IS THERE EVIDENCE OF SOCIAL INEQUITY IN HEALTHCARE FOR CORONARY HEART DISEASE? AN ELECTRONIC-COHORT ANALYSIS USING RECORD-LINKED, ROUTINE DATA

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December 2014

For Amy

DECLARATION AND STATEMENTS

DECLARATION

This work has not previously been accepted in substance for any degree and is not concurrently submitted in candidature for any degree.

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This thesis is being submitted in partial fulfillment of the requirements for the degree of PhD

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This thesis is the result of my own independent work/investigation, except where otherwise stated. Other sources are acknowledged by explicit references.

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ACKNOWLEDGMENTS

I would like to begin with a formal acknowledgement, as stipulated in the Information Governance approval guidelines for this thesis:

> This study makes use of anonymised data held in the SAIL system, which is part of the national e-health records research infrastructure for Wales. We would like to acknowledge all the data providers who make anonymised data available for research

I have been extremely lucky to be treated with great consideration and patience by those working at HIRU, at Swansea University; I am very grateful to all those in the unit who have make this work possible. At the project's inception, Prof Ronan Lyons spent time talking through through the kinds of work that might be undertaken in SAIL; Dr Mark Atkinson gave patient help in explaining to me the structure of the SAIL primary-care dataset; Dr Joanne Demmler helped me to set up a working installation of R within the SAIL Gateway, including providing access to relevant packages; Caroline Brooks, Martin Heaven, and Dan Thayer operated the approval process for export of outputs from the Gateway; I am also particularly grateful to Caroline and Martin for assisting with many other aspects of SAIL processes. Dan wrote and provided access to his routine for determining whether or not an individual is present in SAIL, for which I am very grateful. Cynthia McNerney managed all components of the administration of the IGRP application for this project. I am also grateful to the members of the IGRP itself, for providing approval for this project.

I received assistance with many software and data aspects of the project from technical experts at HIRU, in particular with many DB2-related tasks; I am grateful to all who provided such help, including Chris Jones, Ryan Lever, Dr Jeffrey Peng, Dr Justin Biddle, and Rohan DSilva. I am, in particular, very grateful to Rohan for his tireless patience at the end of a telephone in dealing with my numerous queries about how to get things done in DB2; this project would undoubtedly have been impossible without him.

This project utterly depended on the work of Arron Lacey in writing SQL queries to perform the main data extract. I am extremely grateful to him for all his help carrying this out. Arron was also incredibly

patient with my calls to him out of the blue about many aspects of the process. He has been amazingly supportive in the way he has seemingly instantly performed complex changes to queries in response to my requests.

I am also very grateful to CVRG-C, which provided approval for Arron's valuable time to be used on this work, including to Tinnu Sarvotham, and in particular to Prof Julian Halcox who has also been supportive of this project in many other ways.

I am grateful to Prof Paul Harper for discussing modelling and simulation approaches at the start of this work. Many thanks to Dr Nathanial Hawkins for responding to my enquiry about his conference abstract. Many thanks also to Dr Ian McDowell and Gethin Roberts for discussions about an information relating to the storage of test results in general practice computer systems. I am very grateful to Prof Vernon Farewell for his expert statistical input into the potential for a competing-risks problem. I am grateful to Keith Howkins at the NWIS for responding to data-related queries.

André Miede wrote and made freely available the 'ClassicThesis' LaTeXpackage. David Carlisle wrote me an extremely useful block of code to allow me to accommodate landscape long tables within LaTeXfor which I am very grateful.

While producing this thesis, I have been funded as a WCAT Clinical Fellow in Wales. I am very grateful to all those within that program have helped me with this work, in particular to Dr Donald Fraser, Dr Phil Freeman (WCAT Clinical Fellow in cardiology), and to Prof Sailesh Kotecha. Andrew Emery has performed an invaluable role in administering the scheme, which I appreciate. I am particularly grateful to Dr Keir Lewis and to Dr Sam Rice for showing understanding over the difficulties relating to delays with this project. At a difficult time, they provided invaluable encouragement and demonstrated enormous patience that was vital in allowing this project to be delivered.

I undertook this work as out-of-program training from the Welsh public-health training-scheme. I have maintained links with Public Health Wales while performing this project, and I am very grateful to all those in Public Health Wales who have supported this work during that time, including Dr Mark Temple, Dr Hugo van Woerden, Dr Sarah Aitken, John West, Will Beer, and Dr Marisa Hamilton-Kirkwood. At the project's inception, I received valuable help from Dr Hilary Fielder, Dr Rose Fox, and Dr Sharon Hillier. I received

invaluable librarian support from Nicholas Saunders and Isabel Puscas. Thanks to Emma Palmer, Gareth Holyfield, and John Brassey for head-clearing lunchtime walks. Thanks to the health-protection team (Melanie Thomas, Ceri Harris, Nicola Hathway, and Dr Lika Nehaul) for motivational advice and for on-call reminders. Hugo Cosh, from the Public Health Wales Observatory, has, as always, been impeccably helpful in responding to any data-related query. Thank you also to Rhys Gibbon, from the Public Health Wales Observatory, for help with my query about the episode table. I am particularly grateful to Dr Gillian Richardson, my educational supervisor and Public Health Director for Aneurin Bevan Health Board, for all her support, and to Dr Brendan Mason, director of the public-health training-scheme.

Many individuals at Cardiff University have helped me with this work with advice and support, including Prof Stephen Palmer, Dr Mark Kelly, Dr Jennifer Morgan, Dr William John Watkins, Dr Patricia Gunning, and Dr Giles Greene. Thank you to Dr Mohammed Mustafa for helpful discussion and kind support for this work. I am grateful to Dr John Gallagher for comments and feedback during my first year appraisal. Many thanks to Prof Ian Matthews for his part in the University appraisal process, and for always being ready with kind and supportive comments. Dr Meirion Evans oversaw the University appraisal process, and has been an invaluable source of external support and advice, for which I am very grateful. Prof David Fone and Prof Frank Dunstan supervised this work. I am extremely grateful to them both for all that they have done to make this work possible, particularly at moments of seemingly overwhelming difficulty. In particular, thank you to David for his continuing belief in the importance of my approach and to Frank for his patient support and his expert statistical input. I would like to express my particular gratitude to Dr James White who has been an invaluable support and sounding board in the preparation of this work, and to Dr Daniel Farewell, whose unstinting patience, kindness, and expertise made this work possible.

Finally, I would like to express my thanks to my family and friends who have provided personal support during the preparation of this work. Thanks to Ellie King for PhD coaching and discussion, and to Aidan King, for PhD distraction. Very many thanks to Jane King and Hugh King for providing a bolthole at which I was able to recharge. Thank you to Ashley Moffett and Mike Bate for providing the benefit of their academic experience. I am very grateful to Cari Vallitine for the help that she is provided in numerous ways that has allowed me to

deliver this work. This work would have been completely impossible without the enormous amount of help that I have had from Hugh King, who proofread this document. I am incredibly grateful to Henry King, Rose King, George King, and Amy King (to whom this document is dedicated).

NOTES TO THE READER

This document was produced using the LaTeX 2_ε typesetting system. Doing so made it substantially easier to perform many of the key processes necessary for the delivery of a thesis of this nature: referencing, cross-referencing, tables of contents, tables of figures, acronyms, and so on. There are unfortunately two key disadvantages to its use: firstly, it is quite difficult to obtain word counts; secondly, tables and figures included as 'floats' do not always appear in the most desirable position in the text. In response to the first of these problems, I have presented a word count based on use of the online service TeXcount (version 3.0.0.24), using which I obtain a word count for chapters one to ten of 72,190, substantially below the stipulated limit of 80,000 words, though it is likely that this underestimates the word count slightly because it ignores included tables; I have not found a good solution to the second of these problems, and, thus, tables and figures in the document are at times sub-optimally placed.

Spacing of font throughout the main text was at one-and-a-half line widths, in line with Cardiff University regulations, and was produced using the '\onehalfspacing' latex command. I have used the generous margins which are the default in the 'ClassicThesis' latex package, and which, again, are in line with Cardiff University regulations.

For PhD theses in a scientific or technical areas, stylistic decisions about about the use of the passive or active voice arise. Proponents exist for both approaches; more recent opinion seems to favour the active voice. Using the active voice (which as far as possible I have done) in turn raises the issue of whether to use the first-person singular – 'I' – or first-person plural – 'we', with the former potentially distracting and 'arrogant', and the latter seeming out of place in a PhD thesis where the work is the product of one person. Following useful feedback from the thesis examiners, I have used 'I' throughout (although I have tried to minimise its use) in an effort to make the text easy to read.

Throughout, I have tried to be scrupulous about acknowledging the expert statistical help that I have received with this work, by placing marginal comments in the relevant sections.

I have made a number of stylistic decisions which are based on personal preference: I have employed the word 'significantly' to mean

'statistically significant', I have used the word 'data' as a plural throughout (notwithstanding its increasingly prevalent use as a singular noun), the Oxford or serial comma ('this, that, and the other'), and hyphenation (quite liberally) in compound modifiers – in line with advice from *The Penguin Writers Manual*[1], for example 'high-risk group'. When quoting numbers with a decimal component in tables and in the text, I have generally dropped trailing zeros. The text is in the the past tense when I have described things that I have done for the thesis; I use the present tense when talking about the thesis itself. While carry out this work, I have attempted to relax by reading the works of Charles Dickens. Throughout I have elected to describe anyone that might be reading this text as 'the reader', a decision attributable to this immersion in Victoriana. I have used comments in the margin in this document as a means of directing the reader to other relevant part of this work or to clarify the way I have presented information – I find that these have a less distracting influence on the layout of the text than footnotes.

SUMMARY

This study aimed to establish whether there was evidence of inequity in the utilisation of healthcare for coronary heart disease in the population of Wales during the period 2004 to 2010. Determining whether or not such inequity exists is important, because equity in healthcare is an aim of NHS services and, if present, inequity might contribute to the substantial differences in coronary-heart-disease mortality by deprivation that are seen in Wales.

I used linked general practice, hospital admission, and mortality data from routine sources, and developed a distinctive methodology to evaluate the utilisation, timeliness, and maintenance of appropriate treatment, making comparisons across deprivation quintiles. My approach was based on analysing a pathway of care for coronary heart disease in a comprehensive way. At each stage in this pathway I examined 'clinical triggers' and the extent to which these were matched by appropriate 'clinical actions'.

Findings were broadly in accord with those in the published literature: using multivariate adjustment and taking account of supply-side-effects using frailty models, I detected no systematic evidence of inequity in coronary-heart-disease healthcare provision except in relation to revascularisation. As an illustration of this broad pattern, I found that the adjusted hazard ratio for times-to-receiving revascularisation in the most deprived quintile (compared to the least) was 0.83 (95% confidence interval 0.77; 0.91) in those with myocardial infarction. Further, I found no evidence that indicated prescriptions were reissued over a shorter time-period for more deprived individuals.

In discussing this work, I consider possible explanations for my findings, and address the way that my distinctive methodology, which enabled measurement of important aspects of coronary-heart-disease care, might be applied in other areas. This work has important implications in demonstrating in a systematic and comprehensive way that healthcare inequity for coronary heart disease in the NHS is confined to specific interventions, and is unlikely to be contributing substantially to differences in mortality between deprivation groups.

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ACRONYMS

ACE	Angiotensin-converting enzyme
ACS	acute coronary syndrome
AIC	Akaike information criterion
ALF-e	Encrypted Anonymised Linking Field
APC	Admitted Patient Care
ARB	angiotensin-II receptor blocker
BMI	body mass index
BP	blood pressure
CALIBER	Cardiovascular Disease Research Using Linked Bespoke Studies And Electronic Records
CABG	coronary artery bypass graft
CCB	calcium-channel blocker
CCF	congestive cardiac failure
CHD	coronary heart disease
CI	confidence interval
CKD	chronic kidney disease
CRAN	Comprehensive R Archive Network
CRS	Collaborative Review System
CRP	C-reactive protein
CSDH	Commission on the Social Determinants of Health
CT	computed tomography
CVA	cerebro-vascular accident
CVD	cardiovascular disease
CVRG-C	Cardiovascular Research Group – Cymru

DB2	IBM DB2
DRL	Deterministic Record Linkage
ECG	electrocardiogram
GP	general practitioner
GPRD	General Practice Research Database
GTN	glyceryl trinitrate
HDL	high-density lipoprotein
HIRU	Health Information Research Unit
HR	hazard ratio
hsCRP	high-sensitivity C-reactive protein
HSE	Health Survey for England
ICC	intraclass correlation coefficient
ICD	International Statistical Classification of Diseases and Related Health Problems
ICD-9	International Statistical Classification of Diseases and Related Health Problems, 9th Revision
ICD-10	International Statistical Classification of Diseases and Related Health Problems, 10th Revision
IGRP	Information Governments Review Panel
IMD	Index of Multiple Deprivation
LA	Local Authority
LHCH	Liverpool Heart and Chest Hospital
LDL	low-density lipoprotein
LISI	Low Income Scheme Index
LSOA	Lower Super Output Area
LVH	left ventricular hypertrophy
MACRAL	Matching Algorithm for Consistent Results in Anonymous Linkage

MCCD	medical certificate of the cause of death
MH	Morriston Hospital
MI	myocardial infarction
MICE	multiple imputation using chained equations
MINAP	Myocardial Ischaemia National Audit Project
MRFIT	Multiple Risk Factor Intervention Trial
NHS	National Health Service
NHSAR	NHS Administrative Register
NICE	National Institute for Clinical Excellence
NSF	National Service Framework
NSF-2001	The Wales National Framework for Coronary Heart Disease
NSF-2009	The Cardiac Disease National Service Framework for Wales
NSTEMI	non-ST-elevation myocardial infarction
NWIS	NHS Wales Informatics Service
OA	output area
ONS	Office for National Statistics
OPCS	Office of Population Censuses and Surveys Classification of Interventions and Procedures
OPCS-4	Office of Population Censuses and Surveys Classification of Interventions and Procedures, version 4
OR	odds ratio
PACT	NHS prescription analysis and cost
PAD	peripheral artery disease
PCI	percutaneous coronary intervention
PCT	Primary Care Trust

PEDW	Patient Episode Database for Wales
PHW	Public Health Wales NHS Trust
PRL	Probabilistic Record Linkage
PSALF	Project-specific Anonymised Linking-field
PTCA	percutaneous transluminal coronary angioplasty
PVD	peripheral vascular disease
PYAR	person-years-at-risk
QOF	Quality and Outcomes Framework
RGH	Royal Gwent Hospital
SAIL	Secure Anonymised Information Linkage
SBP	systolic blood pressure
SES	socio-economic status
SIMD	Scottish Index of Multiple Deprivation
SNOMED CT	Systematized Nomenclature of Medicine – Clinical Terms
SQL	Structured Query Language
STEMI	ST-elevation myocardial infarction
TIA	transient ischaemic attack
TRUD	Technology Reference Data Update Distribution
UA	unitary authority
UHW	University Hospital of Wales
UK	United Kingdom
WAG	Welsh Assembly Government
WDS	Welsh Demographic Service
WHO	World Health Organisation
WHS	Welsh Health Survey
WIMD	Welsh Index of Multiple Deprivation

WIMD 2000	Welsh Index of Multiple Deprivation 2000
WIMD 2005	Welsh Index of Multiple Deprivation 2005
WIMD 2008	Welsh Index of Multiple Deprivation 2008
YGC	Ysbyty Glan Clwyd

Part I

INTRODUCTION

1

INTRODUCTION

This thesis is concerned with two potentially linked problems of importance to those involved with healthcare systems, those interested in public health, and to society more generally. The first of these is the difference in age-standardised mortality from coronary heart disease (CHD) between individuals of different socio-economic status in the United Kingdom (UK). The second is the possible existence of healthcare inequity for CHD – systematic differences in interaction with the healthcare system – between individuals of different socio-economic status.

Figure 1.1 shows a schematic representation of the concept from which I developed my ideas. I discuss it here to explain the initial approach to this thesis: its research question, rationale, and methodology. In referring to figure 1.1, there is the opportunity to introduce some of the important concepts discussed in detail later in this work.

The five boxes in figure 1.1 represent points at which comparisons might be made between individuals of different socio-economic status. The graphics in figure 1.1 are based on real figures from Welsh data from the time that this project started. I illustrate comparisons based on socio-economic deprivation, a relative indication of social status, by comparing the population across five evenly-sized groups (quintiles) based on deprivation level. In figure 1.1, I designate quintile 1 as the least-deprived quintile, through to quintile 5 as the most.

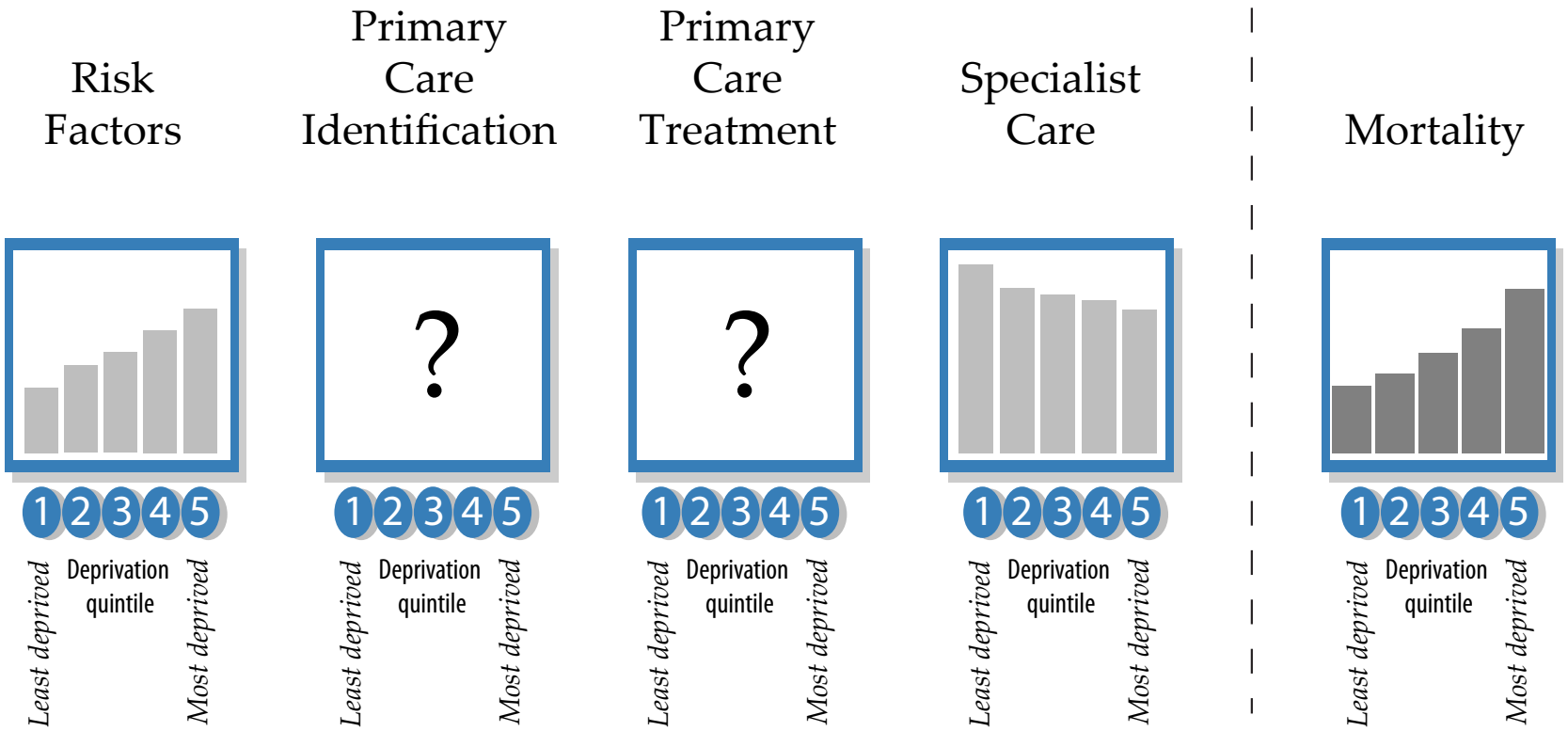
The right-hand box, separated from the others by a broken line, illustrates age-sex standardised mortality from CHD: more deprived quintiles have higher rates. This box corresponds to the first of the problems of concern in this thesis – it is a schematic illustration of the striking differences in CHD outcomes by socio-economic status.

The four boxes to the left of the broken line in figure 1.1, illustrate, in a greatly simplified way, factors expected to have a bearing on outcome mortality. First, on the far left, are represented differences in risk factors between deprivation quintiles, here illustrated by smoking prevalences by quintile: more deprived quintiles have higher smoking prevalences, as well as adverse profiles for some other risk factors. The middle three boxes represent broad components of healthcare for

CHD – the situation in Wales being unclear when I started this work with respect to 'Primary Care Identification' – a process conceived as including measurement of risk factors for CHD, assessment of CHD risk, and the identification of the disease itself – and also for primary care treatment of CHD and its risk factors. The remaining box illustrates a difference in specialist care for CHD, here represented by differences by deprivation in adjusted rates of revascularisation in Wales.

In the construction of figure 1.1, I broadly conceived the four boxes to the left of the broken line as independent variables, with outcome mortality a dependent variable – aiming to give figure 1.1, in a loose terms, the feel of an 'equation', with differences at successive steps, from risk factors through the stages of healthcare, summing to determine the differences in mortality in the right-hand box. I characterise the middle three boxes in figure 1.1 as a 'pathway of care' for CHD.

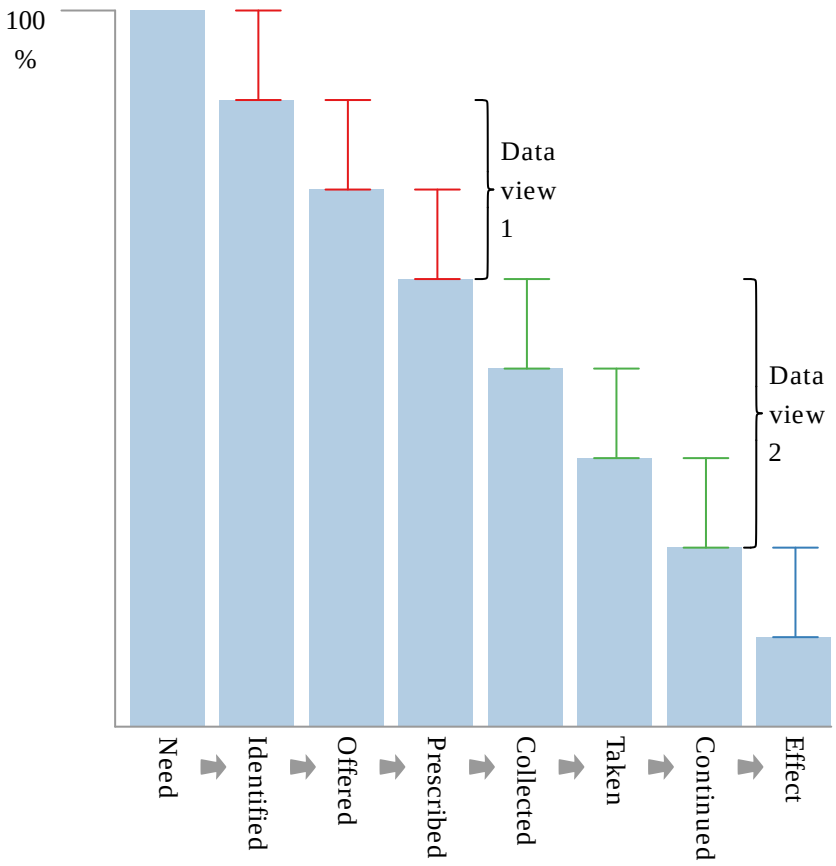
Figure 1.1: Original coronary-heart-disease pathway conception



In a 2006 paper, Tugwell et al[3] discuss the *staircase effect* in which differences in the population-level efficacy of an intervention diminish at each a number of different stages. Describing stages such as awareness, access, diagnosis, targeting, compliance of providers, and adherence of consumers, they characterise differences in the supply of healthcare to different population groups as being the result of more pronounced staircase effects in those groups with worse outcomes[3]. This conceptual approach provides a framework to allow further consideration of the findings from and implications of healthcare-needs-assessment-type investigations. If a particular group is at a systematically lower rate of some intervention for a given level of need, the next step to understanding this finding can be to address it in the light of the staircase effect: for example, is the finding due to a difference in awareness about the intervention? Does it relate to differential acceptability of the intervention? In figure 1.2, I illustrate schematically the staircase effect this I conceive to be operating at each point in the pathway of care for CHD.

An account of the way in which I developed these simple ideas in order to address formal research questions is a major part of this work. In this chapter, I relate the above outline to the overall structure of the thesis. In subsequent chapters, I consider in detail how the content of published literature in this field might modify this simple starting point, and discuss the data sources available for investigation of these issues – specifically the Secure Anonymised Information Linkage (SAIL) databank at Swansea University.

Figure 1.2: Staircase effect



1.1 RESEARCH QUESTION

I begin by formally stating my research question:

> Is there a systematic difference in the utilisation of healthcare for CHD between different deprivation groups across the pathway of care for the disease?

In addressing this question, I have sought to lay the foundations for the consideration in subsequent work of the following question:

> To what extent is any difference in utilisation of healthcare for CHD between different deprivation groups across the pathway of care contributing to differences in CHD mortality between those groups?

In these definitions, by the term 'utilisation of healthcare' I mean the care that was actually received by individuals.

In this thesis, I partially addressed the second research question: if no evidence of healthcare inequity were identified across the pathway of care for CHD, one could logically rule out the contribution of healthcare inequity to differences in CHD mortality. It was clear that, if inequity were observed in the pathway, further techniques involving modelling counterfactual situations would probably be needed to address the second question. I recognized that any contribution from healthcare inequity to differences in mortality could only provide a partial explanation. When referring in subsequent parts of this thesis to my research question I mean the first of the two questions; I have throughout borne in mind that its answer has implications for the second.

1.2 RATIONALE

A number of considerations underpinned the decision to address these questions. They can be summarized as follows:

1. Individuals from more deprived socio-economic groups in the UK have worse outcomes for CHD than those from less deprived groups.

2. Many effective interventions and treatments are now available that have been shown in well-conducted clinical trials to improve outcomes for CHD.

3. Many papers in recent decades have identified potential inequities in the provision of treatment for CHD, but I am not aware of any previous studies that used my approach to the identification of potential inequity across the pathway of care that is developed in this work.

4. There is interest at both an academic and political level in the existence of such inequities.

5. The SAIL databank, hosted by Swansea University, presented a privileged opportunity for researchers from Cardiff University to undertake research using linked routine datasets.

Taking each of these five points in turn, I discuss them briefly in this chapter before signposting to subsequent parts of this work where they are dealt with in detail.

A long history of research, going back as far as the 19th century[4], has demonstrated a relationship between an individual's socio-economic position and their health. A general pattern of poor health in relation to lower socio-economic position has been known for 100 years or more[5]. Research in this area in the UK has received particular impetus from the landmark Whitehall studies, which demonstrated a social gradient in CHD[6,7], and from the publication of the Black report[8] and the subsequent consideration given to its implications.[9,10]

Individuals from more deprived socio-economic circumstances are more likely to die from CHD at a given age than those who are less deprived. For example, McCartney et al[11], in examining trends in social inequalities for premature CHD, found that, in those aged younger than 75 years, men in the most deprived twentieth in England and Wales in 2004 had three and a half times the rate of CHD mortality of those in the least deprived twentieth. When making comparisons across quintiles for Great Britain as a whole, they found that, in men in 1994, the rate ratio for premature mortality from CHD was 1.52 (95% confidence interval (CI) 1.47; 1.57) in the most deprived quintile, compared to the least; by 2008, this rate ratio was 1.84 (95% CI 1.76; 1.93). In women, the corresponding rate ratio was 1.77 (95% CI 1.68; 1.86) in 1994, and was 2.32 (95% CI 2.14; 2.52) in 2004.[11] In simple terms, the findings of this study suggest that individuals in the most deprived quintiles were between one-and-a-half and two-and-a-half times as likely to die prematurely from CHD.

Similarly, Bajekal et al analysed socio-economic differences in CHD mortality in England between 1982 and 2006.[12] The rate ratio in men

between the most deprived and least deprived quintile (this time for all CHD mortality) was 1.52 (95% CI 1.50; 1.54) in 1982, was 1.65 (95% CI 1.63; 1.68) in 1994, and reached 1.94 (95% CI 1.90; 1.93) by 2006. In women, the corresponding rate ratio was 1.64 (95% CI 1.62; 1.67) in 1982, was 1.71 (95% CI 1.68; 1.73) in 1994, and reached 1.90 (95% CI 1.86; 1.94) by 2006. Overall, the findings reiterate the picture seen in the McCartney study. I provide a picture of the situation in Wales, based on the data used in this project, in section 7.2.2.2 on page 204.

I give detailed consideration to some of the important concepts relevant to comparisons between socio-economic groups and which need to be borne in mind when assessing the validity of such findings in chapter 2 (background) and in chaper 7 (data overview and descriptives). Consideration of such detail does not undermine the broad conclusion from the above studies (as well as from many others) that those from more deprived parts of society are more likely, after adjustment for age, to die from CHD. This finding, which has achieved widespread acceptance, is a starting point for the work presented here.

The second broad assumption that I have made is that effective interventions that modify the risk of death from CHD exist – having been developed in recent decades – and, further, that such interventions have been widely implemented in managing CHD in the UK population over a similar period. It seems very likely that such a position would be accepted as quite reasonable by most observers – much of the labour of clinical cardiological research worldwide has focused on the developing and refining of these interventions over recent decades; the plethora of randomised controlled trials, systematic reviews and meta-analyses, as well as the guidelines based upon them, attests to the weight of evidence behind this contention. I provide an overview of specific UK guidance related to the management of CHD in appendix B. Further, other epidemiological research, service evaluation, and clinical audits underpin the suggestion that such treatments are in widespread use at a population level in the UK.

In a UK context, modelling studies suggest that much of the decline in CHD that has been observed relates to implementation of CHD treatments on a population scale, and using similar modelling techniques this finding has been replicated elsewhere.[13–22] It is likely that overall effects on differecnce in outcome at population level relate in greater proportion to differences in risk factor profiles. But these studies, suggesting as they do a substantial reduction in mortality over time, imply that healthcare may by making a considerable con-

tribution to difference: if healthcare can contribute substantially to differences over time (as shown in these studies), I contend that it is, at the very least, plausible that it might also contribute to differences across deprivation groups.

The third underpinning of the rationale is that although many papers have looked at the issue of inequity in healthcare in a UK setting – including in relation to CHD – none has done so in a comprehensive, systematic way across the pathway of care for the disease with a view to addressing potential population-level effects. I discuss the approach to accomplishing this in detail in chapter 5. The meaning of healthcare inequity and the issue of how to quantify it remain problematic; I discuss these issues in chapter 2, where I also set out the justification for using 'utilisation-adjusted-for-need' as an indicator of healthcare equity, and discuss the caveats and limitations inherent in doing so. The contention that my approach is unique is based upon the work presented in chapter 3. Here I present a detailed review of papers looking at healthcare inequity for CHD in a UK context. I discuss findings from these studies in detail there, and consider the methodological implications for my own work – to be sure that my work is novel and unique in this field.

The fourth contention – that the existence of healthcare inequity or otherwise is of interest to a wide variety of stakeholders – is borne out by two different strands of argument. First, the idea of healthcare inequity can be seen as part of the larger field of health equity/inequity, and indeed well accepted definitions of health inequity in the field[23] regard healthcare inequity as being a component of health inequity. The importance of the field of health inequity in principle and policy is evinced in major publications on the subject, thus linking enquiry into the field of healthcare inequity with major concerns about patterns of health in society. Second, healthcare inequity is one of the principal rationales for the constitution of the National Health Service (NHS) in the UK; the field itself rests on considerations of distributive justice and ethics that justify the subject in its own right. I discuss these issues further in chapter 2.

Lastly, I knew that the SAIL databank would provide a technical platform, available for use by researchers at Cardiff University, to allow me to look on a large scale at the issue of healthcare inequity in relation to CHD. I discuss the use of the SAIL databank in chapter 2, as well as in the methods section of this work.

Taking these points together, at the inception of this project, I knew that there was an ongoing problem of inequality in outcomes from CHD in the UK (rationale point 1), that because of the effectiveness and widespread use of CHD healthcare interventions (rationale point 2), together with possible inequity in their utilisation (rationale point 3), the differences in outcomes seen might relate in part to such healthcare inequities. Further, I believed that this work would be of interest to many stakeholders both inside and outside the health service (rationale point 4), and that, with the existence of the SAIL databank, I had access to a technical platform that would allow me to investigate this possibility and address the research questions (rationale point 5).

1.3 AIMS AND OBJECTIVES

1.3.1 *Aims*

The overall aim for this thesis was to address the research question in a way that was methodologically sound, maximizing the chance that valid conclusions might be drawn. I wanted to make this work explicit and thus reproducible, comprehensive in its scope, and unique in its approach. Further, I wished set my methods, findings and conclusions in the context of previous work in this field.

1.3.2 *Objectives*

I identified five broad objectives, which align with the structure of this thesis, and which represent critical steps in the achievement of my aims.

1. Literature review My first objective was to determine in detail the nature of the literature available relating to the provision of healthcare for CHD by socio-economic status. This was necessary to ensure that I was not duplicating research already completed; to ensure that the thesis would add to the existing work in this field; to allow me to set the work in the context of previous work; and to inform the development of my methods.

2. Development of methods In the light of the published literature, and on the basis of my own perspective, I wished to develop a set of methods designed to address as exactly as

possible my overall aim. It was important to develop these ideas clearly before undertaking the analysis; in particular, I had to give detailed consideration to the opportunities and limitations presented by the SAIL databank used for the project. I also had to consider and develop the concept of the pathway of care for CHD as a basis for my analyses.

3. *Data handling and performance of analyses* I recognized that my analyses would depend on accurate processing of extremely large volumes of complex data. I had to ensure that the analyses conformed to intentions and were performed rigorously.

4. *Presentation of results* It was clear that the intention to carry out a comprehensive study meant that the analyses would yield a very high volume of results; a key objective was therefore to present results in an assimilable way while retaining the depth of detail necessary to allow assessment of the study's validity.

5. *Discussion of findings and implications* The final objective was to synthesise previous work and my findings to address the research question posed in this chapter.

1.4 OVERVIEW OF THESIS

In this section, I discuss the way my methods addressed the study objectives, and, in doing so, consider some of the principles governing this work; I also map out the approach that used to present the work in this document.

The detail of the methods by which I searched, reviewed and assessed relevant literature according to the requirements of objective 1, (above) is contained in chapter 3. The methods included detailed tabulation in order to summarize, compare and assess findings from the relevant studies. The review was carried out before I developed the remainder of the project in detail. Because this work predated the final development of my own methods the interventions included in the literature review chapter do not correspond exactly with those eventually included in my analysis. Specifically, although I reviewed the literature comparing the adequacy of glycaemic control in diabetics between socio-economic groups, I did not look at this area in my

analysis – a deliberate omission prompted by concern that a self-care component obscured relationships in this area.

Discussion of data considerations in chapter 4 has focused on the SAIL databank, highlighting its usefulness in providing access to linked datasets within a rigorous information governance framework.

In addition, the concept of the pathway of care for CHD was of crucial importance to the development of my methods. When first considering this project, I produced the schematic simplification of the pathway of care, illustrated in figure 1.1. I recognized that measures of the appropriateness or timeliness of medical interventions and treatments at different stages in the pathway of care could form the basis of my analyses. I developed the concept of 'clinical triggers'. For example, blood pressure (BP) readings above a certain level would be expected to trigger clinical action. The quality of healthcare could be reflected in the relationship between the trigger and the response (the clinical action) and could in turn be expressed by 'trigger-action times'. These 'clinical triggers' could appear at specified stages in the pathway, from routine risk assessment for CHD through to more complex management of established CHD. Further, I recognised that in taking a pathway approach, I would be able to consider knock-on effects in the pathway, in a way that has not been previously attempted. These and other related concepts are discussed in detail in chapter 5.

The linkage of the SAIL data, and the level of detail it provided on individuals' risk factors, interventions and treatments, allowed me to plan realistically to base analyses on such concepts (objective 3, above). I describe in chapter 6 the statistical methods used to take account of uncertainty in my estimates, to adjust for potential confounding variables, to examine for supply-side effects, to take account of missing data, and to examine the sensitivity of findings to underlying assumptions.

Presentation of this thesis required striking a balance between the wish to give a comprehensive picture and the risk of presenting an unmanageable volume of information. Achieving this balance was a key objective of this work (objective 4, above). To do so, I have conventionally separated the content into its narrative component (chapters 1 through to 10) and a set of supplementary appendices that include information extraneous to the main arguments, but potentially of interest for reference purposes. I have not included source code in these appendices, but I am happy to supply this on request.

I present results in three chapters: a first chapter detailing the structure of the dataset; a second chapter presenting detailed results from selected points in the pathway of care for CHD, with referral to relevant appendices for further detail; and a third chapter giving an overview of the results.

I address the final objective – discussion of findings and implications – in chapter 10, where I summarise the findings, appraise the validity of the study, address my research question, consider the study's implications, and outline a potential programme of further work in this field.

In the next chapter, I discuss important background material relevant to this thesis, which is supplemented by information in appendix B.

2 BACKGROUND

In this chapter, I present background material related to socio-economic inequity in healthcare (and related concepts) and to CHD; I also include further material concerning the methods used in this thesis. A number of subject areas have an important bearing on this thesis. These will be considered in turn under the following broad headings.

1. Background information on inequity, socio-economic deprivation and healthcare needs assessment
2. Background information on CHD
3. Background relating to thesis methods

Additionally, background material is included in appendix B, the structure of which is detailed at the end of this chapter.

2.1 BACKGROUND INFORMATION ON INEQUITY, SOCIO-ECONOMIC DEPRIVATION AND HEALTHCARE NEEDS ASSESSMENT

The main subject of this work is inequity in health care by deprivation – specifically, whether it exists in a systematic way in the management of CHD and whether it is important in population terms. In this section summaries of the received knowledge, concepts, and opinions relating to this area are presented. I leave any development of these ideas to chapters 5 and 10.

First, I consider healthcare inequity, as this concept underlies much of what follows; the comparisons in this work are by socio-economic deprivation, so I also address this concept, including a discussion of its measurement; lastly, I present information about healthcare needs assessment conceptualised in epidemiological terms.

2.1.1 *Inequities and inequalities*

The discussion of healthcare inequity ultimately devolves down to issues of distributive justice, ethics, and philosophy. Rather than engaging in detailed discussion of these issues, since this is essentially a data-analysis project, I take the approach of:

- Summarising these concepts
- Distilling a working definition for healthcare inequity, in line with widespread usage in the field
- Highlighting the strengths and limitations of this definition
- Implementing the analysis systematically based on this definition, while acknowledging its weaknesses

It is necessary to distinguish three related concepts:

1. Health inequality/equality
2. Health inequity/equity
3. Healthcare inequity/equity

The third of these is the subject of this work. While the distinction between health and health care is straightforward, that between inequality and inequity is not. Whitehead points out that, in contrast to inequality ("measurable differences in health experience and health outcomes between different population groups – according to socioeconomic status, geographical area, age, disability, gender or ethnic group"[24])

> "The term inequity has a moral and ethical dimension. It refers to differences which are unnecessary and avoidable but, in addition, are also considered unfair and unjust. So, in order to describe a certain situation as inequitable, the cause has to be examined and judged to be unfair in the context of what is going on in the rest of society"[24]

Kawachi refers to inequity as "inequalities that are deemed to be unfair or stemming from some form of injustice"[25], adding that "the crux of the distinction between equality and equity is that the identification of health inequities entails normative judgement". When considering health equity, the World Health Organisation (WHO)'s Commission on the Social Determinants of Health (CSDH) has defined the term as

> "the absence of unfair and avoidable or remediable differences in health among social groups"[26]

In a number of papers, Braveman has examined definitions of health inequity. In her work she looks to generate useful wording for definitions of health inequity.[23,27,28] Importantly, her definition of health

inequity includes ideas about social determinants of health – which themselves might include healthcare. Her broad conclusion is that avoidability should not be used as a criterion for inequity; rather inequity should be identified by the presence of patterns of health in which already socially disadvantaged groups are further disadvantaged. By implication, differences in healthcare (insofar as healthcare can be adjudged a determinant of health) can be regarded as a form of health inequity, though it is by no means clear that this would constitute healthcare inequity according to this definition.

Such an approach is unsatisfactory – being insufficiently specific to underpin the approach in this work, and inferring healthcare inequity from a definition designed to address health inequity. Further, this approach does not address the difficulties that arise when considering healthcare inequity itself. The principal problem to address is 'inequity in what?'. While inequity in healthcare is agreed to be an inequality at some level in the health care system, and one that is also some combination of systematic, unfair, avoidable, and patterned in such a way that socially disadvantaged groups fare worse, it is not by any means clear which aspect of health care one should seek to see equalised. There are a number of different options, which would include equalising the following between groups (adapted from Mooney[29]).

1. expenditure per capita
2. inputs (resources) per capita
3. input for equal need
4. health
5. quality of care
6. funding burden for individuals
7. (opportunity of) access for equal need
8. utilisation for equal need

In the above list, need is conceptualised as a capacity to benefit from healthcare, except in the last point, where the definition is as discussed below (page 26).

Therefore many aspects could be regarded as the target for examining healthcare inequity; different commentators favour different components as representing the concept. There is no consensus in the

literature about which of these approaches is optimal[30–36], and indeed they are very likely to represent contradictory aims.

Using measures of provision of health care without adjusting for need is problematic, because receipt according to need is regarded as a key principle underpinning healthcare equity. This affects points 1 and 2 above. Likewise, even when expenditure is adjusted for need this may be regarded as a poor marker, because costs and efficiencies may vary, discriminating against those with need in areas where provision of health care is more expensive (affecting point 3 above). At the other extreme, judging equity in health care based on outcome levels of health would seem to place unreasonable expectations on the capacity of health care to influence population health (point 4 above). Legitimately, an analysis of healthcare inequity might address issues of quality of care (where quality of care is examined independently of the volume of care) – even if groups are receiving care at the same level, one can address the issue of whether the actual care delivered is of equal quality (point 5 above). In some contexts, inequity in health care might be defined on the basis of the funding burden to individuals receiving that care (point 6 above). The remaining points in the above list relate broadly to access adjusted for need (point 7) or to utilisation adjusted for need (point 8).

Access can be envisaged either as the barriers (typically cost to the individual) to healthcare or as the potential level of healthcare that an individual might utilise, given the opportunity and inclination. Access is thus, in the latter conception, related purely to supply. In contrast, utilisation of healthcare adjusted for need is a reflection of supply modified by demand. In simple terms, an individual might be likely to benefit from intervention (need), be offered it (supply), but turn it down (demand). Some commentators would regard such a situation as equitable, others as inequitable (citing underlying inequities in the education, personal resources and so on affecting an individual's decision-making). Studies looking only at access (pure analysis of supply) are less equivocally investigating the possibility of an unfair situation; in practice, studies examining utilisation as a measure of healthcare inequity are more common, because utilisation is much easier to measure.

Particularly where there is sub-optimal care, the volume of health care, as well as its distribution, matters to patients. In such a situation it is possible that an increased volume of health care might benefit everyone but actually increase inequality between the most and least

deprived. (The most deprived benefit but the least deprived benefit even more).

How would this fit with concepts of healthcare equity? Rawls, addressing the general (not necessarily health-related) issue of distributive justice, derived the concept of the 'difference principle'.[37] Essentially this argued that inequality in the distribution of goods is acceptable only if it is to the advantage of those who are worst off. Daniels argued that health care counts as a 'primary good' and that the difference principle can be applied to it.[38,39] These concepts would have relevance in this thesis to the interpretation of evidence from any studies that show improvements in healthcare in all deprivation groups but widening inequality.

Consideration of these issues has led to adopting the following approach in this work[40–47]:

- I have favoured examination of utilisation of healthcare adjusted for need, given that such an approach is both intellectually justifiable and analytically practical
- I have kept in mind that utilisation adjusted for need gives a picture of the situation in which need, demand, and supply overlap, whereas, in an ideal world, provision of healthcare might be based upon matching of supply to need only, irrespective of demand. Thus, in interpreting any findings in this work, I have kept in mind that any conclusions drawn are potentially beholden to differences in demand between groups – information not available in routine data. Were it found that some aspects of care for CHD were utilised less by more deprived groups, there would be no way of determining whether this might relate to more refusals of care in that group. This represents an inevitable limitation of my approach, acknowledged from the outset.

When considering either utilisation adjusted for need or access adjusted for need, commentators have distinguished horizontal equity (equal healthcare for equal need) and vertical equity (unequal healthcare for unequal need). Such concepts deal with the issue of proportionate access or utilisation for the level of need. The approach in this work has been to look at horizontal equity (equal utilisation for equal need) but to do so at many points in a pathway of care for CHD, so as to build a composite picture of healthcare for CHD from multiple comparisons of horizontal equity; in so doing the aim is also to determine whether higher levels of need at a population level result

in higher levels of utilisation – thus allowing one to address vertical equity considerations as well.

2.1.2 *Socio-economic deprivation*

In this thesis, the concept of deprivation plays a key role in the comparisons made between groups. Deprivation is a term that is not defined or used in the same way by all commentators. Townsend offers the following definition:

> "...a state of observable and demonstrable disadvantage relative to the local community or the wider society or nation to which an individual, family or group belongs"[48]

The concept is thus overlapping with, though not synonymous with, that of poverty[48]. There is no universally accepted definition of poverty, and the distinction is often made between absolute and relative poverty; absolute poverty refers to a lack of the means of physical subsistence; relative poverty extends the concept to individuals as social beings who have psychological needs to participate in a society and share its norms. A common measure of poverty, as used in Child Poverty Act 2010, is 'household income below 60 percent of median income'.[49] Similarly, deprivation itself can take a number of different forms.[48] Material deprivation implies a lack of access to goods and resources; social deprivation involves a paucity in relation to an individual's roles and relationships in society[48]. Multiple deprivation occurs when an individual is at a disadvantage across a number of different domains.

A further related concept is the idea of socio-economic position. Individuals in a society can be classified according to some dimension of socio-economic status, for example income, education, occupation, housing tenure and so on[50]. Again, there is substantial overlap with the concept of deprivation: higher status within society is correlated with an increased capacity to access both material and social resource within that society.[5]

2.1.2.1 *Measures of deprivation*

A number of specific measures have been developed and implemented to characterise levels of deprivation within populations. Particular to the UK are a number of different deprivation measures.

While socio-economic position is more meaningfully measured at an individual level, the concept of deprivation has, in contrast, given rise to measures based on the characteristics of the area in which an individual lives – so-called ecological measures. Such measures have the advantage of being readily ascribed to individuals even in the absence of individual-level data on socio-economic position, because they rely only on information about the area in which an individual lives; the accompanying disadvantage of such an approach is the ecological fallacy: determining an individual's level of deprivation based on the area in which they live may be an invalid inference[51]. For this thesis, area-based deprivation measures have been used, simply because the routine data-sources on which this thesis is based do not provide individual-level indications of socio-economic position (or deprivation). While Office for National Statistics (ONS) mortality data does contain a field for occupation, this is only available for individuals who have died. In theory, individual-level data from the census on income, occupation, and other individual-level characteristics such as ethnicity might be linked to the data employed in this thesis; at the moment this is not possible in practice.

A number of different indices of deprivation have been used in the UK. The majority have employed data from census returns, used in varying combinations, sometimes with a weighting system. Examples of such scores include the Jarman Underprivileged Area Score[52], the Scotdep Index of Carstairs and Morris[53], the Scottish Development Department Index[54], the Matdep and Socdep Indices of Forest and Gordon[54], the Index of Local Conditions[54], the Breadline Britain index[50](census data combined with survey data) and the Townsend index[55,56]. Census-based indices are in general comprised of variables that are proxy indicators of deprivation – an approach dictated by the absence of data on income in census returns. Census data in the UK are only available at 10-year intervals.

The UK Indices of Multiple Deprivation (Index of Multiple Deprivation (IMD), Scottish Index of Multiple Deprivation (SIMD), and Welsh Index of Multiple Deprivation (WIMD)) overcome two of the disadvantages of census-based indices: they are based on data sets updated at more frequent intervals than that collected for the census, and they include data related to income. Constituent nations of the UK use different versions of the Index of Multiple Deprivation, each differing in specifics but sharing underlying principles. The index specific to Wales is the WIMD.

Table 2.1: Domains and weightings for the 2005 and 2008 Welsh Indices of Multiple Deprivation

2005		2008	
Domain	Weighting (%)	Domain	Weighting (%)
Income	25	Income	23.5
Employment	25	Employment	23.5
Health	15	Health	14
Education	15	Education	14
Housing	5	Housing	5
Access to services	10	Access to services	10
Environment	5	Environment	5
		Community safety	5

LSOAs are discussed in section B.1.1

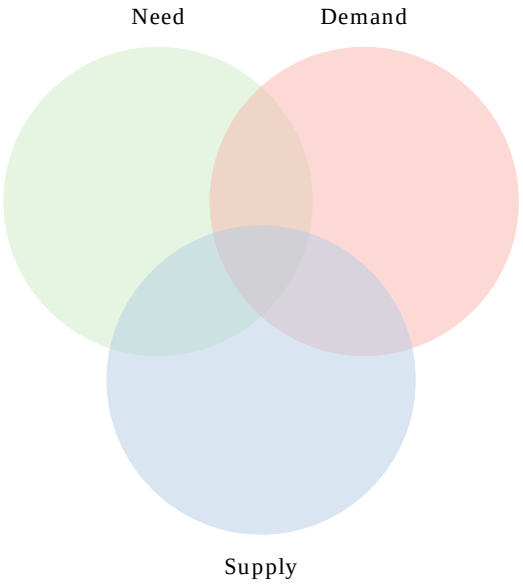
The WIMD is the official measure of deprivation at Lower Super Output Area (LSOA)-level in Wales. The original development of the deprivation index was carried out in the year 2000 by the Welsh Office (and subsequently Welsh Assembly Government (WAG)) in collaboration with the Social Disadvantage Research Group at the University of Oxford[57]. Officials required a replacement to the Welsh Index of Socio-Economic Conditions (the then current index in Wales, which used a number of ward-level indicators from the 1991 census) that utilised new methodologies and sources of data[57]. The Welsh Index of Multiple Deprivation 2000 (WIMD 2000) has been followed in the intervening years by further revisions of the index, Welsh Index of Multiple Deprivation 2005 (WIMD 2005), Welsh Index of Multiple Deprivation 2008 (WIMD 2008), as well as further versions released during the writing of this thesis.[58,59]

Information on the indicators used in the calculation of domains for the 2.1 is provided in appendix A

In common with other indices of multiple deprivation, the WIMDs have a number of domains. The domains for the WIMD 2005 and WIMD 2008 are summarised in table 2.1.[58,59]

The WIMDs contain a health domain. When looking at health outcomes in relation to deprivation using these indices, the inclusion of this domain predisposes to the development of circular logic, whereby an association is sought between deprivation and the particular health indicator when health has already being included as a component of deprivation. Despite this theoretical concern, evidence suggests that the inclusion of a health domain within the index is not important in generating such circularity. Criticisms of the WIMD include the fact that it is unvalidated, and that it is based on the use of the data

Figure 2.1: Need, supply, and demand



Adapted from Stevens A, Raftery J, Mant J; *An Introduction to HCNA*

that are available rather than the data that might *a priori* be sought in attempting to quantify deprivation (though this limitation applies to all deprivation measures that rely on routine data). The decisions about which domains to include, which data to use to derive domain scores, and the weighting to be given to each domain are all subjective decisions. Further subjectivity arises from the technical implementation of the index, with some domains subject to shrinkage techniques, and with the use of statistical techniques to accomplish the ranking of LSOAs[58]. Despite these caveats, the WIMD correlates very closely with other deprivation measures.

LSOAs are discussed further in section B.1.1

The use of the WIMD as a deprivation measure for comparisons is based on my judgement that its disadvantages (ecological nature; validation issues; statistical underpinnings; subjectivity; presence of a health domain; and use of available rather than desirable data) are overall outweighed by its advantages (routine availability; widespread use; widely accepted; frequently updated; available at LSOA level, thereby allowing linkage; and correlation with other similar measures).

2.1.3 *Health care needs assessment*

Healthcare needs assessment is a systematic process used to ascertain the extent to which the supply of health services matches the need for such services. The optimal situation from an efficiency and equity perspective is to match exactly the level of healthcare supplied to the need for it. In reality, mismatches exist. The process of healthcare needs assessment is important in guiding efforts to ameliorate such mismatches.

Underpinning healthcare needs assessments is the idea of need as, "The capacity to benefit from an intervention or treatment". Thus, individuals can be deemed to need an intervention where the balance of risks and benefits is favourable.

Supply can be conceptualised as the rate of health care provided; it is identified by looking at the delivery of interventions and services across populations.

A further important concept is demand: it can complicate the relationship between need and supply. While someone may be likely to benefit from an intervention, they may not ask for, be identified as needing, or consent to it; the converse also applies in that those wishing to undergo an intervention may be unlikely to benefit from it. Thus, demand, the expressed intention of an individual to undergo an intervention, is a distinct concept from need and independent of it.

Indeed, several possible combinations of need, supply, and demand can occur in any one situation, as illustrated in figure 2.1. The ideal lies in the middle of the figure, where an individual with capacity to benefit from an intervention, wishes to and consents to undergo it, and is supplied with the intervention. Other combinations shown in figure 2.1 correspond to situations which are undesirable.

Situations in which healthcare inequity occur, can be considered as systematic mismatches between supply and need between groups within the population that vary with respect to a particular characteristic (for example gender or deprivation level).

Three categories of healthcare needs assessment exist: comparative (comparing need and supply between populations), corporate (asking key stakeholders), and epidemiological. The last of these is the most rigorous, but is often not performed in reality due to data limitations. Broadly, it involves estimating, usually from routine data, the level of need for an intervention in the population and ascertainment of the

level of supply of the intervention in the same population. Gaps in need are identified.

While such assessments can be rudimentary, relying on quite crude estimates of need (in particular), there is no theoretical reason why this should be so. In an idealised situation, valid ascertainment of need would take account of all factors that might affect an individual's capacity to benefit from an intervention, for instance the stage or severity of the disease or risk factor at which the intervention might be directed, comorbidities, allergies, intolerance to medications, and other factors. Similarly, identifying demand requires determining if an individual wants an intervention, independent of whether it is supplied or needed. Where demand overlaps with supply (an intervention is supplied to a consenting individual) identifying demand is fairly straightforward: supply, which is usually quite readily ascertained, accompanies demand. The situation in which there is no demand, despite clinical need and the potential for supply, is difficult to identify: offers of interventions which are declined are not systematically recorded in routine data.

These considerations mean that a number of possible explanations for findings from need assessments can be differentiated. Specifically in relation to CHD, where inequity in provision is observed between deprivation groups (for example), explanations might include the following.

1. The relationship does not in fact exist as postulated. More socio-economically deprived groups in fact have just the same chance of receiving interventions. The relationship that appears to exist is, in fact, a product of methodological weaknesses and random effects.

2. Utilised supply of CHD interventions does, in fact, match the existing need for these procedures, but appears not to. This potential explanation applies particularly to surgical and invasive radiological procedures. Despite an increased burden of CHD in those from more deprived socio-economic groups, they may have a decreased ability to benefit from procedures (need), because of comorbidities and adverse risk factors. This explanation would represent a mis-ascertainment of clinical need.

3. Offered supply does match need. Those in more deprived socio-economic groups may be offered CHD drugs or revascularisation procedures at a rate appropriate to their level of need, but turn

them down more frequently. In this explanation, there is need and supply, but no demand for the intervention from the individual in question, and insufficient information available to ascertain this fact

4. Those in more deprived socio-economic groups are systematically less engaged with the health care system, so that there is less opportunity for care to be offered by the health care system to these groups. This explanation would reflect a lack of demand and supply for the intervention, despite the presence of a clinical need.

5. The healthcare system systematically offers fewer CHD interventions per level of need to those individuals in more deprived socio-economic groups. This situation would reflect a lack of supply, despite the presence of need and demand.

6. Those in more deprived groups are receiving the intervention exactly according to clinical need; the observed gradient seen relates to an over-supply of the intervention to less deprived indervidiuals – a situation in which there is supply and demand for an intervention, but no clinical need.

Such potential explanations are important for this thesis, and highlight some of the problems with epidemiological healthcare needs assessment, which relate particularly to unknown information.

The degree of simplification entailed when using definitions based closely on those postulated by Braveman (see section 2.1.1) becomes clear when considering these permutations of interpretation that can occur with healthcare needs assessment approaches: essentially such definitions simplify the situation to consideration only of need and supply – differences in demand are by definition ignored. Despite this, the overriding advantage of the approach is that it makes it possible to address issues of inequity using routine data.

2.2 BACKGROUND INFORMATION ON CHD

The epidemiology of CHD, is relevant to the background of this work. For the interested reader, I include information on the pathophysiology, classification, and management of CHD in appendix B – as well as information on the organisation of cardiac services in Wales. In the introductory chapter, I discussed patterns of CHD mortality in relation

to deprivation – introduced earlier because of its importance to this work – and that discussion is not reprised here; neither do I cover the detailed epidemiology that underpins the management of CHD here (in other words the randomised control trials and meta-analysis on which guidance is based), but limit the discussion to that in section B.2.3 of appendix B, where I detail the guidance relevant to the management of the condition.

2.2.1 *Epidemiology*

Historically of less importance than infection and trauma, the burden of CHD achieved prominence in Western countries in the middle of the twentieth century. Two factors explained this: firstly, the public health breakthroughs of the preceding decades (including mass immunisation, provision of clean water, perinatal care, and improvements in social conditions) increased survival to older ages and unmasked CHD; secondly, the 20th century, particularly the latter half, saw two of the major risk factors that drive CHD, adverse diet and smoking, become mass phenomena in Western industrialised countries[60]. Further, adverse diet, abetted by sedentary lifestyle, contributed to high population prevalences of other common traits predisposing to CHD: above-optimal levels of serum total cholesterol, raised blood pressure, overweight/obesity, and diabetes mellitus[60].

As late as the 1940s, there was very little widespread understanding of CHD risk factors (a term not coined until 1961[61]) and very few interventions were available to prevent or treat the disease itself. For example, in 1944, a moribund President Roosevelt – smoking, immobile, cocktail-drinking, blood pressure 260/150, with clinical manifestations of angina, malignant hypertension and congestive heart failure – was attended by a personal physician who insisted that his health was good and who believed that his subsequent death from cerebral haemorrhage 'came out of the clear sky'[62].

Since that time, there have been important improvements in understanding of the aetiology of CHD and of effective interventions. Initially, in the years following the Second World War, long-term prospective within-population studies[60], which followed large cohorts of individuals over time, began to implicate a number of patient factors in the development of CHD; best known is the Framingham study[62]. Evidence from such studies was complemented by findings from studies which looked at cross-cultural variations in disease oc-

currence, including in migrant populations[62]. From the late 1960s onwards, increasing numbers of interventional studies evaluated the effects of interventions to treat CHD and its risk factors[62]. All types of epidemiological investigation of CHD have continued apace to the present day, with a resultant continual increase in knowledge about the condition[62].

Increased understanding of risk factors for CHD and other cardiovascular diseases, of effective treatments, and of the public health principles that underpin prevention strategies, have all contributed to a continuing decline in CHD in Western countries since the 1970s. However, in developing areas of the world, economic progress is frequently being accompanied by an increasing burden of CHD[63]. Even in developed Western countries, CHD remains a major cause of death, including of premature death, particularly in economically deprived populations[63].

2.2.1.1 *Descriptive epidemiology*

In North American[64] and Western European populations the burden of coronary heart disease has declined since the 1970s, but this is by no means a global phenomenon. Declining trends in mortality mirroring those seen in Western Europe and North America have also been observed in Japan, Singapore and Hong Kong since approximately 1980[65], but the latter third of the 20th century saw a peak in CHD in Eastern Europe and the countries of the former Soviet Union, particularly prominent in Russia[66]. It is predicted that in many of these countries the proportion of CHD-related deaths as a fraction of total deaths will rise sharply, and that cardiovascular disease (CVD) overall will become the leading cause of death, with CHD as a main contributor[67,68].

The situation the UK is broadly typical of the western European picture[69]. Routinely collected data on CVD mortality is available for the whole of the 20th century for the UK, and corresponding population data is available to allow calculation of mortality rates. Since the 1960s, a clear picture emerges in which the rates of CVD have declined, with a significant part of this trend related to a decline in CHD[69].

In 1961, CVD accounted for 48% of all deaths in men and 55% of all deaths in women[69]; by 2001 this figure was 33% for both sexes[69]. In 1981 CHD accounted for 31% deaths in men and 23% of deaths in women, figures which had fallen to 18% in men and 12% in women by 2009[69]. Further, these deaths tended to occur at older ages, such that

the age-standardised mortality rates for CHD have fallen substantially. In men, the age-standardised mortality rate for CHD fell from approximately 500 per 100,000 in 1961 to approximately 120 per 100,000 in 2009[69]. In women, the rate fell from approximately 240 per 100,000 in 1961 to approximately 60 per 100,000 in 2009[69].

In those under 55 years of age, the age standardised mortality continued to rise until the early 1970s, but has declined since then. In men aged less than 55, from a high of approximately 53 per 100,000 in 1972[69], rates had fallen to approximately 12 per 100,000 by 2009[69]. In women aged less than 55, there was a drop from approximately 9 per 100,000 in 1979 to approximately 2.5 per 100,000 by 2009[69]. Against this background decline, there is some suggestion that declines in CHD may have stopped or be reversing in younger age groups – an effect presumed to relate to increasing obesity and type 2 diabetes prevalence[70].

The adverse trends in obesity and diabetes are clearly of great importance in relation to prevention of CHD. Of particular relevance to this thesis is the evidence of unequal socio-economic patterning in those trends. Hotchkiss et al, in a study of the Scottish population, 1995-2009, considered the relationship between CVD biomarkers and socio-economic patterns. They found significant evidence of persisting inequalities, particularly for the anthropometric measures (including waist circumference and waist to hip ratio) when stratified by education.[71] Agardh et al, in a systematic review of evidence from high-, middle- and low-income countries found that the risk of getting type 2 diabetes was associated with low socio-economic position overall, but that the strength of the associations was more consistent in high-income countries.[72]

The burden of coronary heart disease has not been evenly distributed across the constituent nations of the UK[69]. In 1961, age standardised CHD mortality rates in Wales were 14% higher than in England in men and seven percent higher in women. Similarly rates in Scotland were 30% and 37% higher respectively[69]. This disparity has persisted; in 2009 rates in Wales were 13% higher than in England for men and 17% higher than in England for women; with corresponding figures of 25% and 36% in Scotland[69].

The pattern of decline in CHD since the 1960s predominantly reflects changes in population risk factors, but also relates to improved treatments and survival for those with established CHD[20–22,73,74].

The decline in CHD mortality observed in USA during the 1960's coincided with a marked reduction in cigarette smoking and consumption of animal fats.[75] Dwyer and Hetzel, comparing CHD mortality in Australia, the USA and in England and Wales, noted the sharp decline in rates in Australia from 1966, in the USA from 1968, and the later decline (1972 onwards) in England and Wales. They found correlations with patterns of smoking and diet that correlated with these changes.[75] Capewell, in a study of the Scottish population, estimates that in 1975, when CHD mortality had begun to fall, the relatively limited treatments then available were saving approximately 554 CHD deaths a year, compared with 6203 deaths saved by treatments in 1994. It is estimated that by 1994 40% of the overall decline in CHD deaths was due to cardiovascular treatments, the remainder due to reduction of risk factors.[20] Therefore the broad picture of the decline in CHD mortality since the 1960's appears to be of an earlier phase due very largely to risk reduction and a later phase when increasingly effective treatments contributed substantially.

Unal et al, studying the population aged 25-84 in England and Wales between 1981 and 2000, reported that CHD mortality was reduced by 62% in men and 45% in women. They attributed 42% of this reduction to treatments – 8% to treatment of myocardial infarction, 13% to treatment of heart failure, 3% to treatment of hypertension, and 11% to secondary prevention. The remaining 58% they attributed to due reduced risk factors – this despite adverse trends in physical inactivity, obesity, and diabetes. Hughes et al modelling CHD mortality in Northern Ireland 1987-2007, estimated that 35% of the reduction was due to treatment and 60% due to reduction in risk factors. They also noted the adverse trend in physical inactivity, obesity and diabetes.[15] Unal et al, in a study of the population of England and Wales 1981-2000, estimated that reductions in major risk factors led to four times as many life-years gained as cardiovascular treatments led to.[76]

In Oxfordshire, the case-fatality rate for myocardial infarction declined in all age groups between 1968 and 1998 for both sexes[69]. For example, the case-fatality rate for men aged 80 to 84 declined from close to 90% in 1968 to approximately 70% by 1998[69].

Prevalence data for angina are difficult to compare over time[69], but evidence from both the National Morbidity Survey and the Health Survey for England (HSE) broadly suggest that the prevalence of angina increased (rising from 380 per 100,000 to 1300 per 100,000 between 1955 and 1991 in men); a similar, smaller rise occurred in women. Between

1994 and 2006 prevalence continued to increase – by 46% in men over 75 and by 20% in women over 75.[69]. The increase in incidence and prevalence of angina contrasts with declining CHD mortality. Lampe reports that when the prevalence of angina was assessed according to symptoms and using a standardized questionnaire, the prevalence of angina symptoms appeared to fall between 1978-1996 in men in the UK.[77] However her later study of men in the UK aged 40–59 at entry, over the period 1978–80 to 1998–2000, using NHS central registers and general practitioner (GP) records, showed an increase in the incidence of diagnosed angina. It is suggested that this may be a feature of changes in diagnostic practice rather than a real increase in disease incidence, and that an increase in ascertainment and diagnosis of angina may result from general practitioners prioritising the early identification and treatment of coronary heart disease, as well as from an increase in availability of diagnostic investigations for chest pain.[78] An additional reason for the apparent divergence between increased incidence of angina and decline in CHD mortality is thought to relate to more effective treatment and this may apply particularly to treatment of heart failure (CHD being a major cause of heart failure). An additional effect may be the improved diagnosis of CHD-related heart failure leading to its specific treatment. Cowie, in a UK study of heart failure in all age groups,[79] reported that when diagnosis was based on clinical assessment, electrocardiography, chest radiography and transthoracic echocardiography, the primary aetiologies were CHD (36%), unknown (34%), hypertension (14%), valve disease (7%), atrial fibrillation alone (5%), and other (5%). However, in a separate study[80] in which diagnosis was assisted by angiography Cowie found that CHD was the cause of 52% of incident heart failure in the general population under 75 years, and concluded that clinical assessment without angiography under-estimates the proportion of patients with heart failure with coronary artery disease, and fails to identify those patients who may benefit from revascularization.

There was a less clear-cut picture for MI[69]; the prevalence of heart failure substantially increased between the 1950s and 1970s (230 per 100,000 in 1955 rising to 700 per 100,000 in 1974 women), with a more recent increase likely though difficult to characterise from available data[69].

The incidence of CHD, being largely unaffected by changes in survival, has decreased for CHD, MI (from a peak in the late 1970s) and

heart failure, with the steepest declines occurring in younger age groups[69].

Epidemiological studies have been instrumental in identifying a number of important risk factors for CHD (discussed further in section 2.2.1.2) and changes in their prevalence. Smoking prevalence has declined throughout the UK; it was 46% in 1972; this had declined to 21% by 2008[69]. Consumption patterns of fats has changed: skimmed milk has displaced whole milk; vegetable fat consumption has risen, while consumption of animal-derived fats (butter and lard) has declined; consumption of red meats has significantly declined, being replaced with poultry[69]. Consumption of oily fish has increased since the 1990s, with some suggestion that this increase is at the expense of white fish, rather than other forms of protein[69]. Availability of fruit and vegetables has increased since the 1970s. This increase relates principally to an increase in the availability of fruit[69].

Long-term trends in physical activity levels are difficult to assess accurately in the UK over the long-term. In recent years, compliance with government recommendations for physical activity has slowly increased in the UK,[69]. Proxy measures of physical activity level, such as television ownership, car ownership, and active travel, provide indirect evidence of a reduced level of physical and activity at the population level[69].

Heavy drinking prevalence, measured since 1978 in the General Household Survey, appears not to have substantially increased since the 1970s[69], though difficulties with changing definitions of heavy drinking make interpretation of such data difficult. WHO data on the total amount of alcohol consumed corroborate this finding, suggesting that total intake has not changed greatly since the late 1970s[69].

Data on the population prevalence of obesity from the HSE suggest that, since the 1960s and particularly since the 1990s, the average body mass index (BMI) for both men and women has increased[69].

2.2.1.2 *Aetiological epidemiology*

A prodigious research output in the years since the Second World War has produced an enormous amount of epidemiological evidence – as well as evidence from animal experimentation, pathological investigation, clinical research, and molecular and cell biology – on risk factors for the development of CHD[60,81]. Beyond the major non-modifiable risk factors (age and sex), six modifiable risk factors are now regarded as major established risk factors, classified by Stamler as follows[60,81]:

1. Serum total cholesterol
2. BP were
3. Overweight and obesity
4. Smoking
5. Diabetes mellitus
6. Adverse diet

The exact relative risks from these risk factors vary according to study. By way of illustration, the large Multiple Risk Factor Intervention Trial (MRFIT) study[81] – which includes 25 years of follow-up data on smoking, BP, cholesterol, as well as other risk factors – is sufficiently large to allow stratification by BP, cholesterol, smoking status, and age. The hazard ratios for the 39 to 44 age group are presented in table 2.2. It is clear that for any given level of cholesterol and smoking status, risk rises as blood pressure rises; similarly risk rises with increased serum cholesterol for any given blood pressure in smokers or non-smokers; at a given cholesterol and BP smokers have a higher risk. Moreover, these major risk factors are multiplicative in their effects[81]. Similar patterns and approaches have been used to establish the other major risk factors as strong, graded, and independent risk factors for the development of CHD[81].

At the height of CHD incidence, when many of the studies looking at risk factors were performed, only a small proportion of those individuals included were in low risk categories for all risk factors. This meant that it was initially difficult to infer the extent to which low-risk status was beneficial except by means of statistical interpolation. Pooling of the increasing amount of data from large studies and the increasing proportion of the population that is in low risk groups means that such inferences are now possible based on actual data[81]. This concrete understanding of the benefits of achieving low risk status has important indications for prevention of CHD in the population as a whole, as discussed further in section B.2.5.1[81].

An extensive list of other factors has been considered as potential risk factors for CHD and CVD. The extent to which the aetiological connection has been demonstrated from epidemiological and other evidence varies; such factors include well known risk factors such as physical activity level, alcohol consumption, metabolic syndrome, and psychosocial factors[82,83]; other putative factors include antioxidants, fish consumption and n-3 fatty acids, oral contraceptives, mental

Table 2.2: Serum cholesterol (SC), SBP strata, smoking, and hazard ratio for CHD death, for 149339 MRFIT men aged 39-44 at baseline. All analyses exclude persons with history of MI at baseline; follow up 25 years; 3345 CHD deaths.Hazard ratio adjusted for age, race, and diabetes; substratum for non-smokers with total cholesterol <180 mg/dL and SBP $\leqslant$ 120 mmHg set at 1.00

SC (mg/dl)	SBP (mmHg)				
	$\leqslant$120	121-9	130-9	140-59	160+
Non-smokers at baseline					
<180	1.00	1.38	2.45	4.09	10.25
180-99	1.78	2.50	2.95	4.79	12.64
200-19	1.96	2.26	3.14	5.63	8.57
220-39	2.68	2.84	5.47	7.61	21.72
240+	3.66	6.64	8.65	13.18	26.77
Smokers at baseline					
<180	3.35	3.10	7.55	10.32	37.61
180-99	5.78	6.86	7.82	12.82	24.74
200-19	5.69	7.28	10.22	18.92	22.25
220-39	7.94	10.74	14.74	23.16	41.23
240+	14.53	19.09	20.36	34.46	52.26

Figures from Stamler[81, page 43]

illness, and air-pollution[84–88]. A number of candidate factors are biomarkers thought to relate to the pathogenesis of CHD, for example C-reactive protein (CRP)[89,90], homocysteine[91,92], lipoprotein(a)[93], and haemostatic factors (for example plasminogen activator inhibitor 1, thrombin and platelet-derived factors). The literature in this area is extremely extensive, and a thorough review of all cardiovascular risk factors is far beyond the scope of this thesis; it is useful to note that if consideration is only given to major established risk factors, it is still possible to explain a large proportion of the observed difference in cardiovascular risk between individuals.

A further influence on an individual's cardiovascular risk arises from their experience at the start of life, including their time in utero. The hypothesis that maternal nutrition is an important predictor of chronic disease in later life, including CHD and other CVDs, was first advanced by David Barker, based on evidence from retrospective cohort studies, and is known as the Barker hypothesis or thifty phenotype[94]. The initial hypothesis has received further support from the Dutch famine study (a natural experiment that occured in the Netherlands in the Second World War, when a proportion of the population was exposed to a famine with a fairly discrete onset and cessation); detailed medical records were kept throughout the period of interest. A number of investigators have examined the influence of maternal nutrition on the subsequent health of the affected offspring[95]. Evidence from such studies suggests that children exposed to famine conditions in utero have an altered risk profile as adults, and, specifically in relation to CHD, have increased risks of developing a number of adverse risk factors for the disease (atherogenic lipid profile, disturbed blood coagulation, increased stress responsiveness, and obesity) as well as having an increased risk of CHD itself[95]. These studies present more direct evidence of the effect of maternal nutrition in pregnancy on chronic disease in offspring – as they look directly at maternal nutrition rather than using birth weight as a proxy. In support of the Barker hypothesis, numerous studies have now demonstrated a link between birth weight (and sometimes maternal nutrition) and a number of chronic diseases: CHD, diabetes, hypertension and stroke[96], though the potential for important variables (for example maternal smoking) to confound this relationship must be borne in mind[96] . The mechanism by which a true association is thought to occur is by foetal programing by nutritional stimuli or excess fetal glucocorticoid exposure[96].

2.2.1.3 *Overview*

On consideration of the epidemiology of CHD, a number of clearly-established points emerged:

- The disease is still of major public health importance in view of its effect at a population level, including its implication in premature mortality and its increasing impact in many developing countries
- There has been a decline in the burden of CHD in Western countries in recent decades
- Understanding of the aetiology and risk factors has progressed enormously in recent decades, though some variation remains unexplained
- For many risk factors, population profiles have improved in Western countries (including the UK), though obesity and diabetes prevalence are worsening on a population scale

I discussed in the introductory chapter two further points, which underpin this thesis and are themselves derived from epidemiological investigation:

- Inequalities in outcome between socio-economic groups in mortality from CHD have been consistently observed in epidemiological studies; over time absolute differences between these groups have reduced; relative differences have worsened. Deprived groups consistently have a higher burden of the disease
- Many interventions are now available to manage CHD; the evidence for the effectiveness of these interventions comes from randomised controlled trials and studies that synthesise their results

2.3 BACKGROUND INFORMATION RELATING TO THESIS METHODS

In this section I look at the background relevant to the way in which I addressed the research questions. Specifically, I describe the opportunity presented by the SAIL databank at Swansea University, including an overview of its operation and background information about the relevant datasets held within the SAIL databank. Some additional information on clinical coding has been included in appendix B.3.1, as many readers will already be familiar with this material.

2.3.1 *Anonymised data linkage and SAIL*

The SAIL system is based in the Health Information Research Unit (HIRU) at Swansea University. The unit's aim is to 'realise the potential of electronically-held, person-based, routinely-collected data to conduct and support health-related studies'.[97] To achieve this, HIRU have established the SAIL databank which operates on a DB2 platform (Data Warehouse Edition on AIX), running on an IBM 'P' series supercomputer (Blue-C).[97] The system holds over 2 billion records of health and health-related data, and accumulates additional records over time.

For the purposes of this thesis, I required that data held within SAIL be linked to allow primary-care data, hospital-activity data, and mortality data to be brought together to inform the clinical history of individuals. In general, data linkage has enormous potential to improve the usefulness of the increasing number of health and social service data available for health and social care research, for service planning, and for service improvement, but the process of data linkage raises a number of ethical and technical issues.

Ethical considerations arise because much of the data held is sensitive in nature, and thus steps must be taken to prevent researchers identifying individuals; moreover, the process of data-linkage potentially makes identification more likely, as more information can be retrieved for an individual. The ethical management of large, linked databanks therefore presents a number of Information Governance challenges to those administering them.

A number of approaches might be taken to minimising the risk of any breach of confidentiality associated with the use of linked databanks. These range from simply anonymizing all potentially identifiable information in the data bank, through to a multifaceted approach that includes anonymization but also employs data-aggregation and data-suppression techniques, user-authentication processes, scrutiny of data-use, and disclosure-control at the stages of analysis and publication[97]. The HIRU team at Swansea have addressed in detail the information-governance arrangements required to operate the SAIL databank, and have presented information on these processes in peer-reviewed publications.[97,98] Specifically, they have developed a number of processes that address information-governance concerns:[97]

1. Ensuring data transportation is secure
2. Operating a reliable record-linkage technique

3. Anonymisation and encryption of data to prevent re-identification of individuals
4. Applying measures to address disclosure-risk in data-views created for researchers
5. Ensuring data access is controlled and authorised
6. Establishing methods for scrutinising proposals for data-utilisation and improving output
7. Gaining external verification of compliance with information governance

In adopting a pragmatic approach to the ethical issues surrounding the operation of the SAIL databank, the administrators at SAIL have been able to address the key challenges in establishing a national databank of anonymised person-based records for the purposes of research and evaluation, while at the same time adhering to the requirements of information governance[97].

The formal scrutiny process at HIRU requires applications to be approved by independent adjudicators in HIRU Collaborative Review System (CRS), the panel of adjudicators making up the Information Governments Review Panel (IGRP). Membership of the IGRP is composed of senior representatives from the British Medical Association, the National Research Ethics Service, Public Health Wales NHS Trust (PHW), NHS Wales Information Service, and Involving People (an organisation which aims to encourage public involvement in health and social care research in Wales).Members of the panel assess the application against a number of criteria, including the project's rationale, design, protocol and data specifications.

In addition to developing information-governance systems, HIRU have put in place technical capabilities to deal with very large datasets and with data-linkage between datasets.

When linking data for an individual, it is common for important information, such as a correct NHS number, to be missing or incorrect. This clearly presents issues for the data-linking process. HIRU have developed algorithms capable of matching records together for an individual, even in the absence of complete, correct data.

Deterministic Record Linkage (DRL) of an individual to records in the dataset is very specific (in that those records identified correctly relate to the individual in question), but is frequently not very sensitive as any missing or faulty data in the matching fields will mean that

records are missed. Probabilistic Record Linkage (PRL) can increase sensitivity, because of its ability to identify records in the absence of complete and correct matching fields, but at the cost of some specificity.[98] Thus, the nature of the matching algorithms used in large linked databanks needs to be considered to ensure that the performance of the algorithms used has been ascertained using a valid methodology and to ensure that a sensible balance has been struck between sensitivity and specificity.

The technical solution to record-linkage at SAIL involves the use of the Matching Algorithm for Consistent Results in Anonymous Linkage (MACRAL) algorithm. This is an Structured Query Language (SQL) algorithm that uses DRL and PRL based on a number of matching fields (NHS number, first name, surname, gender, date of birth, and postcode of residence)[98]. On test datasets, this algorithm has been shown to pick up a very high proportion of records with a low error rate, both for general practice (>99.9% sensitivity) and hospital activity data (>99.3% sensitivity)[98]. It is possible to vary the sensitivity of the algorithm by varying the probability threshold of PRL; the optimum threshold for use with MACRAL on the test datasets was 50%[98].

2.3.2 *Routine data sources*

The data in this thesis came from three principal sources. The first was the mortality data collected by the ONS based on death registrations and on information submitted by medical practitioners on death certificates. The second source of data related to admissions to NHS hospitals; this information is contained in the Patient Episode Database for Wales (PEDW), an administrative dataset produced by the collection of information from clinical coding of hospital admissions. The third main source of information was primary care data, routinely collected by general practices in Wales. Each of these datasets is held within the SAIL databank.

2.3.2.1 *Demographic data*

Since 2009 the Welsh Demographic Service, part of a set of services to manage administrative information and demographic data for NHS patients in Wales, has replaced the NHS Wales Administrative Register. Amongst its other functions, it enables authorised staff to trace and verify patients' basic demographic details and their GP registration. This dataset is held in SAIL. It contains information on, for example,

a patient's date of birth, sex, address (available as LSOA of residence in SAIL), and GP. Because the latter two pieces of information change over time, the dataset contains a record of each modification to a patient's address and GP at appropriate time-points.

2.3.2.2 *Mortality data*

Information on deaths in England and Wales comes from the ONS.[99] The information used in mortality statistics is based on information collected when deaths are certified and when they are registered.[99] The information itself may come from three sources: details supplied by the doctor when certifying the death; details supplied by the informant to the registrar (the informant is usually a family member or close friend); the coroner may also supply details. The registration of deaths (as well as the registration of births, marriages, and civil partnerships) is carried out by the General Register Office (part of the Identity and Passport Service).[99] Information is submitted to the ONS. The information includes the usual residence of the deceased, date of birth, sex, marital status, place of death, occupation and employment status, date of death, and underlying cause of death.

The underlying cause of death in mortality data generated by the ONS and used in this thesis is coded using International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) codes (having switched over from International Statistical Classification of Diseases and Related Health Problems, 9th Revision (ICD-9) in January 2000).[99] The raw information provided from the sources listed above is in the form of text. The selection of the underlying cause of death is made on the basis of the condition or conditions provided by the certifier, using International Classification of Disease rules.[99] The underlying cause of death is generally selected from the condition entered in the lowest completed line of the medical certificate of the cause of death (MCCD).[99] In cases where death certificates have been completed ambiguously, the ONS applies 'selection' rules to determine which cause of death should be used.[99] Even in situations where the death certificate has been completed properly, some circumstances or combinations of causes require that 'modification' rules can be applied.[99] The aim of such selection modification rules is to derive the most useful information from the death certificate and to ensure that the underlying cause is comparable between places and times and that each death certificate produces one, and only one, underlying cause of death.[99]

ICD-10 codes are further discussed in section B.3.1

In the deaths processing system within the ONS, there are two distinct sets of data held. The first, termed the 'registration database', contains mostly textual information derived from the death certificate; the second, the 'statistical database', contains only coded information on each death. It is this latter database that provided data for this thesis.[99] The statistical database is continually updated and amended as further information becomes available.[99]

2.3.2.3 *Hospital admissions data*

Data on admission to hospital for individuals resident in Wales and for individuals treated by NHS Wales is contained in PEDW. This data set contains records for inpatient and day-case activity. The dataset contains records reaching back to 1991; substantial changes were made to the format of the data collected in 1997, with the adoption of the mandated Admitted Patient Care (APC) dataset[100].

The data are collected by clinical coders in NHS trusts in Wales (or where patients resident in Wales are admitted to trusts in England by their counterparts there), and are collated by their Information Technology Departments. The data are then submitted from those trusts to the PEDW Data Acquisition Team responsible for the collection, processing and monitoring of the dataset[100].

APC includes clinical, administrative and demographic information on each patient. The dataset also includes diagnostic and operative procedures. Diagnostic information is coded using ICD-10, with up to 14 codes present (a primary diagnosis field; a subsidiary diagnosis field; 12 secondary diagnosis fields); procedures carried out are coded using the OPCS-4, with up to 6 codes being present[100].

ICD-10 and OPCS-4 are discussed further in section B.3.1

Administrative data in the PEDW dataset include details of the treating NHS trust, the method of admission (for example emergency or elective), the discharge destination of the admission, and of episode (time under the care of one consultant) and spell (time in hospital) numbers and dates for the admission.

Demographic data include age, sex, and postcode of residence, from which LSOA- and unitary authority (UA)-codes are derived.

2.3.2.4 *Primary care data*

Primary-care data relating to patients living in Wales are not contained in a comprehensive dataset. The SAIL-databank contains records of primary-care activity for a proportion of general practices in Wales.

The proportion of practices submitting data to SAIL was approximately 40% when this work was carried out.

Read codes are discussed further in section B.3.1

The information in the data imported from general-practice computer-systems into SAIL contains Read codes for general practice activities, measurement values relating to these Read codes, individual codes that allow linking to demographic information, and the date at which the event occurred.

The SAIL-databank stores GP data primarily in the Read code version 2 format. It also includes codes from practices that use more modern versions of the Read code system – Read code version 3.

2.3.2.5 *Socio-economic deprivation*

The data on socio-economic deprivation were incorporated into the SAIL databank as part of another project that used SAIL data (the Wales Electronic Child Cohort). The data contain three deprivation measures: WIMD 2008, WIMD 2005, and Townsend 2001, all derived at LSOA-level. I used WIMD 2005 for the analysis. Background information relating to these deprivation measures is discussed in section 2.1.2.1.

2.4 SUMMARY

Much background material is relevant to the subjects considered in this thesis. To balance the competing requirements of readability and comprehensiveness, I have sought to avoid overburdening the reader by including some background matter in the appendices of this document. The material there has been structured as follows:

> *Additional background material relating to inequity, socio-economic deprivation and healthcare needs assessment:* 'Geographical divisions' in section B.1.1 on page 375
>
> *Additional background material relating to CHD:* 'Pathophysiology' in section B.2.1 on page 375; 'Clinical classification' in section B.2.2 on page 379; 'Treatments and management' in section B.2.3 on page 381; and 'Organisation of cardiac services in Wales' in section B.2.6 on page 400
>
> *Additional background material relating to thesis methods:* 'Clinical coding' in section B.3.1 on 401

In this chapter, I have discussed important background information for this thesis. In the next, I move on to review the published literature relevant to this work, in line with the objectives, as set out in chapter 1.

Part II

DISCUSSION OF PREVIOUS WORK

3

INEQUITY IN PROVISION OF CORONARY HEART DISEASE HEALTH CARE INTERVENTIONS

In section 1.3.2 I highlighted a comprehensive literature review as one of the key subsidiary aims of this thesis. In this chapter, I consider papers in the medical literature describing studies of healthcare inequity relating to CHD. I also discuss in the final section of this chapter papers that enable me to give a brief overview of the National Service Frameworks (NSFs) and Quality and Outcomes Frameworks (QOFs) that formed an important part of the background to my work. My study period coincided with the early years of QOF and therefore evidence about the overall impact of QOF is clearly relevant to my findings. To ground this thesis adequately in previous research, I have necessarily undertaken a review of substantial scope. Many decisions about which areas to review and which to leave out inevitably arose; I include a section detailing the scope of the review and justifying many of the decisions made (section 3.6.2).

3.1 AIMS AND OBJECTIVES OF THE LITERATURE REVIEW

The aim of this literature review is to identify, appraise, and synthesise the literature on healthcare inequities in the provision of interventions for CHD. Underpinning this aim are a number of subsidiary objectives.

1. To develop inclusion criteria for studies
2. To determine which components of the pathway of care for CHD to address, and to justify these decisions
3. To identify papers meeting the inclusion criteria
4. To extract the relevant information from these papers
5. To synthesise the findings from disparate papers so that broad patterns might emerge (accepting from the outset that any meta-analysis based on statistical approaches would be impractical in this case)
6. To consider the findings of studies in the context of common problems with those studies and their methodological limitations

3.2 SCOPE OF THE LITERATURE REVIEW

The inclusion criteria that I used related to relevance to the main thesis, comprehensiveness, and practicality. Some element of trade-off proved inevitable. It was not possible or desirable to review every area that I might have considered; I justify these decisions below.

I wished to consider publications that met the following criteria:

1. They considered inequity of provision of healthcare interventions for CHD, as defined by one of the areas discussed below
2. They described studies that examined inequity from the point of view of socio-economic deprivation or social class at area or individual level
3. They described studies carried out in the UK
4. They described studies carried out in or after 1995
5. The studies are described in the published literature or in the grey literature in Wales

After consideration (see section 3.6.2), I decided to include studies in the review that looked at the following components of the management of CHD and its risk factors:

- Smoking cessation in primary care by means of smoking cessation advice or by means of referral to smoking cessation specialist services
- Primary prevention of CHD by the medical management of risk factors
- Secondary prevention and medical management of chronic disease
- Revascularisation

Primary prevention of disease by medical management was defined to encompass provision of antihypertensive treatments, of lipid-modifying therapies, and of anti-platelet therapies. I also included the medical management of blood glucose in those with diabetes. Because distinguishing between primary and secondary prevention was difficult in the papers relating to diabetes, I combined the review of primary and secondary prevention. For some of the papers, I found it difficult to determine whether or not primary or secondary prevention was

being assessed, and for some it is clear that a mixed group of patients, some with and some without pre-existing CVD, was included (thus implying a mixture of primary and secondary prevention). I have included such studies in the primary care component of the review, but have endeavoured to make clear when I have done so.

As discussed in appendix B, revascularisation can be accomplished either by coronary artery bypass graft (CABG) or by PCI. I included both. Informed readers will be clear that a number of other areas might have been included in this review; I justify the reasons for omitting these in section 3.6.2.

3.2.1 *Agentic versus structural emphasis in the scope of the review*

In a 2010 paper, McLaren et al discuss the potential of prevention strategies to increase social inequalities in health.[101] They draw an important distinction between 'agentic' and 'structural' interventions. They consider that proposed interventions fall on a continuum from 'agentic', where interventions pertain to an individual's capacity to make the choice to act, to 'structural', where interventions pertain to social institutions and norms that shape the actions of individuals.[101] They argue that "population strategies that are more superficial in nature rely on individual agency and aptitude, and as such are potentially more likely to increase (worsen) social inequalities in health."[101]

The focus of this review is interventions whose differential implementation might be contributing to health inequality from CHD. Thus, following McLaren et al, I have limited the scope of my review to interventions towards the 'agentic' end of the above spectrum.

3.3 METHODS OF LITERATURE REVIEW

I employed very similar methods for each of the stages of the pathway of care for CHD examined in this chapter. In overview they comprise:

1. Development of search terms
2. Database searches
3. Selection of papers based on title and abstract
4. Importing records and record storage
5. Review of fulltext papers

6. Snowballing based on relevant papers
7. Tabulation of important information
8. Summarisation of findings

In developing the search terms used, I wanted to have a sensitive definition of the areas considered to ensure that relevant papers were not missed; the subsequent examination of titles and abstracts allowed elimination of irrelevant papers. I wanted to use the same search terms to cover deprivation and to cover coronary heart disease for each of the searches carried out. I wished to employ the thesaurus terms available within the databases, again to maximise the sensitivity of the searches. I started by searching for and reading a number of clearly relevant papers, and then used these as the basis for the systematic searches which followed.

The search terms used for the main six areas are shown diagrammatically in the following figures: smoking cessation in figure 3.1 on page 54; antihypertensive medications in figure 3.2 on page 54; lipid-modifying medications in figure 3.3 on page 55; antiplatelet medications in figure 3.4 on page 56; diabetes management in figure 3.5 on page 56; revascularisation in figure 3.6 on page 57. The search strategies for antihypertensives, lipid-lowering medications, and antiplatelet medications include both terms related to socio-economic factors and to CHD. For smoking cessation, diabetes management, and revascularisation, search terms for socio-economic factors were included but not those for CHD. This distinction was necessary because, without the search terms related to CHD, the searches for antihypertensives, lipid-lowering medications, and antiplatelet medications returned an unmanageably large number of references.

The following databases were searched.*

1. EMBASE 1947 to present
2. Ovid MEDLINE(R) 1946 to present
3. HMIC Health Management Information Consortium
4. ICONDA 1976 to December 2011
5. Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

*Because the searches were carried out before I made the decision to limit the review to papers published after 1995, I employed databases covering periods prior to 1995

6. PsycINFO

The searches were carried out using OvidSP, accessed via the Cardiff University Portal. They were carried out in November and December 2011, and in January 2012. For all searches, duplicates were removed using the OvidSP default algorithm for duplicate removal. Search results were limited to 'English' and 'Humans'. Searches were saved for future reference using the OvidSP save facility. Although initially the time-limit of 1995 onwards was not included, I subsequently added this to the search criteria (though I did not change the databases used in the saved searches); I included papers up to the 'most recent' available. In carrying out the original search,I identified a conference abstract that was clearly relevant[102]. I contacted the authors to determine that a full paper would follow the abstract, and subsequently added this paper by Hawkins et al[103] to the review of secondary prevention of CHD.

Having performed these searches, I examined the titles and, where available, abstracts for those papers within the OvidSP environment. If papers were of possible relevance, I imported them into a file on a local desktop computer (using the RefMan format); there was one of these files for each search. I then imported these files into the Zotero reference management system that I have used for the management of papers for this thesis. Within Zotero, I obtained and stored relevant fulltext papers for those studies relevant to the review.

The identification of relevant papers made use of two separate approaches, firstly, systematic searching of databases of academic papers (as outlined above), and secondly a snowballing approach, in which relevant papers meeting inclusion criteria were back searched (using their reference list) and forward searched (looking at other papers that cited that paper via Google Scholar). For the second of these two processes, I used electronic copies of fulltext papers held within Zotero to identify referenced papers; I copied the paper's title into Google Scholar and examined the 'cited by' papers returned from searching. In turn, I imported relevant papers identified by this process into Zotero.

Having identified relevant papers using the above methods, I ended up with those papers relevant to more detailed review within Zotero in electronic fulltext form.

I decided that if a paper addressed more than one of the points on the pathway of care for CHD

Figure 3.1: Search terms used to look for papers on equity in smoking cessation services

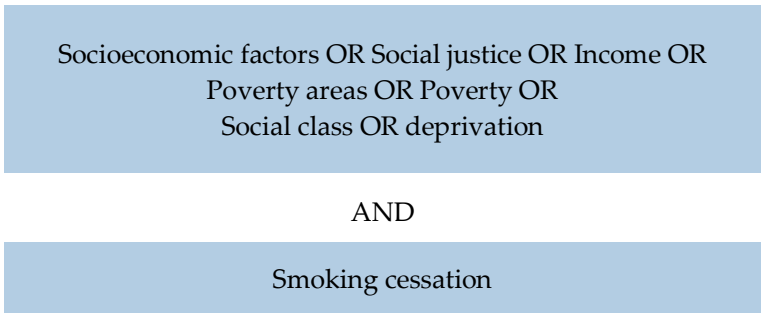


Figure 3.2: Search terms used to look for papers on equity in antihypertensive provision

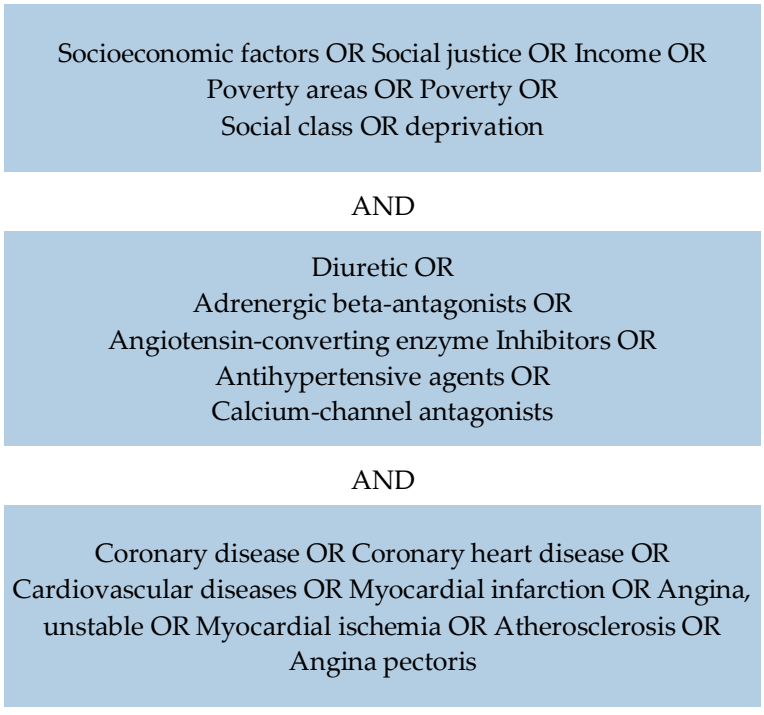


Figure 3.3: Search terms used to look for papers on equity in cholesterol-lowering drug provision

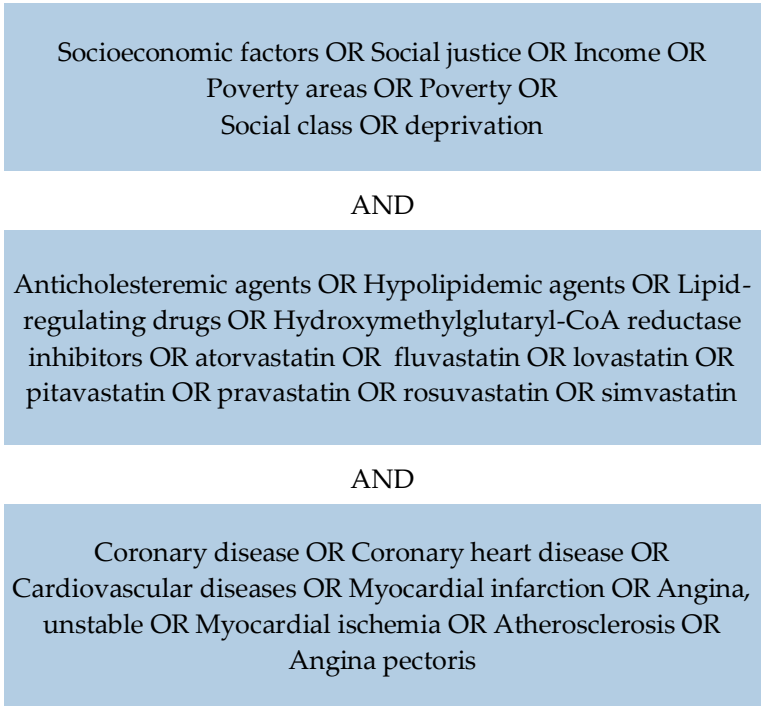


Figure 3.4: Search terms used to look for papers on inequity in antiplatelet drug provision

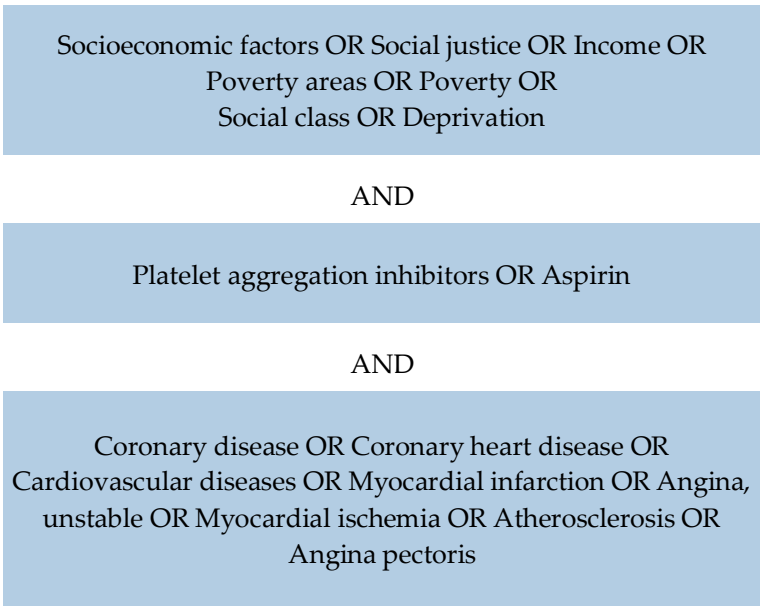


Figure 3.5: Search terms used to look for papers on equity in diabetes management

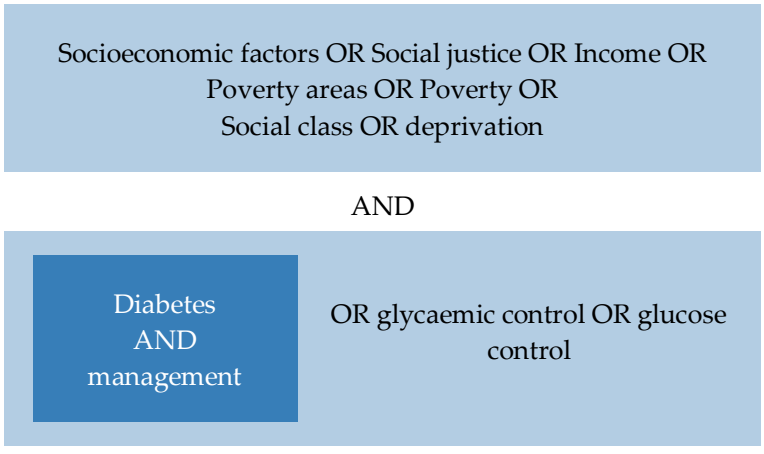


Figure 3.6: Search terms used to look for papers on equity in revascularisation

Socioeconomic factors OR Social justice OR Income OR Poverty areas OR Poverty OR Social class OR deprivation

AND

Angiography OR Coronary angiography OR Coronary artery bypass OR Angioplasty OR Balloon dilation OR Heart catheterization OR Angioplasty, Balloon, Coronary OR Myocardial revascularisation OR Angioplasty, Transluminal, Percutaneous Coronary

I would treat each area addressed as a separate study. This has the advantage of allowing the evidence for a particular part of the pathway to be considered as a whole. Therefore some studies appear in more than one table.

I tabulated important information for each included paper within an access database. The information collected for each paper was as follows: sample size, study type, dimension of comparison, publication date, data collection dates, text summary of study methods, text summary of study results, and comments.

I collected study size information, but in ecological studies particularly, it can be problematic to identify the number of people in the population being studied. Where it was clear that more than 50,000 individuals were included, I collapsed the sample size entry to 50,000 exactly. I did this in order to give as much clarity as possible in the visual summaries of the results, presented later in this chapter. The study type was recorded as ecological, individual-level, or prospective cohort, the distinction between the latter two being made on the basis of whether or not bespoke data were collected on individuals at baseline in a cohort followed up through time (as opposed to the employment of routine or survey data collected on individuals). Technically, any study employing an ecological measure of deprivation might be classified as an ecological study but I have not classified such studies as ecological on this basis alone. The dimension of comparison

field contained the deprivation or socio-economic position measure used in this study (sometimes more than one).

The information obtained and stored in this access database was used to produce figures to summarise the findings from the different papers. (The summaries are shown figures 3.13 to 3.20). Each figure is structured along the same lines. The categories along the x-axis represent the following four categories: 'Favours less deprived', 'No evidence of difference', 'Favours more deprived', 'Unclear'. According to this classification, 'Favours less deprived' would be a result suggesting inequity of provision. Further, studies published later are shown higher up in these figures; thus, the publication date increases at the y-axis. The sample size for the study is shown beneath the study name and date on the left of the figure; this study size is illustrated in the figure, with the size of the marker for each study being proportional to study size; study sizes over 50,000 were rounded down to 50,000 to aid presentation. Study design is illustrated by the colour of the study marker.

3.4 FILTERING OF PAPERS

The results of the processes used to identify papers for inclusion in the literature review are summarised in figures 3.7 to 3.12. The results vary considerably according to the area examined. For example, for smoking cessation 2219 titles were returned by the original search (see figure 3.7); for the search related to lipid-lowering medications 274 titles were returned (see figure 3.9); other searches returned values intermediate to these extreme values. For smoking cessation, quite a large number of papers were retained from the search (261), but, despite this, following the snowballing process and comparison of the papers against the inclusion criteria, I included only four papers in the review (see figure 3.7). I also retained quite a large number of papers from the original search for diabetes (252 papers), and subsequently included 15 in the review (see figure 3.11). For the other searches (antihypertensives, cholesterol-lowering therapies, antiplatelet drug provision, and revascularisation), only a few tens of papers were retained out of those returned by the database search: antihypertensives (42 with 24 papers eventually included – figure 3.8), cholesterol-lowering therapies (52 with 24 papers eventually included – figure 3.9), antiplatelet drug provision (48 with 20 papers eventually included – figure 3.10), and revascularisation (17 with 15 papers even-

tually included – figure 3.12). Because the Hawkins et al paper was identified by a different process (directly contacting the lead author on the basis of a conference abstract), it does not appear in these figures. Thus, one additional entry appears in tables for secondary prevention with antihypertensives, antiplatelet therapies, and statins – each dealing with findings from the Hawkins paper[103].

While the search strategy to identify papers for prevention using antihypertensive therapies, lipid-lowering therapies, and antiplatelet therapies did not distinguish between primary and secondary prevention, I make this distinction in subsequent sections of this chapter.

Figure 3.7: Filtering of papers for smoking cessation inequity of provision related to socio-economic deprivation

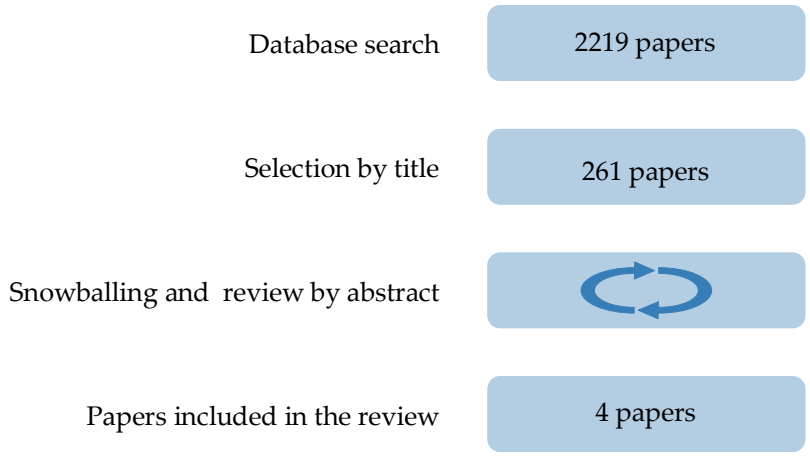


Figure 3.8: Filtering of papers for antihypertensives drug inequity of provision related to socio-economic deprivation

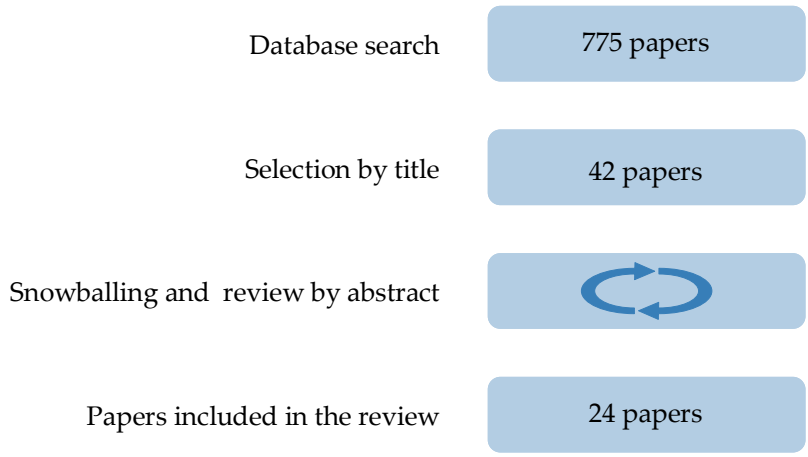


Figure 3.9: Filtering of papers for cholesterol-lowering drug inequity of provision related to socio-economic deprivation

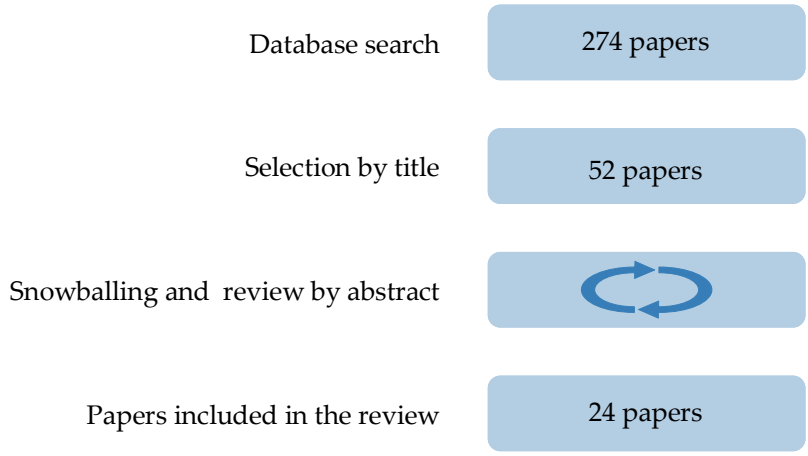


Figure 3.10: Filtering of papers for antiplatelet drug inequity of provision related to socio-economic deprivation

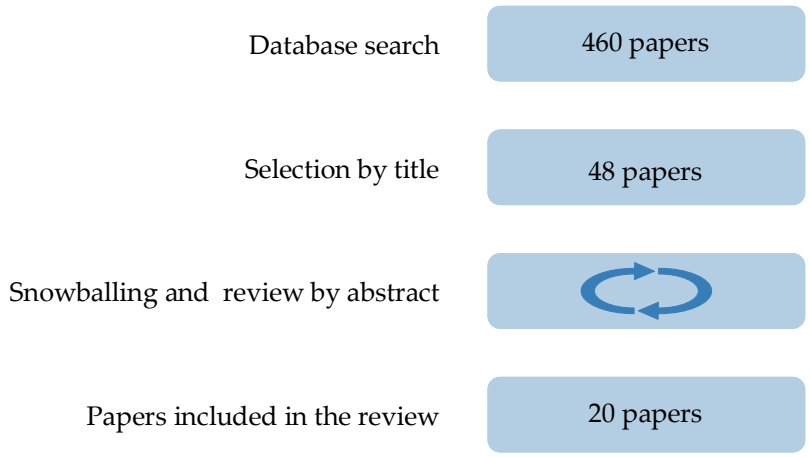


Figure 3.11: Filtering of papers for diabetes management inequity related to socio-economic deprivation

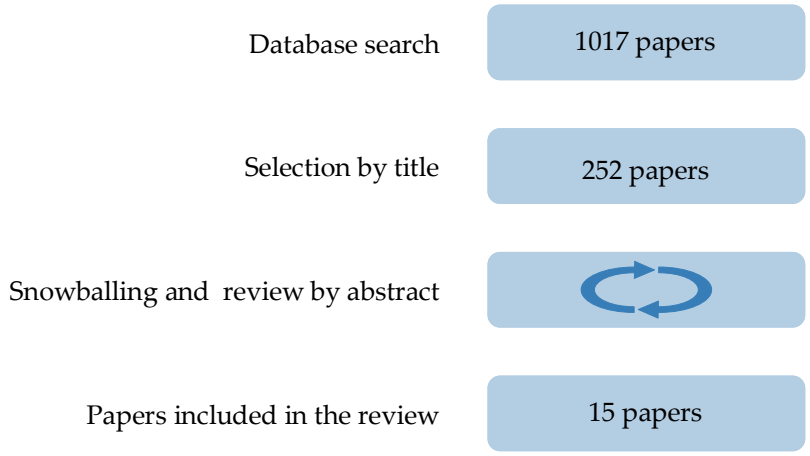
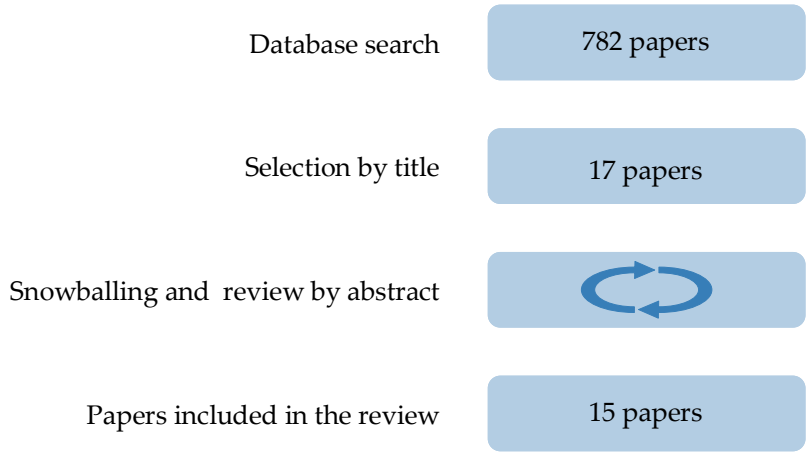


Figure 3.12: Filtering of papers for inequity of provision of revascularisation related to socio-economic deprivation



3.5 REVIEW OF PAPERS

3.5.1 *Smoking cessation*

Italicised name and date references in section 3.5.1 refer to papers in table 3.1 on page 64

I identified four papers that looked at smoking cessation provision in line with the inclusion criteria. These papers are summarised in table 3.1. Two studies looked only at the provision of smoking cessation advice (*Saxena 2007*[104], *Millett, Gray et al*[105]), while two looked at both smoking cessation advice and referral to smoking cessation services (*Strong 2006*[106], *Simpson 2010*[107]). Because of the small number of studies in this area, I have combined these two types of study. Two of the studies were ecological (*Saxena 2007*[104] and *Strong 2006*[106]) and two used individual-level data (*Millett, Gray et al*[105] and *Simpson 2010*[107]).

Of the four studies identified, one, *Saxena 2007*[104], found that provision of smoking cessation advice was increased in areas of decreased deprivation. However, the overall effect size was not large; there was a difference of between one and three percent between deprivation bands in the proportion of smokers offered smoking cessation advice. For example, in practices of size less than 3000, in the most deprived of the three bands, 90.3% of smokers with CHD had a record of smoking cessation advice being offered, compared to 93.3% in the least deprived; for practices with greater than 10,000 patients, the equivalent figure for the most deprived band was 92.7% compared to 94.6% in

the least deprived group. Other results from this study, for individuals with raised blood pressure or with a history of cerebro-vascular disease are comparable.

The other three studies reviewed found no evidence that there was an increased provision of smoking cessation advice (*Millett, Gray et al*[105], *Strong 2006*[106], *Simpson 2010*[107]) or of referral to stop smoking services (*Strong 2006*[106], *Simpson 2010*[107]).

Overall, there is little evidence of a differential effect between population groups based on socio-economic position in the extent to which smoking cessation advice or referral to stop smoking services is provided. Only one study found evidence of inequity of provision (*Saxena 2007*[104]), and here the effect was relatively small.

Table 3.1: Summary of papers examining inequity of provision of smoking cessation referral and stop smoking advice

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Strong 2006[106]; Rotherham Primary Care Trust, United Kingdom, 2003 – 2004 data	Mean IMD (England) 2004; calculated at practice level	Practice-level analysis; mean practice-level index of multiple deprivation. Looks at the Quality and Outcomes Framework CHD registered patients, standardised indirectly for age and sex. Spearman's rank correlation coefficient for standardised CHD against practice deprivation for quality-of-care indicators	The Spearman's rank correlation coefficient for the correlation between the percentage of patients with CHD who smoke and the mean deprivation score for practices was 0.19. This result was not statistically significant, though an exact p-value was not specified	The results suggest that the practice level there is no evidence of increased provision of smoking cessation services and advice in less deprived populations. Indeed, though the result is not statistically significant, the positive correlation coefficient in this case leans towards greater provision of such services in more deprived practices
Saxena 2007[104]; UK, 2004, 2005	IMD 2004. Grouped into three bands	Ecological study using QOF data. Large number of GP practices in the UK. Examination of practice performance in relation to a number of practice characteristics, including practice size, deprivation	Gradient across practices in the proportion of antihypertensive patients, patients with CHD, and patients with cerebro-vascular accident (CVA) receiving smoking cessation advice shows higher rates of smoking cessation advice in the less deprived. Kruskal Wallis exact test p-value is <0.0001	Ecological data at practice level on deprivation; the effect is not large, with the difference of the order of 1– 3% between deprivation bands in the proportion of individuals given smoking cessation advice

Continued on next page

Table 3.1 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Millett, Gray et al 2007[105]; London, 2003, 2005/6	IMD, derived from the postcode of residence of the patient; comparisons made by quintile	Population-based longitudinal study of patients with diabetes identified from diabetes registers in the Wandsworth area of South West London. Comparisons were made at two time points, 2003 and 2005/6. The proportion of patients with diabetes who smoke receiving smoking cessation advice was compared across quintiles (as well as across age, sex and ethnicity)	In 2003, rates of smoking cessation advice were highest in quintile 2 at 52.5% , and lowest in quintile 3 (42.6%). No evidence of a trend across quintiles; In 2005, the rate of being offered smoking cessation advice was highest in the most deprived quintile (88.2%) and declined progressively with decreasing deprivation to 80.2% in quintile 1. The increase in smoking cessation advice rates between the two time points was not influenced by deprivation group (adjusted odds ratio (OR))	Diabetic patients only. Some suggestion of increased provision with increased deprivation, though the relevant statistical analysis to assess whether this is a statistically significant result is not available; no adjustment of the rates in quintiles for other relevant variables

Continued on next page

Table 3.1 – *Continued from previous page*

AUTHOR YEAR; SETTING	INEQUITY DIMENSION	STUDY TYPE	RESULTS	COMMENT
Simpson 2010[107]; UK, 2001/2, 2006/7	Townsend deprivation index 2001; comparisons by quintile	Individual-level database analysis using the QRESEARCH database version 10. Smoking status and smoking cessation provision were identified using Read codes	For in-house smoking cessation advice, in 2001/2 rates of provision were highest in the most deprived quintile at 45.12%(95% CIs 44.61, 45.62), with rates generally declining with decreasing deprivation. The situation was similar in 2006/7, though here the highest rate was in quintile 4 at 84.44%(95% CIs 84.16, 84.72). Referral to stop smoking services had a trend towards decreased provision with decreased deprivation at both time points. In 2001/2, rates were 1.94%(95% CIs 1.80, 2.08) in the most deprived quintile declining to 0.52%(95% CIs 0.43, 0.61) in the least; in 2006/7, the same trend persisted, with equivalent figures 8.56% (95% CIs 8.37, 8.75) in the least deprived declining monotonically to 5.25% (95% CIs 5.04, 5.46) in the least deprived quintile	This study looked at both in-house smoking cessation advice given in primary care, and referrals to stop-smoking services. All analyses were univariate, and so the effects observed may have been explicable by demographic or comorbidity changes. Analysis of the trends across deprivation quintiles are not presented; in view of the results it is possible that there is a significant trend in favour of provision in the more deprived quintiles

3.5.2 *Medical management of risk factors*

In this section of the review I consider interventions that are routinely used to manage risk factors (or in the case of aspirin to manage CHD risk) from the point of view of the equity of their provision.

3.5.2.1 *Antihypertensives*

Italicised name and date references in section 3.5.2.1 refer to papers in table C.1 on page 406

Seventeen studies address inequity in supply of antihypertensives for the primary prevention of CHD; these papers are summarised in table C.1, in appendix C. This table also includes studies that do not allow differentiation of primary and secondary prevention by BP management and prescription of anti-hypertensive medications. The picture that emerges from the studies shown in table C.1 is mixed, but studies predominantly find that both the provision of antihypertensive treatments for primary prevention of CHD and the achievement of BP targets are not related to socio-economic deprivation or social class. Five of the studies (*Pears 2003*[108], *Ward 2004*[109], *Ward 2005*[110], *Edwards 2003*[111], *Crawley 2009*[112]) looked at provision of antihypertensives. Fourteen of the studies examined achievement of BP targets as an outcome (*Edwards 2003*[111], *Chen 2003*[113], *Bachman 2003*[114], *Hippisley-Cox 2004*[115], *Gray 2006*[116], *McLean 2006*[117], *Patel 2006*[118], *Millett, Car et al*[119], *Saxena 2007*[104], *McGovern 2008*[120], *Ashworth 2008*[121], *Crawley 2009*[112], *Hamilton 2010*[122], *Hammouche 2011*[123]). One study (*Pears 2003*[108]) also looked at whether hypertensive patients were 'under-review', 'treated', or 'not-followed-up' with respect to the management of their hypertension. Six of the studies analysing equity in primary prevention by management of BP looked only at diabetic patients: *Edwards 2003*[111], *Bachman 2003*[114], *Hippisley-Cox 2004*[115], *Gray 2006*[116], *Millett, Car et al*[119], *Hamilton 2010*[122].

Saxena 2007[104] found a statistically significant gradient of an increased proportion of hypertensive patients meeting BP targets with decreased deprivation. *Millett, Car et al*[119] found a mixed picture in which a smaller proportion of patients achieved targets in the most deprived practices compared to the least deprived practices, but the proportion was highest for intermediately deprived practices. Statistical significance could not be assessed for this result. *McLean 2006*[117] found a non-significant decline in the management of hypertension as deprivation increased. *Ashworth 2008*[121] found that a statistically significant difference between deprivation groups in 2004-5 (with

more deprived groups less likely to reach BP control targets) had disappeared by 2006-7.

The studies that examined prescription of anti-hypertensive medications either found no association with deprivation/social class (*Edwards 2003*[111], *Crawley 2009*[112]) or found a mixed picture. Of those suggesting a mixed picture, *Pears 2003*[108] suggested that more deprived hypertensive patients were less likely to be on thiazide diuretics, as likely to be on beta-blockers, and more likely to be on Angiotensin-converting enzyme (ACE) inhibitors and calcium-channel blockers; *Ward 2004*[109] found patients from deprived practices were less likely to be on ACE inhibitors and bendrofluazide, and equally likely to be on beta-blockers; *Ward 2005*[110] found that more deprived practices prescribed less bendrofluazide, with no effect for ACE inhibitors or beta-blockers.

The only paper that examined whether hypertensive patients were 'under-review','treated', or 'not-followed-up' *(Pears 2003)*[108], found that deprived patients were less likely to be 'under-review'.

The rest of the studies reviewed found no significant relationship between deprivation/social class and either prescribing of anti-hypertensive drugs or achievement of BP control targets. Examining the studies in which findings suggest an element of inequity of provision of health care compared to those which do not, it is not clear that studies over a particular time period (either the earlier studies which cover periods back to the early 1990s or those from a later period up to 2007) are more likely to provide evidence of an association. One paper *(Ashworth 2008)*[121] found that a relatioship that existed at an earlier time-point, 2004-5, was no longer observable by the second time-point, 2006-7. Methodologically, there is a suggestion that it is the ecological studies that demonstrate inequity in provision of anti-hypertensives or achievement of BP control targets: of those studies suggesting a mixed picture or inequity in management, only that by *Pears 2003*[108] is an individual-level analysis. All the studies that provide no evidence of inequity are individual-level studies.

3.5.2.2 *Lipid-lowering medications*

Italicised name and date references in section 3.5.2.2 refer to papers in table C.2 on page 413

Seventeen papers examine equity in prescription of lipid-lowering medications and achievement of cholesterol targets; these papers are summarised in table C.2. Of these papers, eight deal only with prescription of lipid-lowering medications (*Bradshaw 1998*[124], *Packham 1999*[125], *Packham 2000*[126], *Ward 2004*[109], *Ward 2005*[110], *Ward 2007*[127],

Ashworth 2007[128], *Forde 2011*[129]), seven deal only with achievement of cholesterol targets (*Bachman 2003*[114], *Hippisley-Cox 2004*[115], *McLean 2006*[117], *Gray 2006*[116], *Millett, Car et al*[119], *McGovern 2008*[120], *Hamilton 2010*[122]), and two deal with both (*Edwards 2003*[111], *Crawley 2009*[112]). Six of the studies look only at diabetic patients (*Edwards 2003*[111], *Bachman 2003*[114], *Hippisley-Cox 2004*[115], *Millett, Car et al*[119], *McGovern 2008*[120], *Hamilton 2010*[122]).

Of the papers reviewed, five found a positive relationship between increasing deprivation/social class and reduced lipid-lowering drug provision or reduced achievement of cholesterol targets (*Bradshaw 1998*[124], *Packham 1999*[125], *Packham 2000*[126], *Ward 2004*[109], and *McLean 2006*[117]). The papers that found a positive relationship with lipid-lowering drug prescribing were ecological studies. *Packham 1999*[125] found that the initial relationship between deprivation and statin-prescribing in 1996 was no longer significant in 1997-1998 (*Packham 2000*[126]). The findings from *Ward 2004*[109] need to be seen in light of the fact that there is a similar, but better quality study, published subsequently, which largely repeats the earlier study but uses multivariate rather than univariate analysis (*Ward 2005*[110]).

The findings from all the subsequent studies looking at lipid-lowering medication prescribing equity provide no evidence of inequity of provision. One study suggests a relationship between increased deprivation and worse achievement of cholesterol targets (*Millett, Car et al*[119]), but CIs are not available for the results of this study, so the statistical significance is uncertain. All other studies find no evidence of inequity in the achievement of cholesterol targets between deprivation groups, though in one of these studies the result is hard to interpret with apparent contradiction between CIs and the p-value of the result (*Bachman 2003*[114]). In some of the studies reviewed, the achievement of cholesterol targets appeared to occur more frequently in more deprived groups (*McLean 2006*[117], *McGovern 2008*[120], *Hamilton 2010*[122]).

The results from these studies are only positive (in the sense of demonstrating inequity of provision by deprivation/socio-economic status) in older, ecological studies (*Bradshaw 1998*[124], *Packham 1999*[125], *Packham 2000*[126], *Ward 2004*[109], *McLean 2006*[117]). It may be that the positive results in these studies are a reflection of methodological weaknesses, though they may also indicate that the inequity of provision of lipid-lowering medications that they observed had disappeared

over time; the latter possibility is supported by the findings of *Packham 2000*[126].

3.5.2.3 *Anti-platelet medications*

Italicised name and date references in section 3.5.2.3 refer to papers in table C.3 on page 420

Nine papers looked at primary prevention of CHD using anti-platelet therapies, and are shown in table C.3; some papers may deal with a mixture of primary and secondary prevention, for example *Elwood 2005*[130], *Ward 2004*[109] and *Ward 2005*[110]. One paper looked at clopidogrel provision (*Petty 2008*[131]); the others looked at aspirin. One study (*Edwards 2003*[111]) looked at diabetic patients only.

Of the nine studies identified, the majority suggest either that there is no relationship between deprivation/social class and provision of anti-platelet medications or that those in more deprived social groups are more likely to be taking these therapies. Only two studies (*Ward 2005*[110], *Saxena 2007*[104]) found evidence of inequity of provision. In the *Ward 2005*[110] study, ecological prescribing rates for practices were modelled on a number of practice characteristics, among them Low Income Scheme Index (LISI) score. Results suggested that with increased deprivation there was decreased prescribing of aspirin at the practice level. This is in an ecological study, which was not able to take account of whether individuals specifically had a clinical need for aspirin, as is more possible in individual-level analyses. Instead, this study used a number of proxies to infer the practice-level clinical needs that would be expected for the population. The other study which suggested that anti-platelet medications were prescribed less in more deprived practices used a similar methodology, with similar potential limitations (*Saxena 2007*[104]).

The remaining studies identified in this review suggested no inequity in provision of anti-platelet medications was present, including *Bedson 2001*[132], *Ward 2004*[109], and *Petty 2008*[131]; indeed a number of the studies found that individuals in more deprived social groups were more likely to be receiving anti-platelet therapy with aspirin (*Edwards 2003*[111], *Elwood 2005*[130], *Vinogradova 2009*[133], and *Elwood 2011*[134]), though CIs were not available for the study by *Vinogradova 2009*[133]. All of these studies, and in addition the study by *Bedson 2001*[132] used individual-level data; *Ward 2004*[109] and *Petty 2008*[131] employed ecological methodologies.

Overall, the findings from the review of the equity of provision of anti-platelet therapies suggest that they are provided equitably across deprivation groups and social classes. There is no evidence

of a temporal effect, as the two studies which suggest that a level of inequity of provision might be occurring covered a time period similar to that covered by other studies in review.

3.5.2.4 *Diabetes management*

Italicised name and date references in section 3.5.2.4 refer to papers in table C.4 on page 423

Papers typically do not examine diabetes control from the perspective of primary prevention, though good-quality glycaemic control is a key aspect of the primary prevention of CHD (as well as other macro- and micro-vascular complications); for the purposes of this review papers addressing the quality of glycaemic control by deprivation or social class in individuals who do not have CHD have been examined. The primary prevention component is typically implicit rather than explicit in these papers.

Fifteen papers for the review examined the management of diabetes in individuals without CHD. The majority of papers identified looked at the achievement of glycaemic-control targets, as measured by HbA_{1C}. Only two papers (*Crawley 2009*[112], *Millett, Saxena et al*[135]) examined the provision of prescriptions for hypoglycaemic medication.

A mixed picture emerges, with some papers suggesting that the achievement of glycaemic-control targets in more deprived social groups is worse. *Weng 2000*[136], *Hippisley-Cox 2004*[115], *Bebb 2005*[137], *McGovern 2008*[120], and *Wild 2008*[138] found that patients from more deprived social groups tended to have worse glycaemic control. *Maclean 2006*[117] found that when examining QOF data, the standard of diabetes management did not differ when exclusions from QOF returns were not included in the analysis, but found that when such exclusions were included the percentage of patients achieving glycaemic-controlled targets in more deprived social groups was lower. *Millet, Car et al 2007*[119] found a gradient in the proportion of patients reaching the glycaemic-controlled targets according to deprivation and practice level; a higher proportion of patients in less deprived practices achieved targets. *Crawley 2009*[112] found that there was no difference between the manual and non-manual social class groups in the prescribing of oral hypoglycaemic agents, but that achievement of HbA_{1C} targets was less likely in the manual group in 2003 (when the result were statistically significant) and in 2006 (when it was not). One study (*Gray 2006*), found that patients in the least deprived group were more likely to achieve HbA_{1C} targets, but that the result was non-

significant. *Millett, Saxena et al*[135] found no difference in prescribing of hypoglycaemic agents.

Other papers (*O'Kane 2010*[139], *Edwards 2003*[111], *Bachman 2003*[114], *Millet 2009*[140], *Hamilton 2010*[122]) found that the achievement of glycaemic-control targets between social deprivation groups was not systematically different, with the implication that the management of these individuals is not inequitable across these groups.

In situations in which there is an observed, statistically-significant difference across deprivation groups in the achievement of glycaemic-control targets, the conclusion that can legitimately be drawn is that there is an absence of evidence of equity of provision of care, but not strong evidence of inequity of provision. This is because management of blood sugar by individuals has a very strong self-care component, which may act to a large extent independently of the quality of health care provided to the individual. While this tendency will also operate with achievement of BP-control targets (where adherence to medication regimes may vary systematically across deprivation groups), it is likely to be more pronounced in glycaemic-control management.

3.5.3 *Secondary prevention and management of chronic disease*

3.5.3.1 *Antihypertensives*

Italicised name and date references in section 3.5.3.1 refer to papers in table C.5 on page 430

Thirteen papers were identified that address equity of prescription of anti-hypertensive medications and equity of achievement of blood pressure targets by deprivation or social class for those with a diagnosis of CHD; the papers are summarised in table C.5. The majority (eight) of the papers examined equity in provision of anti-hypertensive medications (*Britton 2004*[141], *Simpson 2005*[142], *Harding 2005*[143], *Ramsay 2005*[144], *Murphy 2006*[145], *McGovern 2008*[120], *Mathur 2011*[146], and *Hawkins 2013*[103]); four papers examined both equity of anti-hypertensive drug provision and equity in achievement of BP targets (*McLean 2006*[117], *Strong 2006*[106], *Saxena 2007*[104], and *Crawley 2009*[112]); one examined only equity in achievement of BP targets (*Ashworth 2008*[121]).

Overall, the findings from the papers identified suggest that the provision of anti-hypertensive drugs and the achievement of BP targets are both equitable in those with CHD. Of the papers identified, only *Saxena 2007*[104] found a unmixed picture of inequity of provision, with a suggestion that, at practice-level, practices with increased deprivation tended to have lower prescribing of ACE-inhibitors and beta-blockers

and to have a decreased proportion of patients with CHD meeting BP targets. A number of other studies found a slightly mixed picture (*Harding 2005*[143], *Ramsay 2005*[144], *McGovern 2008*[120], *Ashworth 2008*[121], *Crawley 2009*[112]). *Harding 2005*[143] found that patients in more deprived communities were less likely to be prescribed calcium-channel blockers and diuretics and received fewer anti-hypertensive drugs, but found that for ACE inhibitor and beta-blocker prescription the gradient suggested some inequity but was not statistically significant – potentially suggesting a lack of power to detect a true gradient. *Ramsay 2005*[144] made numerous comparisons at two time-points for those with angina and those with a previous MI and for different drugs; only one of these comparisons suggested inequity, and the positive results may be a result of multiple comparisons. *McGovern*[120] found that more deprived groups were more likely to receive ACE inhibitors, but less likely to receive beta-blockers. *Ashworth 2008*[121] found that an initial inequity in the achievement of BP targets subsequently disappeared. *Crawley 2009*[112] found that there was no difference in prescribing of anti-hypertensive medications between deprivation groups; in 2003 there was a non-statistically-significant suggestion of inequity in achievement of BP targets; in 2006 this result was significant.

Other studies examined found no evidence of inequity of provision of anti-hypertensive medications (*Britton 2004*[141], *Simpson 2005*[142], *McLean 2006*[117], *Strong 2006*[106], *Murphy 2006*[145], *Mathur 2011*[146]) or in the achievement of BP targets (*McLean 2006*[117], *Strong 2006*[106]). *Hawkins 2013*[103] found that patients in the more deprived individulas with angina were more likely to receive ACE inhibitors or angiotensin-II receptor blockers (ARBs) in 2007 (though not in 1999); in this study, there was no difference for secondary prevention in primary care or following an MI.

No clear temporal tendency in the positive results emerges from the review in this area. *Ashworth 2008*[121] found that an initial difference in the achievement of BP control by deprivation that was found in 2004-5 had largely disappeared by 2006-7; in contrast, *Crawley 2009*[112] found that a non-significant difference in achievement of BP targets in 2003 had become statistically significant by 2006 – though the authors suggest this may be the result of the earlier study being under-powered.

Whether a study was ecological or individual-level appears not to be related to its finding evidence of inequity in hypertension management. Of the papers that examined inequity in achievement of BP

targets, three out of five found some evidence of inequity (though in the studies by *Ashworth 2008*[121] and *Crawley 2009*[112] this was equivocal). When looking at inequity of provision of anti-hypertensive medications, only one paper suggested inequity (*Saxena 2007*[104]); three papers suggested that some individual antihypertensives were inequitably provided but found that others were equitably prescribed or favoured more deprived groups (*Harding 2005*[143], *Ramsay 2005*[144], and *McGovern 2008*[120]). This may provide some indication that 'inequity' in achievement of targets is reliant not only on factors relating to the quality of service (such as identification of clinical need and prescription for appropriate medication), but relates also to the extent to which individuals adhere to any recommended treatment.

3.5.3.2 *Lipid-lowering medications*

Italicised name and date references in section 3.5.3.2 refer to papers in table C.6 on page 438

Ten papers addressed equity by social class or deprivation in prescribing of lipid-lowering medications to those with CHD; they are summarised in table C.6. Eight looked only at equity in prescribing of lipid-lowering drugs (*Reid 2002*[147], *Britton 2004*[141] , *Harding 2005*[143], *Ramsay 2005*[144], *Simpson 2005*[142], *Murphy 2006*[145], *Mathur 2011*[146], and *Hawkins 2013*[103]), one looked only at achievement of cholesterol targets (*Strong 2006*[106]), and one looked at both (*Crawley 2009*[112]).

No studies unequivocally identify inequity in either provision of lipid-lowering medication or in achievement of cholesterol targets, though two do provide evidence of a changing picture over time (*Ramsay 2005*[144] and *Simpson 2005*[142]). *Ramsay 2005*[144] examined the prescription of statins to patients who had CHD. The analysis was carried out separately for patients with angina and for patients with a previous MI. Most of the results showed no evidence of inequity of provision; in 2000 those from the manual social-class group with angina were less likely to receive a statin (prevalence ratio 0.64 (95% CIs 0.45, 0.91)). By 2003 this result was no longer statistically significant for those with angina – prevalence ratio 0.91 (95% CIs 0.76, 1.09); there was no evidence of inequity of provision in those with a previous MI, with the results favouring the manual social-class group in 2000 and in 2003 (though the relationships were not statistically significant). *Simpson 2005*[142] found that an initial relationship in which the most deprived group received significantly less statin treatment than the most deprived observed between 1998 and 2000 was no longer present between 2001 and 2002. Other studies identified in the review did not find any evidence of inequity of prescribing of lipid-

lowering medication (*Reid 2002*[147], *Britton 2004*[141], *Harding 2005*[143], *Murphy 2006*[145], *Mathur 2011*[146], and *Hawkins 2013*[103] – where there was some evidence of increased prescribing in more deprived groups), or inequity in achievement of cholesterol targest (*Strong 2006*[106]), or found neither (*Crawley 2009*[112]). One study, *Strong 2006*[106], found a non-statistically-significant association between increased deprivation and the percentage of patients achieving cholesterol targets at practice level.

3.5.3.3 *Anti-platelet medications*

Italicised name and date references in section 3.5.3.3 refer to papers in table C.7 on page 443

Fifteen papers examined the provision of anti-platelet medications (aspirin in most cases; *Hawkins 2013*[103] looking in addition at clopidogrel) to individuals with a previous diagnosis of CHD. These studies were carried out between 1997 and 2011, with the earliest data for any of the studies going back to 1985.

Of the studies identified, only one (*Saxena 2007*[104]) found any evidence of inequity of provision of anti-platelet medications in patients with CHD, and the association it found was weak. In the study the authors found that at a practice level there was an association between practice-level deprivation (IMD) and the proportion of patients at a practice treated with aspirin, as returned in QOF data. The strength of the association was tested using the Kruskal-Wallis test, but was not examined further using multivariate analysis which might take account of other covariates relating to practices, though analysis was performed separately according to practice size. The ecological nature of this study and the limited nature of the analysis performed, together with the relatively weak evidence of an association, mean that this paper provides only weak evidence of inequity of aspirin provision for secondary prevention.

Other studies in this area did not find evidence of inequity; *Ramsay 2005*[144] found some suggestion that patients with angina or who had previously had an MI appeared to be less likely to be treated with aspirin if they were in the manual social class (compared to the non-manual social class), but these results did not attain statistical significance at either of the time-points studied or for either of the patient groups. Some of the studies in fact found that the more deprived social group appeared more likely to be treated with aspirin; *Trinder 2003*[148] and *Mathur 2011*[146] found some evidence of this, though the results were not statistically significant; other papers (*Elwood 2005*[130], *McGovern 2008*[120], *Elwood 2011*[134]) found evidence of such a pattern;

Hawkins 2013[103] also found such a picture, particularly in younger age groups: this pattern was present in the stable angina group in both 1999 and 2007, in 1999 only in their secondary prevention group, and was not seen in the MI group (either for aspirin or clopidogrel).

Overall, it is clear that the evidence in this area clearly does not support the existence of inequity in provision of aspirin (or other anti-platelet medications) for secondary prevention of CHD.

3.5.4 *Revascularisation*

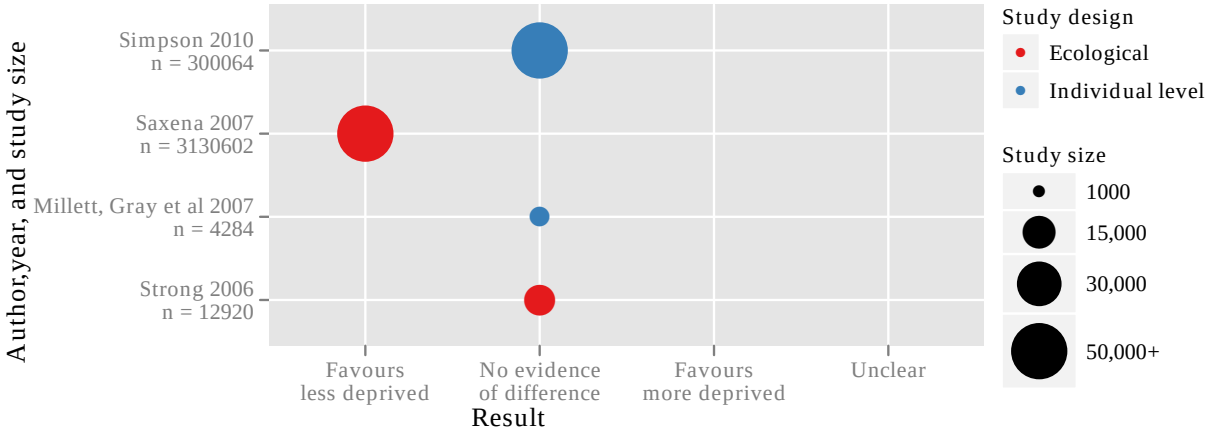
Italicised name and date references in section 3.5.4 refer to papers in table C.8 on page 449

Fifteen papers were identified in the review that examined the equity of provision of revascularisation procedures. The majority of the papers account provision rates of revascularisation procedures (either CABG or percutaneous transluminal coronary angioplasty (PTCA)); one paper (*Pell 2000*[149]) examined waiting times for procedures.

The results from these papers present a mixed picture of the extent of inequity of provision of revascularisation procedures. A number of papers find evidence of inequity of provision, including *Payne 1997*[150], *Manson-Siddle 1998*[151], *Manson-Siddle 1999*[152], *Hippisley-Cox 2000*[153], *Lester 2004*[154], and *Cosh 2008*[155]. *MacLeod 1999*[156] found in inequitable provision of CABG, and though there was some suggestion of inequitable provision of PTCA this result was not statistically significant, which was attributed to the small number of these procedures identified in the study. *Ben-Schlomo 1995*[157] found a mixed picture, with evidence of inequitable provision of revascularisation procedures (CABG) in men: the second and third deprivation quartiles had the lowest rate of revascularisations, while mortality, which was used as a measure of proxy need in the study, increased as deprivation increased. The paper that examined differences in waiting times for revascularisation procedures (*Pell 2000*[149]) found that overall patients in more deprived groups waited longer for surgery, but that when the analysis was repeated separately for routine and emergency procedures there was no longer a significant difference between the groups.

The remaining studies that were reviewed did not find evidence of inequity of provision of revascularisation procedures (*Kee 1995*[158], *Black 1995*[159], *Britton 2004*[141], *Gatrell 2002*[160]). *Morris 2005*[161] found some suggestion of inequity, but the result was not statistically significant. *Mindell 2008*[162] found no evidence of inequity in NHS provision of revascularisation procedures, but did find that provision in the private sector was inequitable.

Figure 3.13: Summary of findings from review of smoking cessation



The majority of the studies identified and included in this review dated from 2004 or earlier (12 out of 15 papers) with many of the studies published in the 1990s (6 out of 15 papers). Only one of the studies found evidence of inequity in revascularisation-provision data from after 2004 (*Cosh 2008*), and this paper used data from 1992 through to 2006. There is, therefore, no evidence of inequity and provision of revascularisation procedures after, at the very latest, the 2000s. Patterns of provision of revascularisation procedures may have changed substantially since that time, due to the large increases in capacity that have occurred.

The majority of studies that identified some level of inequity in provision of revascularisation procedures were carried out using ecological approaches (*Ben-Schlomo*[157], *Payne 1997*[150], *Manson-Siddle 1998*[151], *Manson-Siddle 1999*[152], *Hippisley-Cox 2000*[153], *Lester 2004*[154], *Cosh 2008*[155]). The only paper showing inequity which used individual-level data was *MacLeod 1999*[156]; this paper utilised data from 1991 to 1995.

Two of the papers included in this section of the review were not published, peer-reviewed papers (*Lester 2004*[154], *Cosh 2008*[155]). Their findings therefore merit less weight than those from published studies.

Figure 3.14: Summary of findings from review of primary prevention using antihypertensive medications

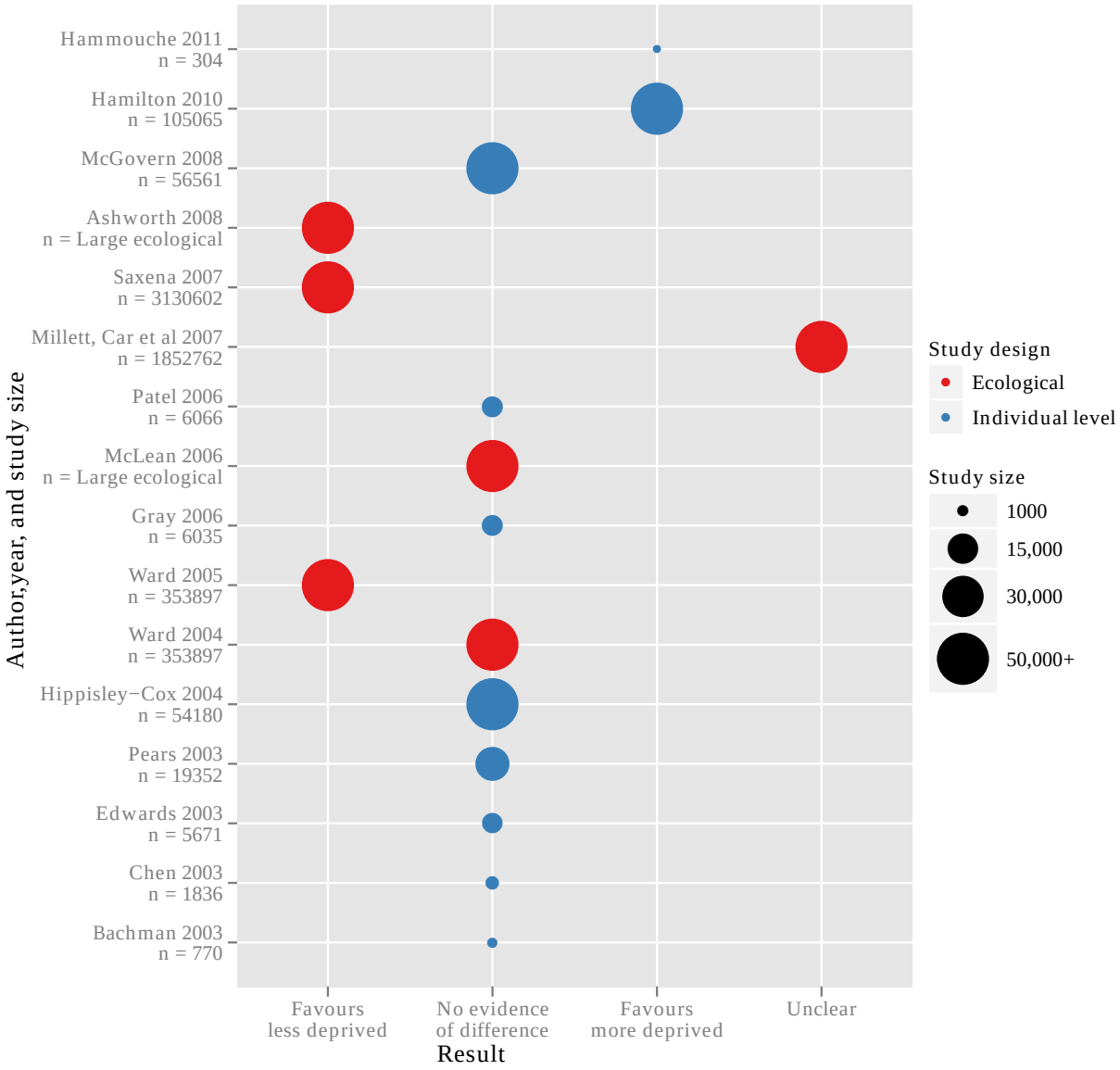


Figure 3.15: Summary of findings from review of primary prevention using cholesterol-lowering medications

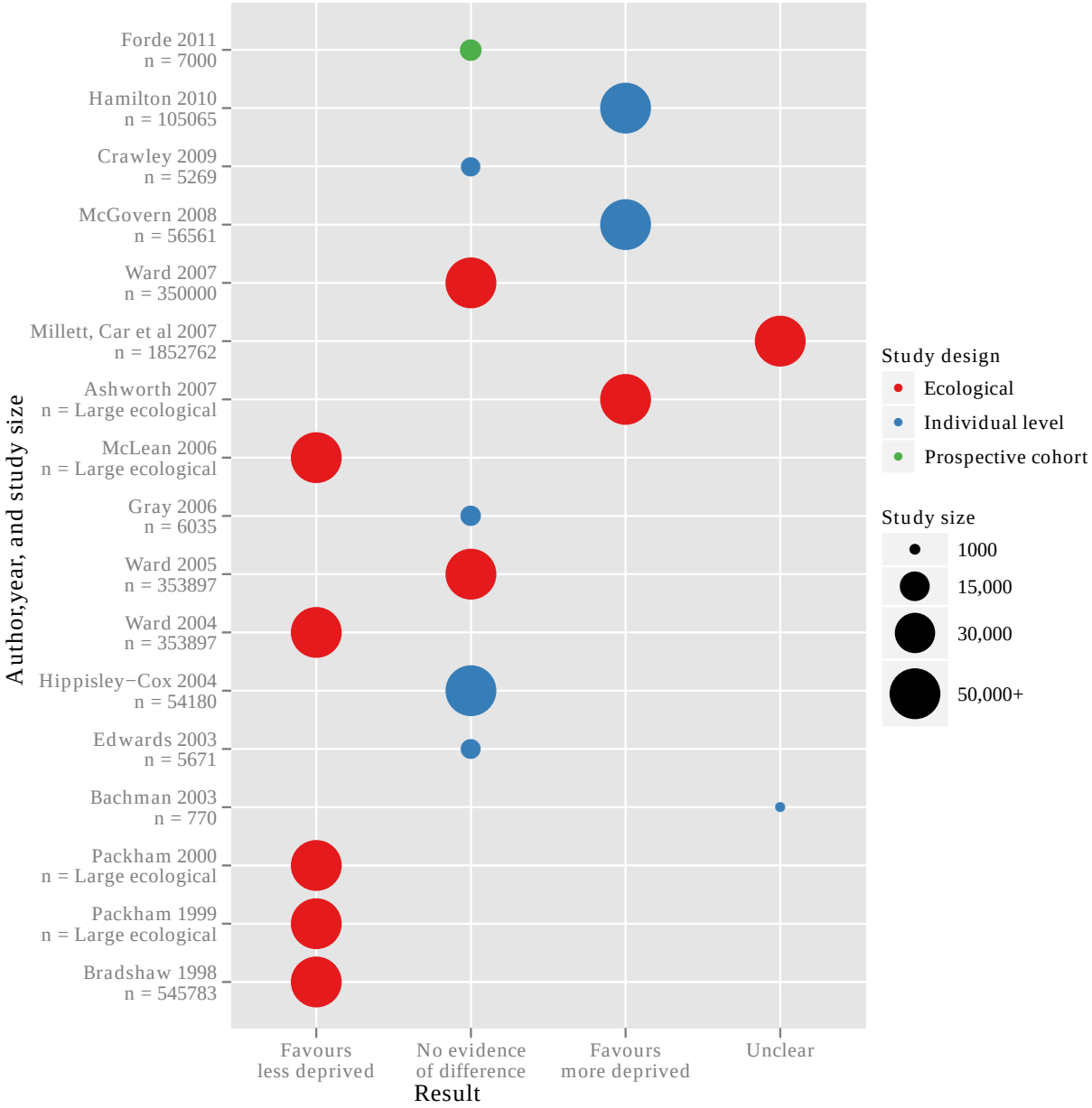


Figure 3.16: Summary of findings from review of primary prevention using antiplatelet medication

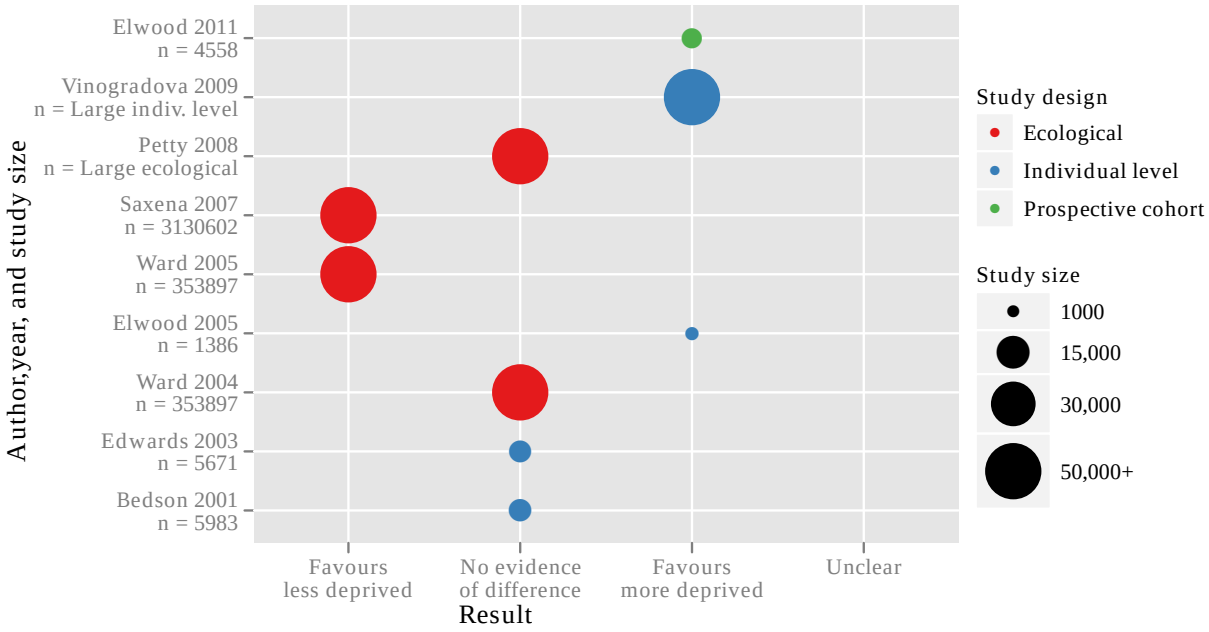


Figure 3.17: Summary of findings from review of diabetes management

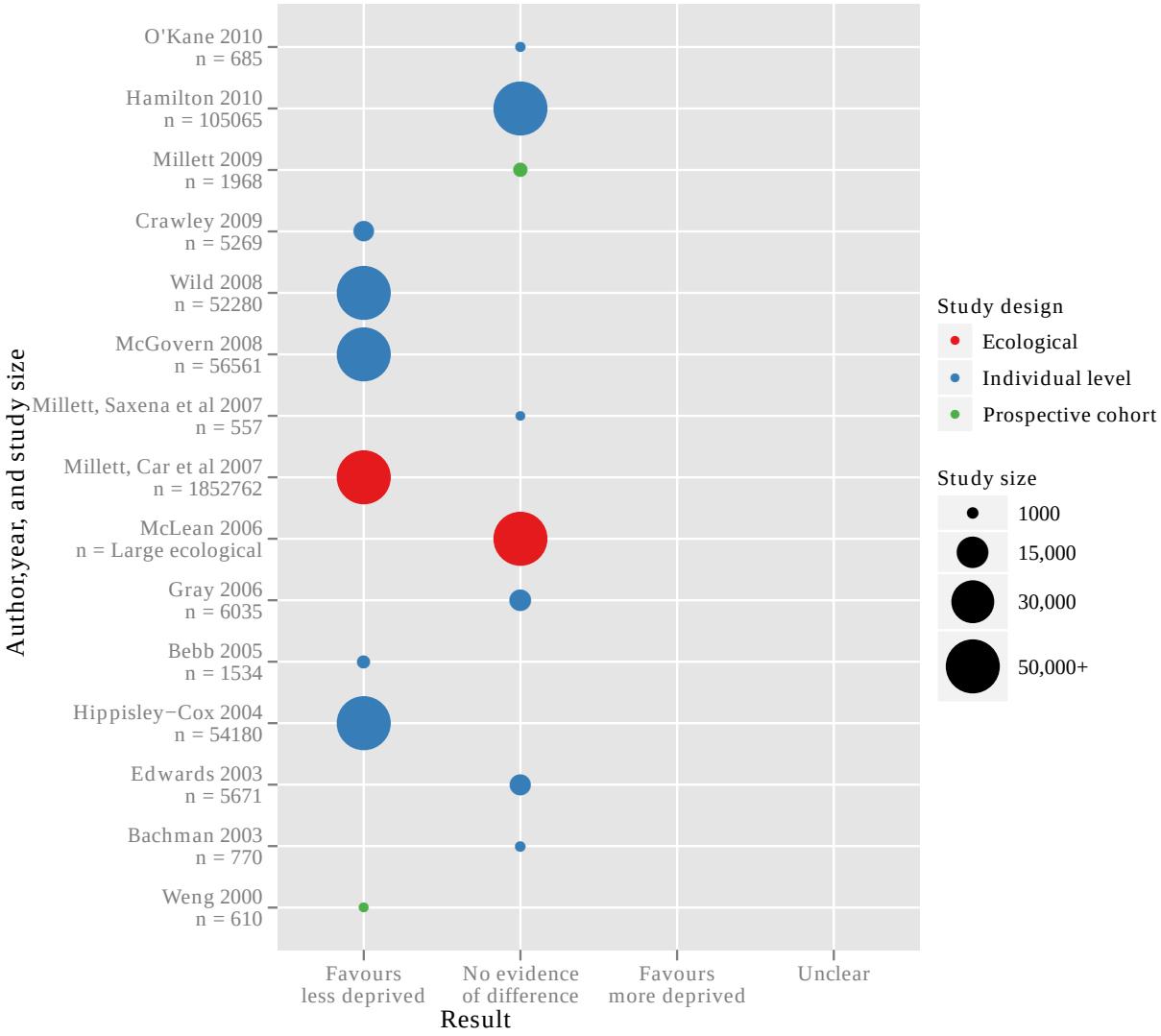


Figure 3.18: Summary of findings from review of secondary prevention using antihypertensives

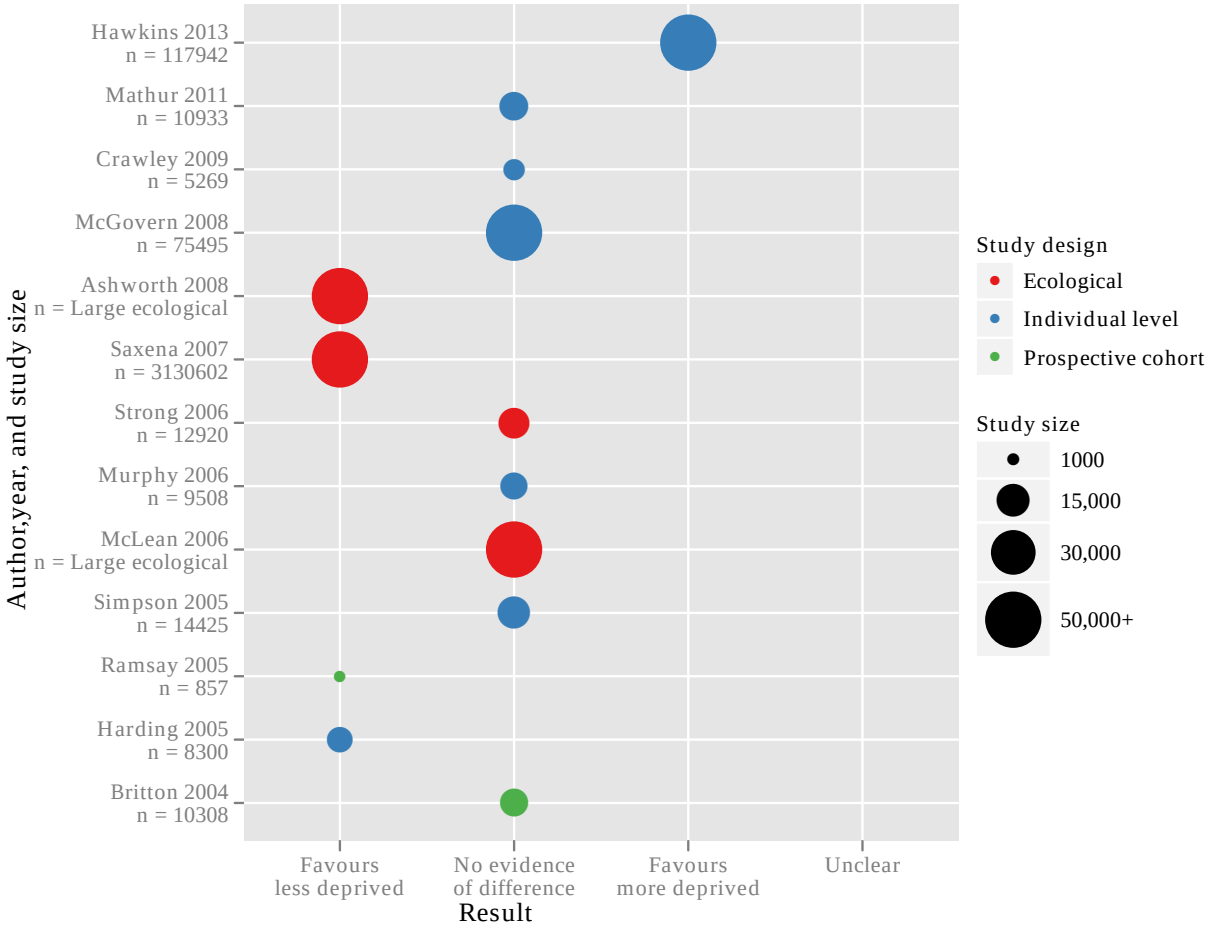


Figure 3.19: Summary of findings from review of secondly prevention using cholesterol-lowering medications

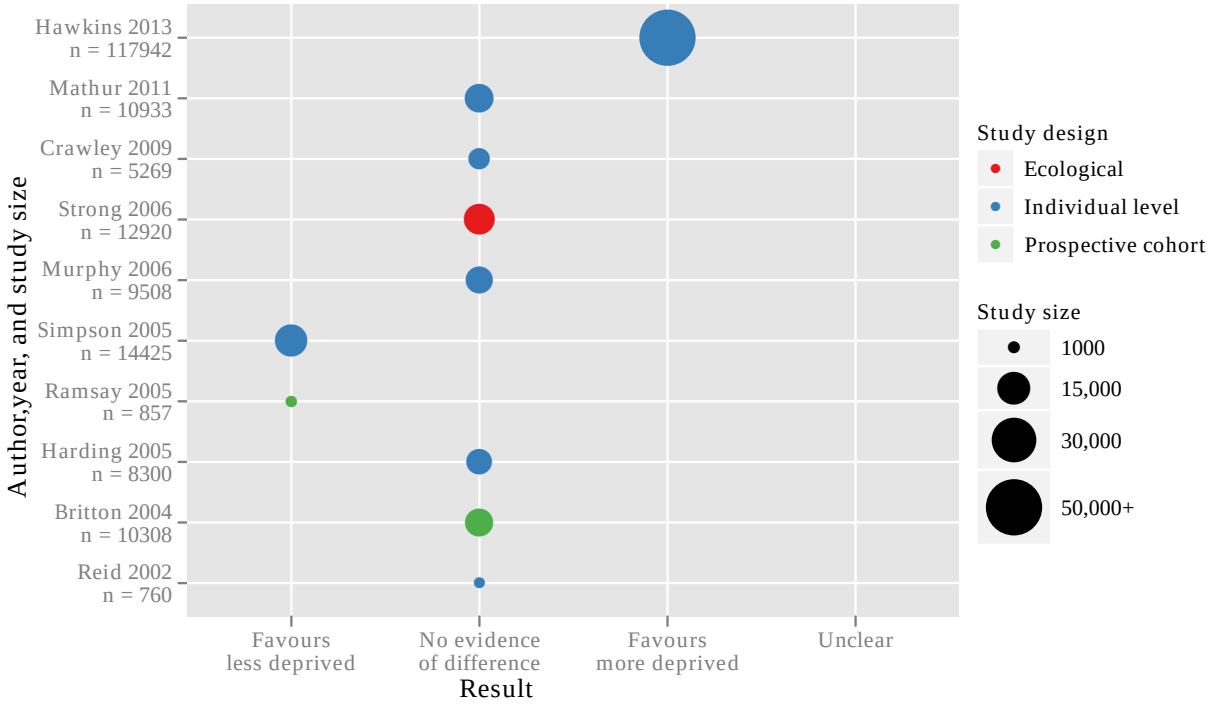


Figure 3.20: Summary of findings from review of secondary prevention using antiplatelet medications

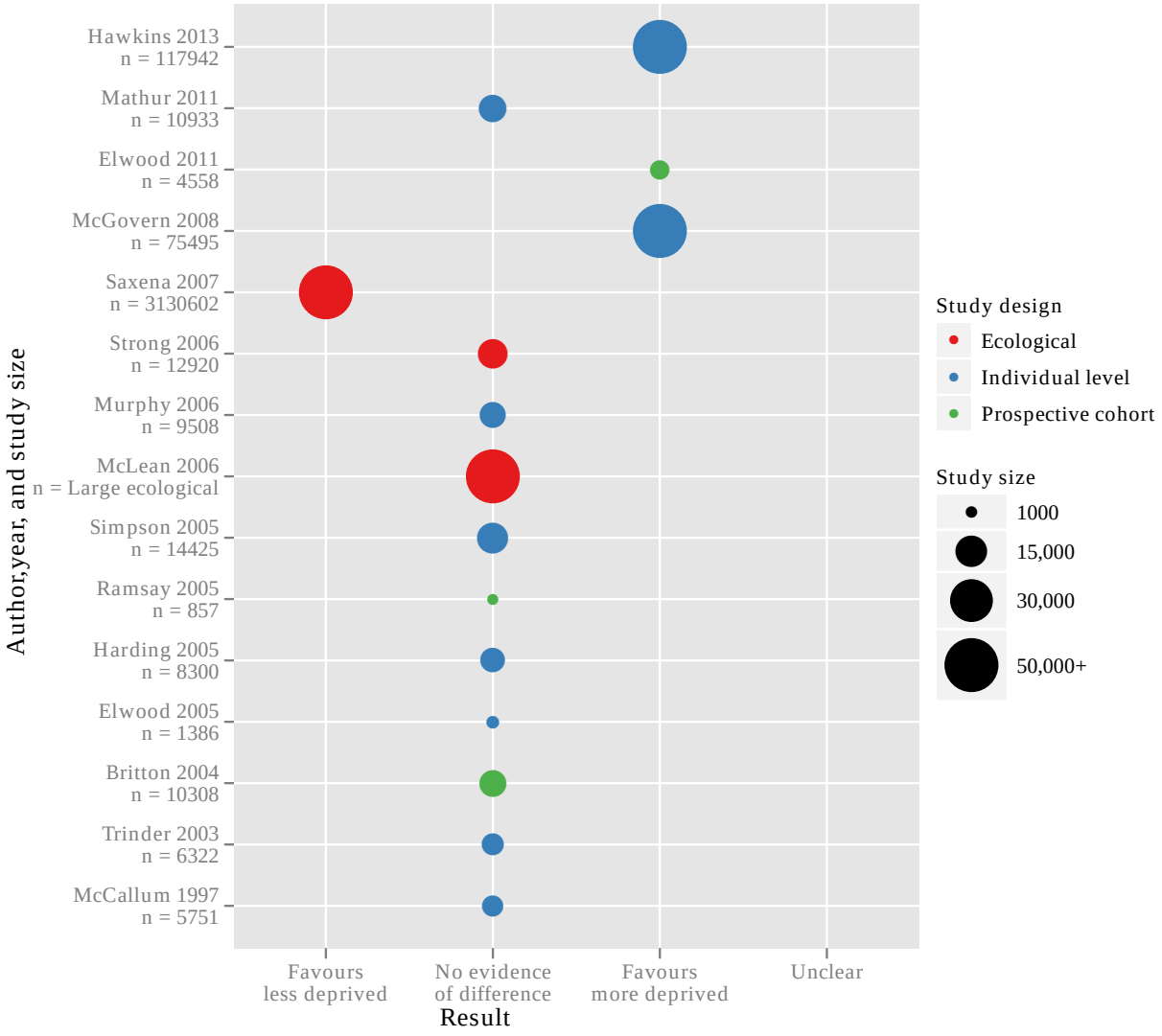
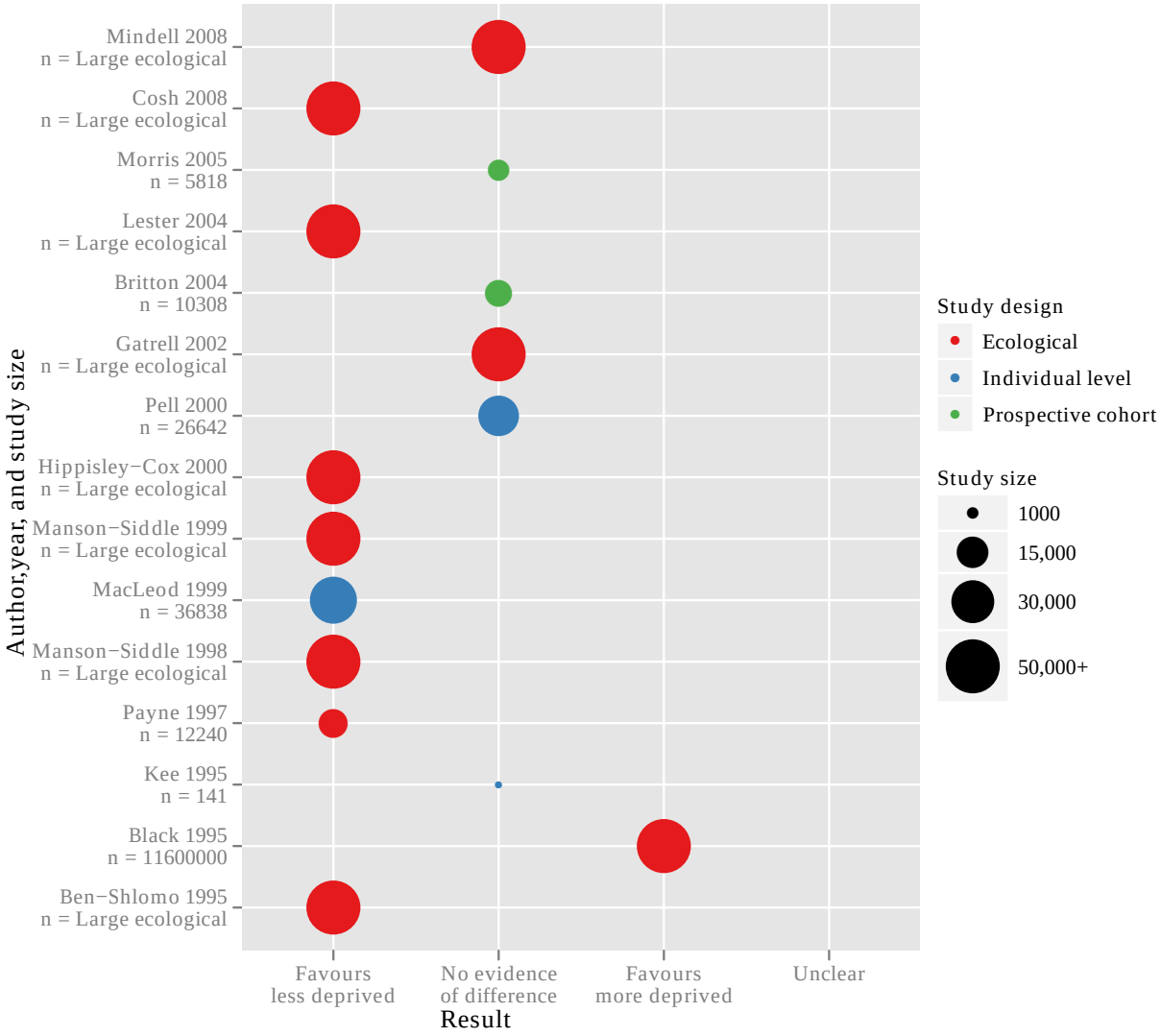


Figure 3.21: Summary of findings from review of provision of revascularisation



3.6 DISCUSSION

3.6.1 *Summary of findings*

The findings from the literature review can be summarised as follows.

1. The findings from the papers examining smoking cessation advice and referral to smoking cessation services are summarised in figure 3.13. Of the studies, only one out of four found evidence of inequity; this represents one out of six of the comparisons made, because two studies made more than one comparison. The effect found was for provision of smoking cessation advice only. The effect was found in a large, but ecological study. The effect was not large

2. Findings for papers for the review of antihypertensives for primary prevention are summarised in figure 3.14. Of the 17 studies, two favour more deprived individuals (individual-level studies), three favour the less deprived (all ecological studies), and 11 studies show no effect. One study has unclear results because there is a suggestion of inequity, but it is unclear whether the effect is statistically significant *Millett 2007*[119]. One of the studies classified as showing no effect (*Pears 2003*)[108], in fact had a mixed picture with more deprived individuals less likely to be prescribed thiazide diuretics and more likely to be prescribed ACE inhibitors – overall it is not clear that such a result suggests inequity (though I have classified it as doing so in figure 3.14). No obvious time effects emerge from the studies, though one study found that evidence of inequity from an earlier time point subsequently disappeared (*Ashworth 2008*[121])

3. The 17 studies looking at primary prevention using lipid-lowering therapies are summarised in figure 3.15. Five studies (all ecological) show some evidence of inequity. Three studies favour more deprived individuals (two of these are individual-level studies). Seven studies, including one prospective cohort, show no effect. For one study, the result is unclear because statistical uncertainty is not taken account of (*Millett 2007*[119]). There is some suggestion of a temporal effect, with all studies suggesting inequity published in or before 2006; in the second of two similar studies (*Packham 2000*[126]), previous evidence of inequity disappeared at a later time point

4. The nine studies examining primary prevention using antiplatelet therapies are summarised in figure 3.16. Of the nine studies included, two studies (both ecological) found evidence of inequity in provision. Three studies (including one prospective cohort and two individual-level studies) found that provision was higher in more deprived groups. Four studies did not find any difference.

5. The 15 studies examining inequity in diabetes management are shown in figure 3.17. Neither study examining provision of hypoglycaemic agents found any evidence of inequity. Of the studies examining differences in outcome, seven out of fourteen studies found evidence of poor achievement in more deprived groups. Of these seven, only one was an ecological study, with one prospective cohort study, and the other five being individual-level studies. One of the studies (*Crawley 2009*[112]) found a significant difference in achievement of targets at only one time point.

6. The 13 studies examining inequity in secondary prevention using antihypertensives are shown in figure 3.18. Of these, the majority of papers found no evidence of inequity. Four papers did find evidence of inequity: *Ramsay 2005*[144] (though here there is a concern about the number of comparisons made, and evidence of inequity was limited to prescription of beta-blockers); *Harding 2005*[143] in the achievement of targets; *Ashworth 2008*[121] in the achievement of targets (though the effect later disappeared); and *Saxena 2007*[104] for both prescription of antihypertensives and achievement of targets.

7. The ten papers examining inequity in the provision of lipid-lowering medications for secondary prevention are shown in figure 3.19. Eight out of the ten studies show no evidence of inequity; the two studies that found evidence of reduced provision of statins to those in more deprived groups found that the effect disappeared over the time course of the study

8. The 15 papers examining inequity in the provision of antiplatelet therapies for the purposes of secondary prevention are shown in figure 3.20. Only one, poor-quality, ecological study found evidence of inequity. Two studies found evidence that more deprived individuals were more likely to be receiving antiplatelet therapies

9. The 15 studies examining inequity in the provision of revascularisation procedures are shown in figure 3.21. Eight found evidence of inequity (only one of which was an individual-level study). Of the seven studies finding no difference or favouring the more deprived individual, two were individual-level studies and two were prospective cohort studies. If the non-peer-reviewed studies are discounted (*Lester 2004*[154], *Cosh 2008*[155]), there is no study showing evidence of inequity after the year 2000

A standout finding from the overall set of results from this literature review is that most studies find no evidence of differential provision of health care for CHD across deprivation groups or between individuals with different levels of deprivation. This overall picture is summarised in table 3.2. From the total column, 28.4% of studies find evidence of inequity. Moreover, in compiling these figures, I have credited a study as having provided evidence of inequity if any component of the study (including comparisons at different time points or for different types of intervention within an intervention type, such as antihypertensives or antiplatelet drugs) provides such evidence. Thus, if all comparisons made were treated separately, this figure would be lower.

Taken at face value, such results imply that inequity in provision does not appear to operate systematically (if at all); the effect is, at most, limited to particular interventions at particular times and in particular places. Prior to making such conclusions, consideration is owed to the methodological limitations of studies, including to the issue of which study type was employed.

In relation to study type, a further clear pattern emerges from the review: ecological studies tend to find relationships suggestive of an inequity of provision more frequently than individual-level or prospective cohort studies. I illustrate this further in table 3.2. A higher proportion of ecological studies find that provision of healthcare (or proxy measures of provision of healthcare) favour less deprived groups: 53.7%, compared to 13.1% for individual-level studies, and 21.4% for prospective cohort studies. Two lines of argument might be invoked to explain this. The first is based on three considerations that relate to ecological studies: they are, in general, poorer quality, due to inherent methodological weakness; they are typically easier to carry out than studies using individual-level data; they are potentially (as with other studies) subject to publication bias (the phenomenon whereby positive results are more likely to result in publication). Therefore one might

Table 3.2: Findings for different study types in the literature review. The percentages indicated show the percentage of studies in the relevant column with each result type

	Eco (%)	Ind (%)	Pro (%)	TOTAL
Favours less deprived	22 (53.7%)	8 (13.1%)	3 (21.4%)	33 (28.4%)
No evidence of difference	15 (36.6%)	42 (68.9%)	9 (64.3%)	66 (56.9%)
Favours more deprived	2 (4.9%)	10 (16.4%)	2 (14.3%)	14 (12.1%)
Unclear	2 (4.9%)	1 (1.6%)	0 (2.7%)	3 (2.6%)
TOTAL	41	61	14	116

Eco = ecological study; Ind = individual-level study; Pro = prospective cohort study

conceive a scenario in which poorer-quality, ecological studies, which can be readily carried out, arrive at invalid conclusions (due to methodological weakness), and, due to the existence of publication bias, disproportionately achieve publication of this result; equally, there may be a large number of unpublished ecological studies that showed no evidence of inequity. The differing rates of inequity identified in individual-level studies might relate to the fact that such studies are less likely to draw invalid conclusions, so that publication bias has no (or few) positive studies on which to operate.

The second plausible possibility is that, due to their differing approaches, ecological and individual-level studies are systematically gathering different information. Ecological studies typically use a proxy measure of need, such as the death rate or admission rate for CHD. In using such an approach, ecological studies may identify need that is hidden from individual-level studies, because they are inferring levels of need in populations; this will include need in individuals who may not themselves have presented to health services nor have been included in cohort studies. In the event that more deprived individuals are less likely to present to health services at earlier stages in the pathway of care for CHD, ecological studies might uncover an apparent 'inequity' that is hidden from individual-level studies, because ecological studies take account of inferences about the level of need that might exist, regardless of whether that need results in presentation to healthcare services.

A further theme that emerges is the possible effect that time may be having on inequity in provision of CHD services. In a number of studies an effect was observed at an earlier time point, but later in the

study period the previously observed effect was not there. It is notable that the inequity is generally observable at an earlier time period and disappears later, rather than vice versa. Over the period considered in the review, organisational and clinical changes are known to have occurred, for example in the development and implementation of NSFs and the QOF; such changes may have had an influence on inequity in provision, as might a generally increased awareness of its possible existence, or other factors. However, he overall pattern of findings when comparing different studies does not appear to suggest that earlier studies are more likely to find evidence of inequity then later studies.

For ease of visualisation and discussion, I have simply classified studies as 'Favours less deprived' (that is to say provides evidence of inequity), 'No evidence of difference', 'Favours more deprived', and 'Unclear'. Synthesising the findings from different studies using their individual effect sizes was impractical because of the heterogeneous nature of the measurements used. The approach taken has the advantage of simplicity, but fails to convey the magnitude of any effects uncovered. In this approach, I have only classified as 'Favours less deprived' results which were statistically significant, but statistical significance depends on study size and gives no information about whether result is clinically important.

I now consider the magnitude of the effects uncovered in the selected studies. It is notable that five of the comparisons which provided results suggestive of inequity arose from one study (*Saxena 2007*[104]), and in each case the effect size was small (comparisons were for smoking cessation, primary prevention using antihypertensive therapies, primary prevention using antiplatelet therapies, secondary prevention using antihypertensive therapies, and secondary prevention using antiplatelet therapies). This study used a fairly simple, ecological method. The authors examined practice-level achievement of QOF-indicators in relation to practice characteristics, including practice-level deprivation (IMD separated into three bands). While the patterns across deprivation suggest inequity in the areas mentioned, the actual percentage difference in achievement is small. Taking the example of smoking cessation, results (which are divided up by practice size) show that in practices sized 0 to 2999, the percentage of individuals CHD offered smoking cessation advice rose from 90.3%, through 91.4%, to 93.3% from the most to the least deprived third of practices. Similar magnitudes of effect was seen for other practice sizes.

Likewise, for achievement of BP targets in those with hypertension, for the smallest practices the percentage of patients achieving the target rose from 70.3%, through 72.4%, to 74.0%. For practices sized 5000 to 7999, equivalent figures were 69.8%, 71.9%, and 71.7%; for the practices sized 10,000 and over, equivalent figures were 70.2%, 71.7%, and 72.0%. Figures for prescription of antiplatelet therapies in those with a history of CHD, are, for the smallest practices, 87.5%, 88.5%, and 88.9%; for middle sized practices 89.3%, 90.3%, 91.1%; for the largest practices 90.1%, 90.7%, 91.2%. Though not reproduced here, the figures for the other comparisons mentioned above (primary and secondary prevention using antihypertensive therapies) show a similar pattern. What is notable for these comparisons is that, though the trend shows an increase in the percentage of patients that achieve the QOF target as the deprivation level of the practice decreases, these differences are between one and three percent for almost all of the comparisons made. All of these differences achieved statistical significance using the Kruskal-Wallis test, but, in view of the fact that the interventions will only be effective in a proportion of cases, even if they are given, these small percentage differences seem insufficient to be meaningfully contributing to any difference in outcome. It is notable that data were collected during the first year after the introduction of QOF, (2004-2005) a period when most general practices made rapid and significant changes in the way they collected and reported data required by QOF, and faced new administrative challenges. It may be that practices with certain characteristics coped better with these challenges. For example, the authors suggest that the better performance of larger practices may reflect the wider range of staff roles they could deploy. It is conceivable that the administrative aspects of QOF performance in practices in deprived areas were affected by the additional pressures (such as consulation rates) that such practices may experience.

Determining the clinical importance of the results of many of the studies can be very difficult on the basis of the results provided. Furthermore, this makes it impossible to pool the analyses from different studies. For example, some studies[109,110,117,124–126] provide results in terms of correlation coefficients between prescribing rates and deprivation rates at practice level or area level. It can be hard to infer from such information the extent to which the correlation coefficients presented would impact on patients and on the difference in outcomes seen between deprivation groups.

It is quite clear from all the studies that, from the outset, a key data limitation goes some way to undermining all the published studies; this was alluded to in sections 2.1.1 on page 17 and 2.1.3 page 26: data are not available on whether or not individuals have been offered an intervention but turned it down.

The inadequate information about demand for interventions means that it is very difficult for studies to definitively identify inequity – for reasons detailed in the earlier discussion of health needs assessment.

A further related issue, is that data generally give little or no information on adherence. Adherence to treatment, and consequently the effectiveness of interventions in practice, is known to differ according to deprivation (for example in the effectiveness of smoking cessation and in the quality of blood sugar control in diabetics). When examining differential outcomes between deprivation groups, studies are generally unable to determine the extent to which achievement of outcomes relates to provision or to adherence or other patient-related factors.

A number of issues relating to the ways in which statistical techniques were employed in the papers arose in the course of the review. First, in some of the studies a large number of comparisons were carried out, only some of them turning out to be statistically significant in suggesting inequity. If enough comparisons are made random effects make it likely that some positive results will emerge. Second, the level of uncertainty in the result was not always adequately quantified, particularly in relation to *Millett, Car et al*[119]. Further in the paper by *Saxena 2007*[104], it is not clear that the Kruskal-Wallis test used to determine statistical significance in terms of the difference between the groups is adequate.

In a number of studies, even in relation to a particular area such as provision of antihypertensives, more than one comparison may have been made, and these results may conflict. Particularly in relation to the prescription of antihypertensive medications this raises a question: if a deprived individual or group has inadequate provision of one particular drug class, but provision for others showed no evidence of inequity, is this provision unfair overall? There is a recognised ladder of treatment for the management of hypertension (see appendix B), and simply measuring the provision of each of the drugs that can be used in the treatment of hypertension is a blunt mechanism for assessing the overall equity of provision of such a ladder of treatment. Clearly, for practical reasons studies have simplified their approach,

and gaining a really detailed picture of the extent to which treatment meets quite complex treatment recommendations is frequently impractical.

3.6.2 *Strengths and limitations of the review*

While, in carrying out this review, I have endeavoured to be comprehensive, I was inevitably obliged to leave out some potentially relevant material. I now justify the decisions made in this respect. The scope was limited to a subset of available interventions for CHD, based on a number of considerations: the availability of routine data relating to that intervention; the exclusion of activities that are not necessarily, in themselves, risk modifying; the exclusion of studies addressing inequities in provision of interventions that are no longer used in routine practice. Furthermore, the final selection in the review was limited on the basis of other criteria, including the nature of the inequity under consideration (whether it be by area-based socio-economic deprivation, individual-level socio-economic deprivation, race, income, employment, education, or gender), the population in which the study was carried out, and the time period which the study covered.

To rationalise the selection of literature summarized in this chapter, papers have been reviewed only if they address inequity in interventions that are addressed in the subsequent parts of this thesis. Inequity in other interventions for which adequate information is not available in routine data, though it does have the potential to influence the gradient in CHD outcomes observed, is less directly relevant to this thesis.

A number of activities directed at an individual might be inequitably provided, but not result in modification of an individual's risk; such activities include referral to specialists or investigation of CHD. For example, it may be that individuals from different area-level socio-economic deprivation groups are referred to cardiology specialists at different thresholds. In such a situation, less deprived individuals might be seeing cardiologists at an earlier stage in their disease. It would be possible for papers in the published literature to study whether such phenomena were occurring, but such papers have not been reviewed in this chapter because the process of being referred to a specialist is not considered to directly affect the risk of progression of CHD.

Behaviour change interventions available to primary care practitioners include in-house delivery of advice relating to smoking cessation, weight loss, diet, and exercise, and referral to specialist services to provide relevant programmes.

Weight loss, dietary, and exercise interventions are not reliably recorded in routine data. It is hard to tell, on the basis of the Read code employed, whether the intervention was truly agentic or part of a bigger programme. Therefore, in relation to behaviour modification, I have limited ourselves to considering only differences in smoking cessation provision.

Smoking cessation advice is a fairly discrete intervention, with a dedicated service, that operates at an agentic level. Records in routine general practice data (on the basis of preliminary examination of the GP data in Wales) are much more substantial than for other behaviour change interventions. It is possible to look at differences in outcome, because smoking status is a fairly well recorded variable in GP records.

This thesis specifically looks at area-level socio-economic deprivation. In view of this , only papers which include area-level socio-economic deprivation or some other measure of social class (either at individual or area level) as one of the individual characteristics for assessing equity were selected for detailed review.

The focus of this thesis is the Welsh population and the geographical area of Wales; papers have, therefore, only been included if they describe studies carried out in Wales or in other constituent countries of the UK. I made this decision because, while patterns in other areas are certainly of interest, it is likely that the extent of any inequity that exists relates to the organisation of health services.

Likewise, papers of potential relevance have been published over several decades, with the earliest papers on this theme published in the 1980s. Papers included in this review describe only studies performed in or after 1995. I judged that evidence about the existence of inequity or otherwise from early periods is not necessarily generalisable to the current time.

Papers from the grey literature relating to Wales stimulated my original interest in the subjects addressed in this thesis, and for this reason I wished to include them, though I have taken account of their unpublished nature.

I wanted , as far as possible, to summarise the findings from the review in such a way as to allow the reader to grasp fairly quickly the main findings. Because of the differing nature of the studies included,

I elected to summarise findings purely on the basis of whether the results did or did not suggest inequity. Using this approach meant that I left out information about effect size and that, where studies had mixed results, I classified such studies as demonstrating inequity. Despite the limitations of the approach I have taken, I believe that the means used to present the findings will aid the reader in interpreting the literature.

Carrying out a literature review of this nature is a major undertaking. I wished to complete the review at a relatively early stage in the time-period allotted for this thesis. Having done so, I have not attempted to systematically update the findings, but have tried to take account of any new information that I have identified subsequently through non-systematic means, for example the paper by Hawkins et al[103].

3.6.2.1 *NSFs and QOF*

NSFs are policies set by the NHS in the UK to define standards of care for a number of major medical conditions including CHD, stroke, cancers, chronic obstructive pulmonary disease, diabetes, kidney disease, and mental illness. They set clear quality requirements for care based on the best available evidence, and offer strategies and support to help organisations achieve these. The NSF for CHD was introduced in England in 2000, and in Wales in 2001.[163–168] The The Wales National Framework for Coronary Heart Disease (NSF-2001) set out the standard of cardiac care that should be provided for the Welsh population.[163] Subsequently this document was updated with a revision that also includes non-CHD cardiac disease: The Cardiac Disease National Service Framework for Wales (NSF-2009)).[163] There is ample evidence that, in relation to CHD, there was marked in improvement in both quality of care and in mortality, during the period following the introduction of the NSFs. It is, of course, impossible to quantify how much of this improvement is directly attributable to the NSFs.

The Coronary Heart Disease National Service Framework: Building on excellence, maintaining progress – Progress report for 2008[169] details the progress made in implementing the Coronary Heart Disease National Service Framework in England in the eight years since its publication. It describes rapid and significant changes during the period 2000-2008, marked improvements having been seen in resources. Waiting times for CABG were shorter, and cardiology units were better resourced and staffed. Smoking rates were lower. CHD mortality had continued to decline. Hippisley-Cox et al[170] reported that there were

substantial improvements in both the recording of coronary risk factors and disease control measures following the implementation of the National Service Framework for Coronary Heart Disease. Ramsay[144] reported that between 1998-2001 and 2003, statin uptake and the use of combined drug treatment in elderly men and women increased markedly. Campbell[171] measured changes in the quality of care for three major chronic diseases (CHD, asthma, and type 2 diabetes) between 1998 and 2003. He found substantial improvements relating to all three, but most marked for CHD. An implication of such evidence is that standards of CHD care were already significantly improving before the introduction of QOF in 2004.

The QOF, an unprecedented public health intervention operating within primary care, is a system for the performance management and payment of GPs in the NHS in the UK. QOF was introduced in April 2004 as part of a revised contract for GPs. It offered financial incentives relating to a range of performance indicators including those for CHD. (A typical clinical indicator would be the proportion of patients with coronary heart disease who had cholesterol measured in that year.)

In this chapter I have already discussed, in relation to healthcare inequity, a number of studies whose evidence is based on QOF data.[104,106,112,117,121,128] A large volume of literature exists in relation to other aspects of the impact of QOF and provides evidence of relevance to this thesis in the following respects.

There was marked improvement in clinical activity indicators (including those for CHD) in the early years of QOF. This means that my study period coincided with a period of rapid change in activity in primary care in relation to CHD. QOF achievements tended to plateau after the initial improvement.[172–176] During this period of improvement there was some evidence of narrowing of the deprivation-gap.[121,174,177] There was little evidence of 'gaming' through exception reporting: this is relevant to the reliability of QOF data used in studies discussed earlier in this chapter.[178] QOF was associated with a decrease in hospital admissions for incentivized conditions including CHD.[179] There was evidence of limited effects of the characteristics of a general practice on its QOF achievements.[180]

3.6.3 *Implications for thesis*

A number of important influences on my approach to this work arose from the findings of the literature review.

First, it is clear that difficulty arises when studies attempt to disentangle true inequity in healthcare provision from patient-related factors. This is particularly the case when looking at differential achievement of intermediate outcomes (for example blood pressure or blood sugar control) between groups, but also applies to other ongoing interventions (for example any long-term drug therapies), where differential adherence to treatment across groups may lead to differential outcomes. Empirical evidence of this effect appears to emerge from the review: a higher proportion of the studies looking at diabetes management appear to suggest inequity (7/14) – with only one of these studies being ecological. With the exception of revascularisation (where all but one of the studies suggesting inequity are ecological), other areas reviewed do not have such a high proportion of study suggesting inequity. It is conceivable that this pattern relates to the fact that there is a very strong patient component in the management of diabetes.

On this basis, it is clearly important that in subsequent parts of this thesis, I use caution in ascribing any differences observed to healthcare inequity, when they might actually be due to healthcare inequity or patient-related factors, or a mixture of both. Information is not available in routine data sources to allow accurate determination of whether a difference in the level of treatment that an individual receives might relate to differences in demand, or to differences in adherence. It is inevitable therefore that this thesis will suffer some of the limitations that studies identified in the review evinced – exact discrimination of the detail of the nature of the differential staircase of care (discussed in chapters 2 and 5) would not be possible except using a bespoke dataset that would be extremely difficult and expensive to acquire.

In many ways, the overall findings of the literature review are surprising: evidence for the healthcare inequity in relation to the NHS and CHD is, except perhaps in relation to revascularisation, very limited. Even if the possibility of publication bias is discounted, the majority of published studies do not find evidence of inequity. Furthermore, in those studies that do, the effect sizes tend to be fairly small. Additionally, in papers finding evidence of inequity, the extent to which the effect relates truly to healthcare inequity, rather than to some combination of healthcare inequity and patient-related factors are, for the most part, difficult to ascertain.

A further theme that emerges from the literature is the possibility that a temporal effect may be operating in relation to health care inequity, CHD, and socio-economic position. There is some suggestion from the literature that earlier papers may have been more likely to identify inequity; certainly, a number of papers identified inequity at an earlier time point, with the observed inequity subsequently disappearing.

Clearly, if the healthcare inequity is not occurring systematically in relation to CHD and socio-economic position, this represents an important finding. The existence of healthcare inequity by deprivation has implications for health inequalities, in the sense that any agentic intervention might have the potential to worsen health inequalities where inequity occurs. In contrast, if this is not the case, as the findings from the literature reviewed in this chapter seem to imply, this not only obviates the need for concern that such a phenomenon might be contributing to health inequalities, but also raises the possibility that systematic implementation of agentic interventions might in itself contribute to a reduction in the inequality in outcomes from CHD seen across deprivation groups.

It is clear that the existing literature on healthcare inequity related to CHD and socio-economic position is limited in terms of methodology and scope. Moreover, absence of a clear pattern of inequity in care for CHD contrasts with what is known about uptake of screening services by more deprived groups. There is a clear need for a whole-pathway, population-based approach to systematically address the existence or otherwise of healthcare inequity related to CHD. In the next chapter, I discuss the methods employed in this thesis to allow the accomplishing of this task.

Part III

METHODS

4

DATA PERMISSION, SPECIFICATION, EXTRACTION AND PROCESSING

4.1 INTRODUCTION

At the start of this thesis, I developed a research rationale and research questions that I wished to address. I identified the SAIL databank as the best source of the data in which to find answers to the research questions. Having decided to use this data source to underpin the thesis, a number of challenges immediately presented themselves, which can be summarised as follows:

1. Obtaining permissions for data access
2. Producing a detailed specification of the dataset required for the thesis
3. Arranging for the extraction process to be performed within HIRU
4. Processing the extracted data to make it usable for this project

In this chapter I discuss the means by which I addressed these challenges: I outline the methods used to move from the aim of using SAIL data through to the production of a cleaned dataset suitable for subsequent work.

As well as outlining the nature of the steps taken, I seek, where necessary, to provide justification for the methods used to achieve the aims. The problems presented were considerable, and it is certainly the case that they could have been solved in many different ways. While at every stage I have attempted to solve problems in the best way that I could devise (subject to limitations of programming capability and experience, and to the constraints of working on a remotely-hosted system), the approaches taken are not necessarily optimal, and with hindsight I appreciate that many things might have been done differently. With a view to aiding future research of this type, I also attempt in the following pages to reflect on the difficulties encountered, the means employed to circumvent them, and how one might avoid them were it necessary to perform these processes again.

In discussing how permissions were obtained to use data and the way the data required were specified (point 1 and 2 in the above list), I describe the processes separately. In reality, quite a substantial amount of crossover existed between the two processes: to obtain permission to use data requires a specification of what is to be used; specifying the structure of the dataset has, to a certain extent, to take account of what is likely to be permissible from an information governance perspective.

In this chapter, I detail the methods have used to obtain, extract, clean and appropriately format the data for subsequent use. Further detail of the methods that I needed to use to address the research questions is discussed in chapters 5 (where I have looked at the methods used to examine the data from a pathway perspective) and 6 (where I have set out the analytical and statistical methods used).

4.2 PERMISSIONS FOR DATA ACCESS

In the background chapter to this thesis I discussed the Information Governance processes operated by HIRU in relation to SAIL – discussed on pages 39 to 40. In interacting with HIRU, I have followed scrupulously the appropriate Information Governance procedures relating to requesting and using data from SAIL – as outlined in the background material.

In practical terms, to meet the Information Governance requirements relating to the SAIL databank, I undertook the following.

1. Preliminary discussions with HIRU to consider the feasibility of the project
2. Formal application to HIRU to obtain permission to use SAIL data
3. Permission from the Cardiovascular Research Group – Cymru (CVRG-C) to use analyst time at SAIL to carry out the data extraction from the main databank

On the basis of preliminary discussions with HIRU staff over several weeks, I refined the data specification that was included in the subsequent formal request to SAIL. These preliminary approaches included discussions with the co-director of HIRU and with data analysts from the HIRU Management Team. In discussing the issues around the data extract, I examined the detailed structure of the data

tables relating to general practice data, PEDW data, and mortality data and discussed the issues relating to extraction from these tables.

I modified the formal application to HIRU before submitting it for Information-Governance approval in the light of feedback from preliminary discussions.

Because I intended that a data analyst employed by the CVRG-C would perform the extraction of the specified data tables from the main SAIL databank, I also submitted a further application to the CVRG-C for permission to engage the analyst's time.

4.3 DATA SPECIFICATION

In specifying in detail the nature and structure of the data required for this thesis, I aimed to aid the IGRP in their considerations related to the CRS to facilitate the data-extraction process.

Specifically in relation to the data extraction from the SAIL databank, I aimed to facilitate the writing of SQL queries (which was the computer language by which data were retrieved from SAIL). This meant that I needed to specify the structure of tables, linking fields, and additional fields required in each table. For each table, I set out explicit criteria to allow selection of records for inclusion in that table; because the extract that I wished to use contained several tables, I specified the means by which these tables should be linked together.

In summary, I needed to make three things as clear as possible in this specification:

1. The relationships between the tables
2. The criteria by which I wished data rows within these tables to be selected and included in the extracted dataset
3. The fields (variables) within each of the three main tables that I needed

In the remainder of this section, I discuss these aspects of the data specification in turn.

4.3.1 *Table relationships*

I specified five tables.

1. Main demographic table

2. Mortality table
3. PEDW table
4. Primary care table
5. Geography and deprivation look-up table

The specification required that tables 1–4 be linked together on Project-specific Anonymised Linking-field (PSALF) – a unique individual identifier within the project. The effect of using this linking field was to allow the establishment of relationships between the tables, so that for each individual listed in the main demographic table, it was possible to identify the associated mortality, PEDW, and primary care records in tables 2–4 (on the basis of PSALF). The relationship between the demographic table and tables 2–4 was a one-to-many relationship, in the sense that one row in the demographic table could be linked to many rows in the other tables.

I also linked the the geography look-up table, table 5, to the main demographic table by an encrypted LSOA code – this being an identification number specifying one of the 1896 LSOAs in Wales. Using a similar linking process, where I knew the LSOA area-of-residence for an individual, I could determine the associated area-based decile for WIMD 2005 (and thus quintile) and also the Local Authority (LA).

4.3.2 *Selection criteria*

For each of the required tables, I needed to specify selection criteria that clarified which records from the main SAIL databank tables should be included in the tables for the extract.

For table 1, the main demographic table, I requested inclusion of records for individuals that met the following criteria.

- The individual had a date of birth in or before 1975
- The individual had any primary care data in practices that submit data to the SAIL databank

For table 2, the mortality table, I requested that records from the SAIL main mortality table should be included in the data extract if the PSALF for that record was present in table 1 (the demographic table for this project). I asked that if the cause of death code was one of the codes shown in appendix E table E.1 (ICD-10 codes only) the ICD-10 code retrieved be included unchanged in the extract; if the

ICD-10 code was not in the list then then I specified that it be recoded to 'Non-cardiovascular death'.

For table 3, the PEDW table, I asked for records that met the following criteria.

- The PSALF for that record was present in table 1
- The spell in which that record occurred contained a diagnosis or procedure code from appendix E table E.1 (ICD-10 and Office of Population Censuses and Surveys Classification of Interventions and Procedures (OPCS) codes only) in any episode in that spell in any coding position

For table 4, the primary care table, I asked that records be included if they met the following criteria.

- The PSALF for that record was present in table 1
- The event code for that record contained one of the Read codes in appendix E table E.1 (Read codes only)

A very large number of Read codes (over 4000) defined inclusion of records in the primary care table (those shown in table E.1 in appendix E. These codes included those relating to primary care diagnosis, investigation, and treatment of CHD and of its risk factors. I took the codes themselves from a much larger dataset of Read codes (version 2) for clinical activity and drug prescription. I downloaded the full set of codes from the Technology Reference Data Update Distribution (TRUD) website[181]. I imported the main dataset into an SQLite database, so that I could extract codes relevant to this thesis. The aim in selecting Read codes for the data extraction was to maximise sensitivity, by including as many codes as possible relating to each particular clinical area, leaving open the possibility for refinement of the coding definitions of different clinical states at a subsequent time.

Ethnicity data would have been useful in this thesis, partly because I would have liked to use it for adjustment when examining effects related to deprivation; partly, because variation by ethnicity in utilisation of healthcare is of inherent interest. Though Read codes exist for ethnicity, these are not widely used. Ethnicity availability in GP systems was insufficient to underpin analysis in this area. I argue that the impact of the absence of ethnicity data is likely to be very small; from the most recent census data, 7% of the Welsh population is from minority ethnic groups. Further, CHD is predominantly a disease of

older age groups; older age groups have lower proportions of minority ethnic groups.

I extracted the codes in SQLite using SQL queries that used 'LIKE' clauses to identify codes in which the code description matched the required clinical area. The 'LIKE' search terms used are shown in table 4.1 (the '%' sign is a wildcard character signifying an arbitrary string of characters of arbitrary length). In a small number of cases I used two, three, and four digit Read code stems to identify lists of codes in a particular branch of the Read code version 2 system. I identified such code stems using the NHS Read Browser software package, available from TRUD, which allows the Read codes system to be visualised and navigated.

To identify drug treatment Read codes, I worked back from the codes for specific drug treatments where the code was known, to allow searching by broader categories relating to that code. This is possible using Read codes version 2, because the five-digit code describes a branching hierarchy. By working back to earlier digits in the five-digit sequence, I was able to identify the broader category from which the code derived. For example, the Read code for ramipril 1.25 mg capsules is 'bi61.'. From this, using the NHS Read Browser, it is possible to work up the hierarchy and to identify the code 'bi...', which is the code for ACE inhibitors. The search string 'bi%' can then be used in a 'LIKE' statement to identify all the Read codes for ACE inhibitors. Using this approach, I identified Read codes for the following drug groups.

- Antihypertensive medications including ACE inhibitors
- Antiplatelet medication
- Oral hypoglycaemic medication
- Insulins
- Statins and other cholesterol-lowering agents

The SQL queries that I ran using these 'LIKE' statements yielded a large number of codes (7894), many of which were not relevant. I then examined the code descriptions relating to these codes individually to determine whether or not they should be included. Following this process, I retained 4155 codes.

At the time of the data specification, I was unsure whether there might also be some GP activity coded using version 3 Read codes

Table 4.1: LIKE statements used in searching for Read codes

DESCRIPTION	LIKE STATEMENTS USED IN SQL
CHD	%isch%, %coro%, %cor a%, %cor th%, %ang%, %myo i%, %myoc%
Stroke	%CVA%, %strok%, %sient isch%, %H/O: TIA%, %pected TIA%
Heart and renal failure	%fail%, %CKD%, %CRF%, G58%, K04%, Kyu20
Glomerular filtration rate	%glom%, %GFR%, 451A%, 451F%, 451G%, 451J%
Diabetes and HbA1c	%diab%, %fast%, %impair%, %gluc%, %sugar%,%HbA%, %Hb. A%
Rheumatoid arthritis	%rheu%
Family history	%FH%, %fam%
Cholesterol and lipids	%chol%, %LDL%, %HDL%, %triglyceride%
BMI and weight management	%wt%, %weight%, %bmi%, %body mass%, 162%
Exercise and exercise management	%exer%, %acti%, %phys%
Hypertension	%hyp%, %press%
Smoking	%smok%
Diet	%diet%

or the Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) coding system. Because of the possible existence of these alternative coding systems within the SAIL GP data, I 'translated' the list of version 2 Read codes into these alternate systems. I performed the conversion from version 2 Read codes to version 3 Read codes using the file 'rctctv3map_uk_20110401000001.txt' downloaded from the TRUD website. This file contains a field 'V2_ConceptID' (which contains version 2 Read code concepts) and a field 'CTV3_ConceptID' (which contains version 3 Read code concepts); I carried out the conversion in R version 2.12 using the 'match' function to match the version 2 Read codes from the original list to version 3 Read codes. I then compared the resulting codes in version 3 with the original codes, and I retained and added to the code list those codes that were different. I matched Version 2 Read codes to SNOMED CT codes using the NHS Data Migration file RcMap_uk_20110401000001.txt, matching on the fields 'ReadCode' (version 2 Read code concept) and 'ConceptId'(SNOMED CT concept). Following this process, the list of codes included 7379 codes. I added a classification field to this list that I asked the HIRU analyst to add to the general practice data when performing the extract. I passed this list to the HIRU analyst performing the data extraction.

For table 5, I specified that all 1896 rows, one for each LSOA in Wales, should be included in the extract table.

4.3.3 *Data fields*

For each of the tables 1–5 above, I requested a number of fields in the data specification. For the main demographic table, table 1, I specified the fields PSALF, week and year of birth, sex, encrypted LSOAs on 1 January at yearly intervals (2003 to 2010), and encrypted practice codes on 1 January at yearly intervals (2003 to 2010). An individual's LSOA of residence or practice code can change at any time, and over a given period can change several times. In order to capture as many such movements as possible, while at the same time still making the analysis of the small-area deprivation status of individuals tractable, I used the approach of requesting the LSOA for individuals on 1 January annually.

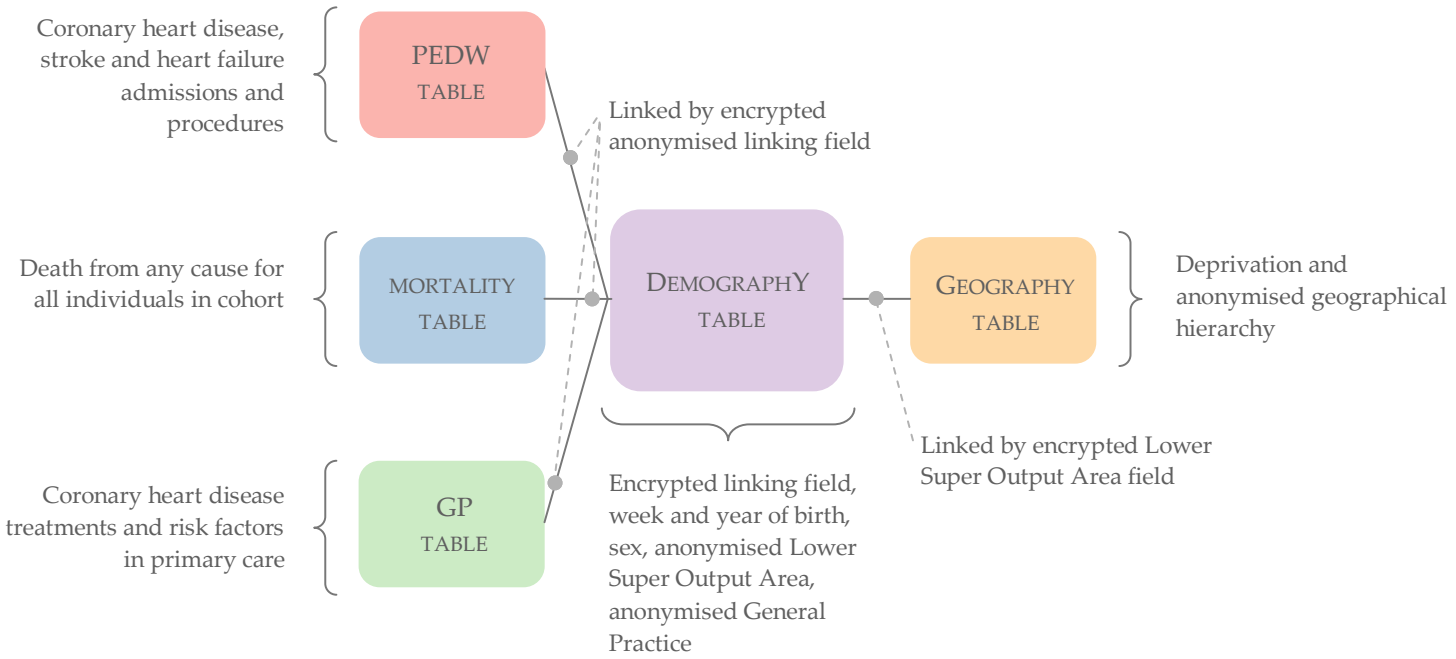
For the mortality table, table 2, I specified the fields PSALF, date of death, place of death, primary cause of death (ICD-10 code), and underlying cause of death (ICD-10 code).

For the PEDW table, table 3, I specified the fields PSALF; spell number; episode number; spell start date; spell end date; episode start date; episode end date; diagnostic codes (ICD-10) and descriptions, all 14 positions; procedure codes (OPCS-4) and descriptions, all 6 positions; admission method; source of admission; referring organisation code; duration of elective wait; provider unit code; and discharge destination.

For the primary care table, table 4, I specified the fields PSALF, event code (Read code), Read-code description, event date, and event value.

Table 5, the deprivation and geography look-up table, is a table created as part of an earlier project using the SAIL databank. The table contains one row for each LSOA in Wales for the 2001 census (totalling 1896). I asked that, for this thesis, the table contain encrypted LSOA code, LA code, WIMD 2005 deprivation decile, and Townsend deprivation decile.

Figure 4.1: Overview of the database structure for the data used in this thesis



4.4 DATA EXTRACTION

The data for this thesis were extracted from the SAIL databank, managed by the HIRU team at Swansea University. Two HIRU analysts performed the data extraction. The first of these wrote the SQL queries needed to extract the data as set out in the data specification.

Before any data could be made available for research purposes, in line with SAIL Information Governance procedures, the Encrypted Anonymised Linking Field (ALF-e), a unique identifier for each individual, was re-encrypted with PSALF – a newly-encrypted version of this identifier, used only for my data extract. Similarly, LSOA codes were encrypted.

The process of beginning the data extraction brought to light some issues with the data specification, and as a result I made a number of changes. First, I identified a number of additional clinical codes (Read codes and ICD-10 codes) that were not included in the original data specification. Second, it was not possible to create the primary care table simply by the use of a simple SQL query, because the large number of records in the main SAIL GP table and the very large number of Read codes in the data specification made this approach programmatically unfeasible. HIRU analysts therefore created used techniques based on cursors within the IBM DB2 (DB2) framework. Using this approach I was able to take advantage of the strength of relational-database software to match the primary care data to the records in the temporary intermediate table. This did not affect the file structure of the primary care data.

Data-processing and the data extraction were iterative processes, because I encountered a number of problems that necessitated revisions. I discuss these further in section 10.3 on page 329.

4.5 DATA-PROCESSING

I performed the data-processing stages described below with the aim of producing a usable dataset. Doing so required that a number of challenges be overcome. These included the difficulty of working on a remotely-hosted computer, the large size of the dataset, the necessity to clean the dataset adequately prior to use (from the point of view of missing, duplicate, and implausible data), and formatting the data for use. I describe below the means used to address these challenges. In doing so, I address four areas:

1. Working on a remote system
2. An overview of the decisions made about the programming languages and software used
3. An overview of the structure of my software
4. A detailed description of the cardiovascular-dataset-generating software that I wrote to perform the first stage of the data processing

4.5.1 *Working on a remote system*

Due to information governance regulations set out by the data access agreement with HIRU, I performed all analytical activity within the SAIL Gateway – the remote access facility for SAIL projects. Over the course of the analysis, I used two versions of the Gateway system. Version 1 was in use throughout 2012 and the first half of 2013. I switched over to version 2 of the Gateway in June 2013. The principal difference between systems is that version 2 of the Gateway requires an additional token, which acts as an electronic one-time pad. This provides additional security for access to the system.

Although working on the Gateway allowed access to the necessary data sets in a way that would not have been possible otherwise, I was subject to a number of practical restrictions on the way data processing might be accomplished. I discuss these further in section 10.3.

4.5.2 *Programming-language choice*

Before engaging in any analysis, I had to make a number of decisions about the likely approach that I would employ. In deliberating, I had in mind a number of principles: given that at the outset, I was unsure of the exact nature of the processing needed (as is perhaps inevitable), I wanted to use an approach that was as flexible as possible; similarly, I wanted an approach that gave the maximum level of control over the handling of the data; I wanted an approach that would be able to handle very large volumes of data, especially as at the start of the project it was not clear how large the final dataset might be; I wanted to employ programming languages that I had used before, and with which I was at least reasonably familiar; I wanted to, if at all possible, design and produce software that was configurable, thus giving it

potential use in future projects other than this one; any software that I used had to be available within the Gateway.

With these principles in mind, I decided not to use the DB2 database within which the SAIL data are held. Rather, I exported data from this system to a separate file structure generated by my software. I did this for two principal reasons: performing the intricate algorithms on individual-level data that I had in mind would be very difficult in SQL (though not necessarily impossible); using my own file structure would give additional control over the data, as compared to the data held within DB2 (though I hasten to make clear that this additional control in no way reduced data security; the data was just put in a different part of the Gateway). This approach had one obvious drawback. For very large data handling, DB2 is a highly optimised, fast approach. Given that most of the processing that I wished to accomplish would only require running once, rather than multiple runs in a performance-critical situation, this was a trade-off (some loss of speed in return for greater control and more straightforward coding) that I thought worthwhile.

I selected programming languages that I have previously used: C# (for general programming; I chose this over other general-purpose programming languages simply because it was familiar); the SQLite dialect of SQL for writing queries (again because I had used it before, but also because SQLite is a lightweight relational database software that can be incorporated into C# fairly readily; I used the dynamic linked library System.Data.SQLite to do this); R for statistical analysis and production of graphics.

I considered a number of other possible options before rejecting them, including using Microsoft Office applications (Excel and Access), using SPSS, and using Stata. I also considered using R for the preprocessing of the data, instead of simply for the analysis of the processed datasets. While it may have been possible to perform the necessary processing using these approaches, rather than using the C#/SQLite/R combination that I used, I think that it would have been much more difficult. Factors bearing on this decision include speed considerations, ability to handle large datasets, flexibility and ease of programming, ability to implement an object-orientated approach, and greater or lesser familiarity with certain software. Clearly there was more than one way to approach the task: I believe that, in view of the uncertainties I faced at the start of this project, the approach chosen represented a sensible balance of performance and flexibility.

Having decided which software to use, I then progressed to plan an overview of the necessary software structure.

4.5.3 *Software structure*

The raw data produced by the extract, and held in project-specific tables within the DB2 was not suitable for addressing the research questions. The data required modifying in a number of respects. The first set of problems related to the fact that the data had not been cleaned. Duplicate entries were present in the mortality table (but quite obviously an individual dies only once), in the general practice table (where the same Read code for the same individual for the same date quite frequently occurred, but with a different Read code description), and in the demography table (where some unique individual identifiers were duplicated). Also in the demography table, some of the LSOA codes did not relate to Welsh LSOAs, because the residents registered with a Welsh practice ended up in Welsh Demographic Service (WDS) data. Further problems arose because some general practice data contain values for results or readings. In many cases these values were either missing or were clearly implausible. Thus, I had to develop an approach to handle these entries. Because I was unsure of the nature of the distributions of these values, I needed to visualise them in order to determine meaningful cut-offs.

The second broad category of problems related to the structure of the data. I wished to get the data to a state where I could use one master algorithm to cycle through the records for each individual and derive information on the individual based on these records (a process described in chapter 5). In order to facilitate this, I generated a cleaned dataset with an appropriate structure. The raw dataset contained four tables (and one lookup table) in different formats. Moreover, the PEDW data was in a 'long' format, with one row for each unique combination of spell, episode, operative code, and diagnostic code – making it more difficult to use. The data in the separate tables were unsorted, making it difficult to access all of the data on one individual in turn. To provide usable data, I restructured the data to two tables: a demography table and a common format table (containing general practice, mortality, and the restructured PEDW data in the same format). The lookup table was unchanged. The data in both of these tables needed to be sorted by the individual's unique identification number (PSALF).

A further problem with the raw data was its size. While there are only a few hundred thousand mortality records, there were approximately 2,000,000 entries in the demography table, 40 million entries in the PEDW table, and 130 million entries in the general practice table. This meant that I had to write software capable of handling this large number of records; moreover, at the time of development, I was unsure of the exact final size of the data set because the extraction process was ongoing, and because SAIL data are periodically refreshed.

I wished to resolve some of the enormous numbers of clinical codes (particularly Read codes) into a more tractable set of events. For example, there are, for many classes of drugs of interest, many different Read codes relating to that class. Likewise, some diagnoses may have a number of Read codes associated with them, for example diabetes. I thus wished to develop the means of adding a classification to a particular record based on clinical-coding criteria; and in fact I determined that a two-level system was necessary. For example, I wanted it to be possible to have a broad category for all the general practice entries relating to raised blood-pressure, but also to be able to further classify these entries on the basis of whether they related to blood-pressure readings, blood-pressure diagnoses, blood-pressure comments, or blood-pressure treatments. I wanted this to be possible for all types of general-practice data, but also for mortality and PEDW data. Given that I knew it was unlikely I would get this classification right first time, I wished to develop a system which allowed me (and potentially others) to specify fairly easily the nature of the classification to be used.

Finally, developing the cardiac-dataset generator provided opportunities to check the original data extract, allowing me to identify any associated problems. This inevitably resulted in the processes of data extraction and creation of the cardiac dataset generator becoming intertwined and iterative. Such an approach allowed me to identify a number of problems, which are discussed below in section 10.3.

4.5.4 *Dataset processing*

In this section, I provide details of the structure and workings of the cardiac-dataset generator. I discuss the following areas:

1. Overview of the process carried out by the software
2. A discussion of the configurability of the software

3. The software structure
4. The processing methods used in a number of key areas
5. The visualisation of data necessary for processing general practice value fields

4.5.4.1 *Overview of the process*

I begin with a discussion of the processing of the general practice data. The processing of the other main datasets (demography; mortality; PEDW) was similar though necessarily slightly different. The differences are discussed below.

The data processing approach taken for the GP data is summarised in the schematic diagram in figure 4.2, which indicates the main files used to process the data. Due to the large size of the dataset in question, I split the data up into subsets. I did this using a classification code which was specified in the original extract specification and which allowed each GP data line to be categorised into the broad area to which it referred on the basis of its Read code. Thus, the first level of classification of the general practice data that I wished to achieve was accomplished as part of the extraction process (discussed to above) using the linkage between the general practice table and the table of Read codes that I provided to the HIRU analyst performing the extraction. This allowed me to deal with different types of GP data separately.

First, I extracted the GP data from the main SAIL databank (❶ in figure 4.2). I did this for each of the classification types, which included for example 'hypertension', 'coronary heart disease', 'calcium-channel blocker' and so on. I then imported each of these extracted raw data files (❷ in figure 4.2) into an SQLite database (❸ in figure 4.2) from where I could further query the data and remove duplicates. I added a further sub-classification field to the data in the SQLite database by linking the GP table to a sub-classification table (also imported into SQLite, and derived from the user-specified classification files). This allowed extraction of fields based on more detailed descriptions, for example 'Hypertension reading', 'Hypertension diagnosis', 'Coronary heart disease comment', and so on.

Once this process was complete, I ran each line of the data through a C# algorithm (❹ in figure 4.2) which processed it based on its classification and sub-classification. I kept relevant fields for further analysis; where readings or results were present, I processed these

so that the units were standardised, and zero values and implausible values rejected. This process was, again, based on user-specified formulae. As a result of this process, I created a set of event files (❺ in figure 4.2), which contained processed GP event data, and which could subsequently be combined with PEDW and ONS mortality data, in a common format which could store all event types. The event files contained processed data separated by event classification ('hypertension', 'coronary heart disease', 'glomerular filtration rate', and so on). Analysis required examination of data at individual level. Therefore in the next stage of data processing I ran a C# algorithm against each of the event files (❻ in figure 4.2) and categorised events by individual. Because a single individual file would be too large to be manageable, there were a number of individual files which each contained processed data on a subset of individuals (❼ in figure 4.2). At this stage I combined the general practice data with mortality and PEDW data that had been processed along a similar but distinct pathway.

Finally, in order to work properly, the derived dataset generator required the records in the event files to be sorted in order of ascending PSALF. I accomplished this by writing an external merge sort algorithm. This allowed me to produce a set of event files which were sorted, which contained all the records relevant to a particular individual, and through which the derived dataset generator algorithms could cycle.

Although the algorithms for processing the PEDW data were similar to those used for the general practice data, there were a number of differences. The classification system for these data was more straightforward, with the higher-level classification set as 'Admission' and the lower-level classification based on the type of admission (for example, CVA, MI, PCI, and so on). No values were present in these data, so processing was more straightforward

I substantially restructured the PEDW data. The data in the original extract contained one row for each combination of individual, provider unit code (indicating the hospital site in which the admission occurred), spell number, episode number, diagnosis number, and procedure number. For my analysis, I wanted this table to contain one row per episode. I restructured the data at the stage of importing from the SAIL DB2 database.

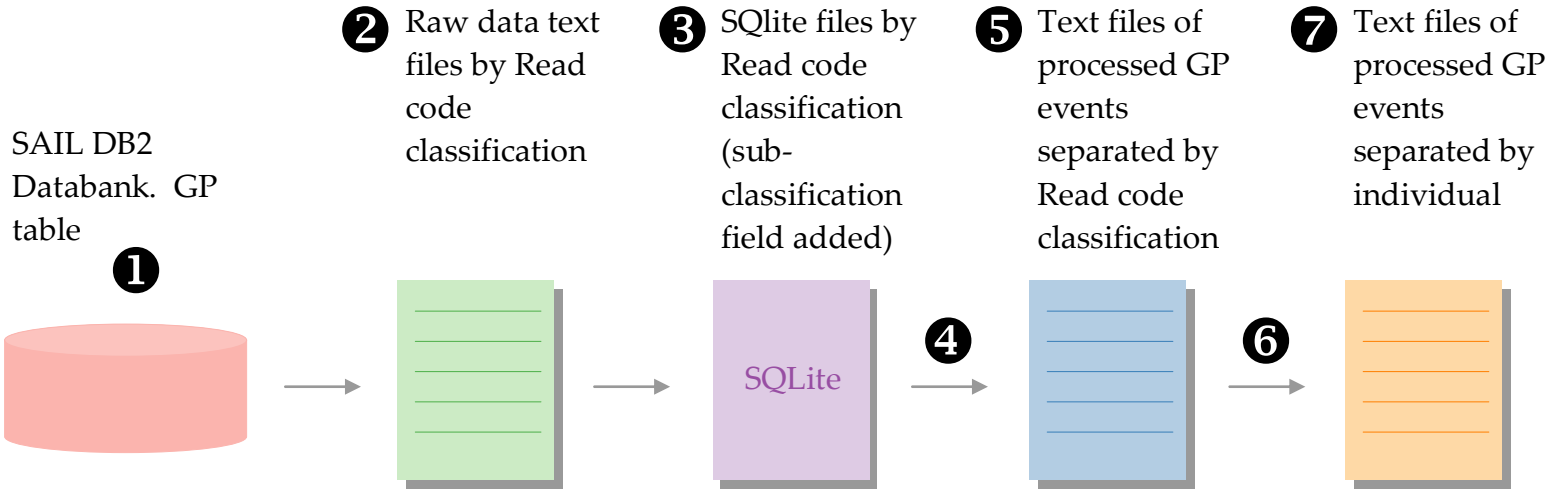
Similarly, the mortality data required less processing than general practice data. I imported the data through the equivalent system of files, with the high-level classification code set to 'Death', and the low-

level classification code set to either non-cardiovascular cause of death, or a specified cardiovascular cause. At this stage, I removed duplicates from the mortality table, which arose where the same individual had more than one entry in the table. In each of these cases, the cause of death code and date of death were identical, and so I removed one of the entries at random.

Once I had imported and classified the PEDW and mortality data, I was able to alter the format in line with the common format for the tables that I had previously used for the general practice data. I then combined all of these data lines into separate files; each file contained data relating to a range of PSALFs. I used the external-merge-sort to sort the files by ascending PSALF. As a result of this process, I was then able to obtain a set of cleaned, classified, sorted event files, which contained data derived from the general practice, PEDW, and mortality tables.

I required the demography table to be available separately. I imported this table into a file in a separate section of the cardiac dataset file structure. During this process, I used queries sent from C# to the SAIL DB2 database to remove non-Welsh LSOA codes. At this stage, during the process of writing the cardiac dataset generator, I discovered that there were a number of duplicates in the demography table. I arranged for the HIRU analyst performing the data extract to remove these duplicates in a refreshed extract. I imported into the classification-files section of the cardiac-dataset file-structure an unchanged version of the lookup table from LSOA to other LSOA-level variables.

Figure 4.2: Schematic representation of data processing of GP data



4.5.4.2 *Configurability*

One of my aims in producing the cardiac dataset generator was to produce a system that could be reused in future to generate similar datasets, using refreshed data from SAIL and using a different specification of codes and classifications. With this in mind, I sought, throughout the process of writing the software, to provide options for users to specify the nature of the final dataset.

Simple variables that the user may specify include the location of the file structure, the dataset name, and the file size for processing records. I wished to make it possible for users to specify which type of records they wish to select from the raw data, how they want to classify such records, and how they wish to process values in the general practice data. To do this, I developed a system whereby the software checks a directory of Excel spreadsheets (termed the classification files), to look for user-inputted information. The advantage of this approach is that most users are familiar with spreadsheet software, and the specification of the dataset itself does not require programming knowledge. The classification files are generated on the basis of the unique types of classification in the raw data. For each classification file, there is a list of Read codes, Read code descriptions, the number of entries for that Read code in the raw data, and a field to flag whether or not that Read code and Read code description is a duplicate combination. A further field is used to hold formulae that allow users to define how they wish the value field for that particular Read code to be handled.

In using the system, the user assigns a sub-classification to each of the Read codes. The process of such an assignment means the records related to that Read code will be included in the final data; otherwise the codes are ignored. For codes where the user will wish to use the value field (typically this is a measurement reading such as blood pressure or cholesterol), the user specifies a means of handling this in the formula field. Here, there are functions available to specify the handling of the data, which are parsed later by the software. There are three formulae that I have written, which proved useful for this project.

- RANGE: This function allows the user to specify a range within which the value should be retained, and the record used. If the value falls outside the range, the sub-classification of the record is changed, by adding the suffix 'EMPTY OR OUT OF

RANGE'. The arguments to the function are the lower and upper boundaries for the range.

- SPLITRANGE: This function allows the user to specify two ranges, for handling mixed distributions. This situation arises where the same Read code has value fields whether measurement or reading entered is not always in the same units. The function converts values within the second specified range into values within the first specified range using a formula entered by the user as one of the arguments to the function.
- BLOODPRESSURE: This function allows the user to specify the handling of blood pressure readings, again using two ranges. This time the first range is used for diastolic blood pressure and the second for systolic blood pressure.

For each of these formula types, the formula used for the processing of any sub-classification is taken from the entry for the first Read code entry related to that sub-classification. All subsequent Read codes of the same sub-classification are processed in the same way. This saves the user having to repeatedly enter formulae.

In using these functions for the processing carried out for this thesis, I based the decisions made about which ranges to employ on visualisation of the distributions of the values in the data, and on discussions with a chemical pathology clinician and a laboratory technician, based on the graphed distributions.

4.5.4.3 *Visualisation of data*

I needed to visualise the distributions of raw data within the value fields of the general practice data at an interim stage, before they had been processed. I achieved this by writing code in R that extracted the relevant data from the SQLite event files (using the R package, 'RSQLite', available from the Comprehensive R Archive Network (CRAN) repository). The graphics themselves were produced using the R add-on package, 'ggplot2', also available from CRAN.

I automated this process in such a way as to allow large numbers of distributions to be generated and exported from SAIL for discussion with people with expertise in the area, facilitating decision-making about which ranges to include.

4.6 CONCLUSIONS

In this chapter, I have outlined the stages through which it was necessary to progress in order to produce data appropriate for use in later parts of this thesis. This has included outlining the processes by which information governance approval was sought and obtained from the relevant quarter; I have detailed the process by which the requisite dataset was specified, such that extraction might take place and inform information governance procedures; I have outlined the extraction process undertaken; finally, I have detailed the process by which the extracted data was processed, formatted, and cleaned.

In carrying out these processes, the aim was to progress the work to a point at which a suitable dataset was available for the purposes of subsequent work. These later data-processing and analytical tasks were in themselves quite detailed programming projects. I describe them in the next two chapters.

5

PATHWAY OF CARE FOR CORONARY HEART DISEASE

5.1 INTRODUCTION

When first developing ideas for this thesis, I conceived the idea of a pathway of care for CHD as illustrated in figure 1.1, and discussed in chapter 1. In chapter 3, I reviewed the literature around inequity of healthcare interventions for CHD; I found a mixed picture, and no studies that attempted to look in a comprehensive way across several areas of care. In the light of this review, and taking into consideration the aims of my work, I developed an approach to take account of the flows and knock-on effects that might potentially operate in the system of care as a whole. I devised an approach to analysis that focused and comprehensiveness, with a view to examining systematic effects. The intention was to develop a detailed approach to the idea of a pathway of care that was explicit, reproducible, and rigorous. It is this approach that I discuss in this chapter. I hope to set the methods of this thesis in the context of previous important concepts in this area, to show how and why I have extended previous conceptual frameworks, and to provide a detailed description of the methods used to implement this approach.

I will examine two areas:

1. An overview of the methodological concepts developed around a pathway approach
2. The detailed implementation of these concepts to generate the data to address the research questions

5.2 METHODOLOGICAL CONCEPTS

In the this section, I discuss what I mean by the pathway of care for CHD, how I determined what should be included in it, the idea of indication patterns for individuals the concept of the 'clinical trigger–clinical action' approach taken at each point in the pathway, and the assumptions and limitations of this approach.

5.2.1 *Pathway of care for CHD*

This idea of a pathway of care for CHD, as conceived here, involves a comprehensive overview of the different components of healthcare that can be delivered to an individual at different times in managing CHD. Clearly, the requirements for healthcare activity related to CHD vary from individual to individual, and from time to time for that individual. Thus, at any one time an individual will have a specific indication pattern consisting of the set of components of healthcare for CHD that are indicated for that person at that time.

5.2.2 *Inclusion in pathway*

There are a large number of interventions that relate to CHD. (The concept of interventions here is deliberately broad, ranging from from simple measures to ascertain CHD risk, through management of risk factors and chronic disease, to revascularisation. Deciding which of these to include and which to leave out was a key stage in developing the pathway. It was necessary to develop an approach that considered up-to-date interventions that have been shown to be effective, and which were appropriate during the period studied. I kept a number of principles in mind:

- I wanted to include in the pathway interventions that had been shown to reduce mortality from the disease or affect identification of individuals so that they could receive such interventions subsequently. For this reason, for example, I did not look at therapies that provide symptomatic relief of angina
- I wanted to look at interventions that could be regarded as generally accepted in practice (allowing that there are always clinical situations in which clinical judgement will override generic guidance). For this reason, I focused on interventions recommended in National Institute for Clinical Excellence (NICE) guidance
- The pathway was limited by the data available. I could not look at all relevant interventions. In particular, I could not look in any detail at the inpatient management of acute coronary syndromes (ACSs), because information about prescribing in secondary care was not available in routine data

- I limited examination of the pathway to looking at treatments that were in general use during the period of the cohort. I did not look at experimental or unusual interventions
- I wanted to look at cessation as well as commencement of prescribing of appropriate medications

With these principles in mind, I then developed the overall principle of the pathway. In figure 5.1, I illustrate the overview of the pathway schematically. At the top of the figure is shown the potential progression of an individual through different stages of CHD. At first an individual will not have the disease, but may become at high risk of developing it; they may then progress to have stable angina, unstable angina and other ACSs. On the left-hand side of the figure, I illustrate the kinds of healthcare activities that can be appropriate in CHD. This includes a spectrum of care running from primary care identification of risk factors and risk, through primary care management of such risk factors, to medical and surgical management of established disease.

I wished to develop the idea of visualising the pathway of care for CHD based on figure 5.1. Though this was not straightforward (I discuss some of the issues with it below), I intended to develop an approach that allowed consideration of an overview of the pathway of care, and, in particular, a way to visualise it. The eventual overview diagram that I developed is detailed in section 5.3 on page 133.

5.2.3 *Points in the pathway*

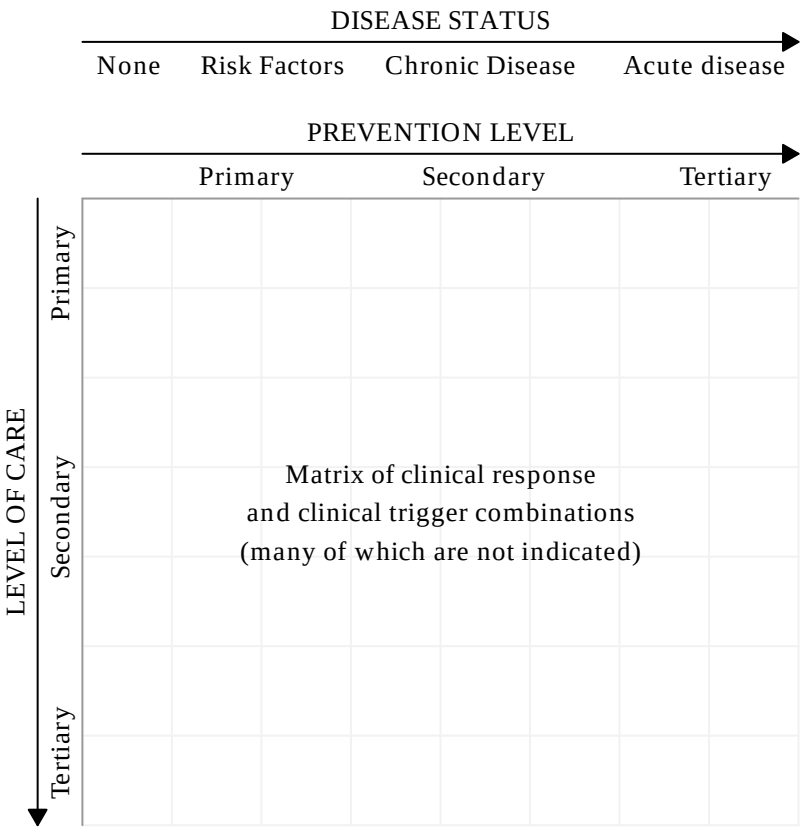
Having developed the idea of viewing the pathway in overview, I then sought to determine how I would address each particular point in the pathway. In the first instance, I developed an approach to thinking about what was happening at each of these points, and about what I would be able to determine from available data with respect to health care provision at each point.

5.2.3.1 *Staircase effect*

In chapter 2, I discussed healthcare needs assessment on page 26 and I also introduced the staircase effect on page 6.

These concepts were important for this thesis. I characterise the delivery of a healthcare interventions as a staircase, following Tugwell[3], but with the addition of the idea that at each step in that staircase a particular factor is involved, either related to need, demand, or supply.

Figure 5.1: Pathway concepts



Need-related factors are those that have a bearing on an individual's capacity to benefit from intervention; supply-related factors are those pertaining to health-service considerations; demand-related factors are those to do with whether an individual seeks an intervention, wishes to undergo it, consents to it, and, where relevant, adheres to therapy.

In figure 1.2, I have classified different stages in the staircase as supplied-related, demand-related, or need-related. In this conceptualisation, only a proportion of those reaching any particular stage will move onto the next, with the drop-off related to the factor in question. (By drop-off, I mean the proportion who fail to move onto the next step). Effective delivery of an intervention requires that an individual passes through each stage. At each stage, the drop-off can be characterised as related to supply, demand, or need; in figure 1.2, I have illustrated this by colouring drop-off blue when related to need, read when related to supply, and green when related to demand.

Thinking about the staircase effect for the intervention in this way means that one can distinguish, if only in theory, between drop-off related to supply-related factors (which are principally health-service related), need-related factors (related to the efficacy of the technology in a particular population group), and demand-related factors (determined by individual behaviour, but clearly related to health service and societal influences).

For any intervention, there are several stages that need to be gone through in a critical pathway, each one of which needs to be met before the theoretical efficacy of the intervention is brought to bear. Tugwell et al[3] defined stages of awareness, access, diagnosis, targeting, compliance of providers, and adherence of consumers. The exact sequence of steps conceived might vary according to intervention and according to the level of 'magnification' required in thinking about the staircase effect. In figure 1.2, we start with all individuals in the population with capacity to benefit from the intervention, and progress through to the proportion of those with this need in whom the intervention is eventually efficacious. Along the way, we incorporate drop-offs in a number of individuals identified as having the need for the intervention, being aware of that need, being identified as having that need (by the health service), being offered the intervention, consenting to the intervention, being prescribed the intervention or being listed for a procedure, collecting the prescription or attending for a procedure, taking the intervention, and persisting with treatment. The exact sequence of these steps will vary by intervention.

In my conceptualisation of the staircase, supply-related factors would include identification of need, offer of intervention, and prescription of intervention (when the intervention is a drug) – these principally relate to the activity of the health service; demand-related factors will include awareness, consent, collection of medications, attendance, and adherence – as these principally relate to individual choice and behaviour; need-related factors would be limited to the number of individuals in the population with the need and to the efficacy of the intervention.

The above theoretical division of the staircase effect is useful, because it allows one to think about what 'views' of the staircase one is able to get for any one intervention. Typical academic studies of healthcare inequity examine drop-off across a number of steps in the staircase – and these steps may be some combination of demand-related, supply-related, and need-related. They do this because they have to; data are usually not available on all of the potential drop-offs in the staircase. This limits the extent to which studies can accurately ascertain the existence of healthcare inequity – where healthcare inequity is conceptualised as a differential drop-off between social groups in supply-related steps of the staircase. Where demand-related and need-related steps exist in the segment of the staircase examined, the possibility of the drop-off being related to differences in these cannot be discounted. Again, this is important for studies of healthcare inequity: if one social group is turning down an intervention at a much higher rate than another, does this represent healthcare inequity?

The limited extent of routine data means that in this thesis I had to think carefully about which segments of the staircase I would be looking across for any one intervention. In an ideal world, routine data would contain information on identification, offering of interventions, consent, refusal, and so on. This is not the case in reality. Keeping the idea of the staircase effect in mind, I determined that I would have to examine a simplified situation. When looking at a non-drug-related intervention, the data only allowed one to look at the drop-off from the proportion of individuals with need to the proportion of individuals to whom the intervention was given. Clearly, this conflates several drop-off steps in the staircase: one does not know who is offered intervention, who consents to it and who refuses it. For most diagnoses, one does not know whether individuals have been identified as having the diagnosis. These issues are an inevitable consequence of using

routine data. Cognizance of the staircase effect allows one, I believe, to keep these limitations carefully in mind.

For interventions that involved a continuous prescription of a drug, I was able not only to look at prescription of the drug, but also at the continuation of prescription. Thus, for such interventions, it was possible to get to 'views' across the staircase. This approach allowed me to examine another potential differential drop-off in the staircase between deprivation groups.

While the conception of the staircase effect is necessarily theoretical, it underpins the way chosen to develop methods for this thesis, and I hope that the foregoing explanation provides the reader with some insight into my thought processes.

5.2.3.2 *Clinical trigger-action*

In considering the pathway of care, I have distinguished two important concepts: first, the idea of a clinical indication for some action to be performed; this indication can vary with time, according to the course of disease for an individual as well as other individual characteristics, such as age; at one time, an individual may have activated a number of different clinical indications. Second, I have considered the idea of a clinical action; while this might typically be thought of as a drug prescription or procedure, I have extended the idea to include more general actions such as appropriate referrals, appropriate advice, and appropriate measurements. In the above discussion, I have referred interchangeably to interventions, triggers, indications, actions and so on. In subsequent parts of this chapter and thesis, I have used the following definitions to cover these concepts:

> *Clinical trigger* The time point at which an individual enters a state where a particular clinical action (measurement, investigation, referral, drug prescription, or procedure) would be recommended for the individual according to generally accepted practice
>
> *Clinical action* A particular clinical action that would be recommended for an individual according to generally accepted practice on the basis of their current clinical state
>
> *Indication period* The time-period from the clinical trigger up to the point at which the clinical action is no longer indicated

For example, according to NICE guidance, individuals whose risk assessment (by any appropriate risk-assessment tool) suggests a CVD risk over 10 years of greater than 20% ought to be offered a statin medication. The time point at which that individual is known to be at high risk is a clinical trigger, subsequent to which a statin is indicated; initiation of prescription of the statin is the clinical action. I detail each of the clinical trigger-clinical action combinations examined in section 5.3.

In considering clinical trigger-clinical action combinations, the aim was to analyse differences that might be occurring between individuals from different area-level-based deprivation-groups. In evaluating differences, I sought to look firstly at the time from the clinical trigger to the clinical action for different groups. Secondly, in the case of drug prescriptions, I set out to examine the time from the initiation of prescription with the medication to the time of cessation. Both of these means of proceeding would allow use of a time-to-event analytical approach.

I also wished to develop an alternative concept when looking at prescription medications: drug-coverage proportion. Here, I would look at the proportion of the indication period covered by the drugs prescribed.

5.2.3.3 *Further considerations*

This approach raised a number of issues. I have discussed these in principle here, and in detail in the second part of this chapter, section 5.3. Broadly they relate to the fact that the available data only provide a seven-year window in which to examine activity. Prior to the start of the study period, some data were available from general practices and from PEDW. The data therefore sometimes identifies individuals with a clinical trigger that had initially occurred prior to the period of the study. Moreover, in some cases the data allowed one to identify the situation where an individual had received the clinical action prior to the clinical trigger. I discuss how I handled these issues when implementing my methods in section 5.3.

5.2.4 *Cohort of inclusion*

This study was based on a cohort of individuals followed up from January 1, 2004 to 31 December 2010. For any individual, there was a defined start point and defined end point (or censoring point),

demarcating a designated cohort period for that individual. During that time, any one individual could have several clinical trigger-actions occurring. It was necessary to develop a conceptual framework to handle the relationships between an individual's presence in the cohort (and therefore capability to contribute time to the analysis) and the timing of any clinical trigger-actions for that individual.

For example, clinical triggers occurring prior to an individual's cohort period could be identified in our data (because there was data from a lead-in period prior to the start of the study period). I therefore conceptually differentiated these clinical triggers occurring before the cohort period of observation for the individual (prevalent clinical triggers) from clinical triggers occurring during it (incident clinical triggers). I also needed to ensure that an individual's cohort period was taken into account when considering the times for which a clinical trigger-action could be followed up. I discuss the detailed implementation of algorithms to address these issues in section 5.3.5.

5.2.5 *Assumptions and limitations*

Inevitably, in order to simplify my methods for analysing the pathway of care for CHD, I needed to make a number of assumptions and simplifications. Such a process provided me with an analytically tractable problem; potentially, this is at the expense of introducing some limitations into the analysis.

Ratcheting effect of indication states I made the assumption that individuals could only move in one direction in the indication states that they could occupy. For example, in the case of an individual being at high risk for CVD (this is discussed further below), I assumed that they could not subsequently become low risk. Likewise, I assumed that if an individual with stable angina had a ACS they could not subsequently have returned to a stable angina state. I believe that such assumptions do not generally introduce major limitations into my approach, and they contribute subsequently to simplifying the analysis.

Overlaps in pathway presentation In seeking to present a graphical representation of the overview of the pathway of care, I have simplified the combinations of clinical triggers and clinical actions displayed, at the expense of producing

some overlaps. In other words, clinical trigger and clinical action states illustrated in the pathway diagrams (shown later in this chapter) do not represent mutually exclusive states. For example, individuals throughout the pathway care can combine the first smoking clinical trigger with any other trigger state. Similarly, the revascularisation clinical action is a composite of the clinical actions for CABG and PCI. I have deliberately sacrificed some conceptual rigour to achieve simpler presentation.

Risk assessment NICE simply states that when assessing risk for CVD, an appropriate risk tool should be employed. The more commonly used risk assessment tools, particularly towards the start of the period covered by our data, were the Framingham risk assessment tools. I have performed the main analysis using the Framingham non-laboratory risk assessment tool, as this requires less information for completion then other tools – making fewer demands in the ascertainment of risk factors. This allowed me to make an assessment of risk on a greater proportion of the study population, though this does need to be balanced against the potential disadvantages of using this measure, including the lack of inclusion of deprivation and ethnicity data and the evidence that risk is overestimated for contemporary UK populations.[182]

Drug cessation By setting the analysis out as I did in order to examine times to cessation of medication prescription, I made a further assumption: what does cessation of medication actually mean? Obviously, prescriptions cease at or after the censoring points for the cohort. To coherently identify drug cessation during the cohort period, I had to define a minimum length of time before the cohort end that would count as cessation of prescription.

Multiple comparisons By setting out multiple points in a pathway at each of which I examined the possibility of healthcare inequity, the possibility arose that by making multiple comparisons one would simply identify some statistically significant results by chance. While I have not formally adjusted for this effect, for example the use of Bonferroni corrections or some similar approach, I have

born this consideration in mind, and discussed this in detail in chapter 10.

Contraindications and informed dissent Read codes exist that would allow determination of whether or not individuals had contraindications to a particular intervention or whether they turned intervention down (informed dissent). QOF business rules take account of such situations. I elected not to in my analysis, because I was interested in the population-level implementation of clinical actions, regardless of contraindication or dissent. In other words, the overall aim of the project being to examine the possibility that differences in intervention utilisation drive population-level inequalities outcome, I felt it was important to look at unrestricted population denominators to gain insight into potential effects of differential healthcare utilisation at a population level.

In the first section of this chapter, I have outlined the conceptual underpinnings used when developing a pathway approach to looking at healthcare inequity. This has been a somewhat abstract discussion in many places. By contrast, in the next section, I now turn to the concrete details of the implementation of these concepts.

5.3 IMPLEMENTATION

5.3.1 *The problem*

In chapter 4, I discuss data-processing tasks that produced a cleaned dataset. The ensuing problem was to derive from this data the necessary dataset with which one could implement the pathway approach using clinical trigger-actions.

Having completed the processes discussed in chapter 4, I had produced two main tables (held in a number of separate files because of their large size): one for demography data; one for the common format data, containing general practice, mortality, and PEDW data. To implement the methods described in this chapter, I developed an additional programme called the the derived dataset generator that took these tables as input data and produced the data for final analysis as an output.

Firstly, I needed to determine which individuals met the inclusion criteria for the cohort, and to determine their relevant demographic information. It was necessary to define time-periods of inclusion in the cohort by examining censoring events.

Having decided which components of the pathway of care to include in the analysis, I needed, at each point in the pathway, to determine the important events for each individual, including CVD diagnoses, risk factors, changes in risk score, and treatments. The core of the analysis required that I use this information to implement the clinical trigger-action approach at each point.

5.3.2 *Inclusion in the pathway*

I determined on a number of broad areas to include in the pathway of care for CHD:

1. Risk and risk factors attainment
2. Smoking management
3. Blood pressure management
4. High-risk statin management
5. Drug management of chronic CHD
6. Drug management of ACS
7. Revascularisation of chronic CHD
8. Revascularisation of ACS

For each of these I then identified specific clinical trigger-action combinations that I wanted to examine. In doing so, I took account of NICE guidance and of the availability of data to examine each potential clinical trigger-action combination. I discuss the resulting set of clinical trigger-actions below.

5.3.2.1 *Risk and risk factors attainment*

With a view to determining whether identification of individuals at high risk of CVD differed between area-based deprivation groups, I sought to examine the group of individuals for whom measurement of risk factors and ascertainment of overall risk would be important

in determining the need for treatment, particularly smoking management, statin treatment, and BP management. I examined clinical actions following the first identified instance of an individual becoming aged 40 in the absence of any CVD-diagnoses (CHD, diabetes, CVA or transient ischaemic attack (TIA), or peripheral vascular disease (PVD)). I refer to these subsequently as 'high risk diagnoses'. Saying that would be useful in avoiding misunderstanding in later text. To identify these diagnoses, I used the diagnostic codes in appendix E. I looked at both Read and ICD-10 codes; when looking at the latter, I considered codes in any coding position. For individuals with this trigger, I wanted to look for a number of clinical actions:

Ascertainment of smoking status I defined the presence of this clinical action to be indicated by the presence of a Read code indicating smoking status. The full list of codes is detailed in appendix E.

Measurement of BMI Defined as the presence of Read codes for BMI, as shown in appendix E.

Measurement of BP For simplicity, I looked only at systolic blood pressure, defining the clinical action as being represented by a systolic blood pressure reading, according to the list of codes shown in appendix E.

Measurement of cholesterol Defined as the presence of a Read code for measurement of cholesterol, as shown in the list of codes in appendix E.

Full cardiovascular risk assessment Defined as the first time point at which a complete set of data points was available such that an assessment of risk using a risk tool would have been possible (whether or not this were carried out). For the main analysis, I used the Framingham non-laboratory risk assessment tool, which requires (in addition to age and sex) a BMI, a systolic-BP reading, a known smoking status, diabetes status, and antihypertensive medication treatment status. Diabetes status was defined on the presence or absence of diabetes codes, while age and sex were always known. Thus, in practice, achievement of this clinical action required that an individual had a systolic-BP reading, a BMI, and a smoking status all recorded. In a sensitivity analysis, I used the original Framingham risk-assessment tool, which required left ventricular hypertrophy (LVH) on

Cardiovascular risk tools are described in appendix B

electrocardiogram (ECG) – assumed not to be present for anybody (because this information was not available), and a cholesterol-ratio reading; BMI was not required; other variables are required for both tools. Regardless of the risk-tool used, I put no time limit on the relevance of variables. For example, if the final required variable, say smoking status, was not recorded until three years after the most recent systolic BP, I considered this BP reading to remain valid, an assumption discussed in chapter 10.

5.3.2.2 *Smoking management*

I wished to examine potential differences in smoking management between deprivation groups in primary care. I identified smokers by finding the earliest time point in the dataset at which an individual had a Read code indicating that they smoked. Thus, the clinical trigger in this case was defined as being the earliest occurrence of one of the Read codes in chapter E. The indication period for these individuals was ended by the presence of a Read code for the individual being a non-smoker, again shown in chapter E (as well as by other censoring events). I had to take account of the situation in which an individual was recorded as being a smoker, then recorded as no longer being a smoker, and then recorded as a smoker again. In this or similar situations, I looked only at the period from the first trigger to the first non-smoking code; I disregarded subsequent clinical triggers and indication periods; using this approach simplified coding. In subsequent parts of this thesis, this clinical trigger is referred to as 'First smoking'. In individuals with this clinical trigger, I looked at two clinical actions.

Provision of stop smoking advice This clinical action represented advice given by clinicians in primary care to individuals who smoke, with a view to encouraging smoking cessation. I defined it using the codes shown in E

Smoking cessation referral In this case, I was looking for referrals to smoking-cessation services. The clinical trigger is defined using the code shown in E

5.3.2.3 *BP management*

I had to decide how to handle different situations in which high BP needs to be managed. In individuals not otherwise at high risk of

CVD, the cut-off for managing BP is different from that in those who are already known to be at high risk (either through diagnosis or through risk assessment).[183] I treated these two situations separately. Furthermore, I needed to determine how to employ BP readings – should one use systolic readings only, or also look at diastolic readings? How many readings should one look at? After consideration, and as far as possible in line with NICE guidance[183], I decided on two separate clinical triggers for BP management.

> *BP raised and low-risk* This clinical trigger arose in a situation in which an individual whose risk assessment suggested that they were low risk, or whose risk assessment was unknown, had three consecutive blood pressures recorded each with a systolic value greater than 160. In the event that the individual subsequently became high risk, the indication period for this clinical trigger was terminated, and a separate period initiated classified as 'BP raised and high-risk'(see below)
>
> *BP raised and high-risk* I defined this clinical trigger as arising when an individual who was known to be a high risk for CVD, either through risk assessment or the presence of other high-risk diagnoses, had three consecutive blood pressure readings recorded where each systolic blood pressure was greater than 140. Alternatively, if a high risk individual had a hypertension diagnosis recorded, I initiated this clinical trigger. For simplicity, I did not differentiate clinical triggers for situations in which an individual was at high risk as a result of risk assessment from clinical triggers where an individual was at high risk due to a high-risk diagnosis

I based assessment of cardiovascular risk on my own algorithm that calculated risk using the Framingham non-laboratory risk assessment tool (or for the sensitivity analysis the Framingham 1991 risk assessment tool). This algorithm calculated risks at all possible time-points; I then determined on the basis of these risk assessments, for any one individual, the time periods when they were: unknown risk; unknown low risk; of known high risk based on risk assessment; of known high risk based on a high risk diagnosis; I used the codes is shown in appendix E to define high-risk diagnoses. Likewise, the codes used to search for hypertension readings and hypertension diagnoses are also

shown in E. Further algorithms combined information on risk and BP reading to identify these clinical triggers. When referring to these clinical triggers in the rest of this document, I have used the above terms For both of these hypertension related clinical triggers, I looked at prescription of antihypertensive medication. Clinical protocols for the management of hypertension are quite complicated: there is a ladder of treatment, with individuals having additional treatment added according to action and tolerance of treatment; the order in which drugs are prescribed for individuals depends on patient characteristics such as age and ethnicity. Many of the medications that can be used to treat hypertension can also be used for other conditions. While I did consider developing algorithms to address the complexities of the management protocols for hypertension, I ultimately decided to reduce the complexity of the investigation and look only at a simplified 'clinical action'. While such an approach overlooks the intricacies of hypertension management, I hoped that by looking in broad terms at the provision of antihypertensive medications, I would be in a position to identify gross levels of inequity in provision of them.

> *Treatment with antihypertensive medication* I defined this clinical action as being indicated by treatment with any one of a number of antihypertensive medications. The list of codes used to define this clinical action are shown in appendix E

5.3.2.4 *High-risk statin management*

In ensuing text of this thesis and in the wording of figures and tables, I refer to clinical triggers and clinical actions using the names shown in italics section 5.3.2

For statin management, I considered two clinical triggers separately: one for individuals at high risk due to risk assessment; another for individuals at high risk due to a high-risk diagnosis. In either case a statin is indicated, but I wished to differentiate the situations, because of the likelihood that the levels of clinical action would be different. When considering high-risk diagnoses, I did not include CHD. I did this to avoid duplication: I consider the provision of statins to individuals with CHD when examining clinical triggers at other points in the pathway (clinical triggers 'Stable angina', 'Stable angina diabetes', 'Old ACS', 'Unstable angina', and 'MI').

> When *Risk assessed high* This clinical trigger arose at the time point at which an assessment of cardiovascular risk was possible using the Framingham non-laboratory score and where the result of the risk assessment gave a cardiovascular risk over the next 10 years of greater than 20

percent. My algorithm to assess cardiovascular risk calculated the 10-year risk at every possible time point for every possible individual: possible time points were defined as being when one of the measurement variables changed (for example, following a systolic BP reading, the score would be recalculated); I also recalculated the score annually on each individual's birthday.

High-risk diagnosis This clinical trigger arose at the earliest time-point at which one of the diagnostic codes shown in chapter E appeared in the patient's data. CHD diagnostic codes were not used for this clinical trigger, for reasons explained above. On the appearance of a CHD diagnostic code in the data, the indication period for this clinical trigger was terminated, and the relevant CHD clinical trigger was initiated

5.3.2.5 *Drug management of chronic CHD*

I defined the two different clinical triggers for the management of chronic CHD. The first related to stable angina (and other unspecified diagnoses of CHD); the second relates to stable angina in individuals with diabetes. I make this distinction because the presence of diabetes affects whether or not ACE inhibitors are indicated. The clinical triggers I looked at for chronic CHD were:

Stable angina This clinical trigger was defined by the presence Read or ICD-10 codes shown in appendix E. In the event that an individual developed diabetes the 'stable angina' indication period ended, and a clinical trigger for 'stable angina and diabetes' was initiated. I also terminated the indication period in the event of a clinical code for ACS.

Stable angina and diabetes Defined the same as for 'stable angina' using the same codes, but with the additional requirement that the individual have diabetes. The codes used to define diabetes are shown in appendix E. I terminated this indication period in the event of a clinical code for ACS.

For 'stable angina', I looked at two clinical actions:

Statin This clinical action was defined by the presence of a Read code indicating prescription of the statin, as shown in appendix E

Aspirin Defined by the presence of a Read code for aspirin, shown in appendix E

I also examined these two clinical actions for 'stable angina and diabetes', but in addition, in line with NICE guidance, I examined the following:

ACE inhibitor Defined by the presence of a Read code for ACE inhibitor or angiotensin II receptor antagonist, as shown in appendix E

5.3.2.6 *Revascularisation of chronic CHD*

In addition to the above medication-related clinical actions for the chronic CHD clinical triggers, I also looked at revascularisation. For both the 'stable angina' and 'stable angina and diabetes' clinical triggers, I examined the following:

PCI This clinical action was defined by the presence in PEDW records of a code (in any position) indicating that the individual concerned underwent a PCI. I have listed the codes used to identify this clinical trigger in appendix E

CABG Similarly, the CABG clinical action relied on OPCS-4 procedure codes in PEDW. Again, I have included the relevant codes in appendix E

Revascularisation In many instances, a PCI or CABG might both be used to manage a patient's disease and achieve revascularisation. I considered the possibility that inequity in the provision of PCIs and in the provision of CABGs might interact to obscure the overall picture. For example, by finding inequity in the use of PCI one might in fact simply be identifying increased use of CABG in more deprived groups, with a consequent reduced need for PCI – reflected in reduced utilisation of PCI. To allow for this possibility, I also included a composite clinical action defined using the above codes for PCI and CABG combined

Revascularisation for patients with CHD is performed either where patients have symptoms unresponsive to optimal medical treatment or

to improve prognosis in those with a substantial burden of ischaemia.[184] CABG is the established treatment, with demonstrated survival benefit; in recent years PCI has increasingly been considered as an alternative.[184]

There has been extensive debate about whether PCI should be considered as equally efficacious (as CABG) in terms of key outcomes (survival, freedom from MI, and freedom from recurrent angina).[184]. In recent years PCI has improved in sophistication (balloon angioplasty, to bare-metal stents, to drug-eluting stents) and complications from the procedure have gone down. At the same time outcomes from surgery have improved, with use of improved medical therapy, anaesthesia, surgical technique, and technical developments such as off-pump surgery.[184]

A 2009 study, which pulled the results from 10 randomised controlled trials, concluded that overall there was no significant difference in the risk of death between those treated with CABG versus PCI (hazard ratio (HR) 0.9; p-value 0.12).[185] In this study, subgroup analysis suggested that those over 64 and diabetics did have significantly improved survival with use of CABG. Evidence from disease registers consistently suggests benefits of between 4 and 5% for CABG over PCI at 3 to 5 years.[184,186–189] In the recent SYNTAX trial (which compared treatment in a much less restricted patients), PCI failed to achieve pre-specified criteria for non-inferiority as compared to CABG.[190].

During the time-period covered by the study I present here, the parity of effectiveness of PCI could have been regarded as a legitimate conclusion on the basis of findings in the literature. For this reason, I included this intervention when examining the clinical trigger for chronic CHD. Clearly, subsequent findings suggest that PCI does not in fact improve outcomes to the same extent as CABG.

5.3.2.7 *Drug management of ACS*

When considering ACSs, I defined three clinical triggers. Because of limitations of the data it was necessary to use as one of these triggers the diagnosis 'old MI'. Codes exist in PEDW for old myocardial infarctions; sometimes Read codes for ACSs appear in GP data. For these situations, I defined a clinical trigger for the situation in which PEDW data suggested an old MI or in which GP data suggested an ACS in the absence of a corresponding in-patient record. The possible classifications of ACSs that might be derived from the data are quite numerous, and include unspecified ACS, MI, unstable angina, ST-elevation

myocardial infarction (STEMI), and non-ST-elevation myocardial infarction (NSTEMI). I discuss this further in section 5.3.6.2. After much exploration of unfeasible alternatives, I settled on a simple three-way classification of ACSs, as follows:

> *Old ACS* To define this clinical trigger, I used a PEDW code for old myocardial infarction and Read codes for ACSs. I have listed the codes used to define these trigger points in appendix E. The indication period for this clinical trigger ended at the date of any subsequent codes for MI or unstable angina, again listed in E. In the event that *old ACS* codes (those related to old myocardial infarction or myocardial infarction recorded only in primary care) occurred after PEDW ACS codes, the implementation algorithm disregarded them. The algorithm also disregarded *Old MI* with an indication period less than one month in duration
>
> *MI* I initiated this clinical trigger on the appearance, in any coding position, of a code for MI in a patient's data. I did not differentiate between NSTEMI and STEMI. Where repeat ACSs occurred, I terminated the indication period for the previous MI or unstable angina clinical trigger and created a new one. When looking at clopidogrel as an action, I terminated the indication period 12 months after the clinical trigger date, as the drug is no longer indicated after that time
>
> *Unstable angina* I defined and implemented this clinical trigger exactly as for MI, with the exception that I used different codes. I show the codes in appendix E

Because of the way that I defined the clinical triggers *MI* and *Unstable angina*, it was possible for one individual to have more than one of these clinical triggers – thus, the unit of comparison here was an *MI* or *Unstable angina* clinical trigger rather than an individual.

For each of the above three clinical triggers, I looked at four clinical actions. I defined and implemented the first three of these, 'statin', 'aspirin', and 'ACE inhibitor' as described in section 5.3.2.5. The fourth was as follows:

> *Beta-blocker* The presence of one of the Read codes listed in appendix E defined this clinical action

In addition, for 'MI' and 'unstable angina' I also looked at:

> *Clopidogrel* This clinical trigger was defined by the Read codes shown in appendix E

5.3.2.8 *Revascularisation of ACS*

For the three clinical triggers relating to ACS, I also looked at revascularisation clinical actions. These three, 'PCI', 'CABG', and 'revascularisation', were defined in the way detailed in section 5.3.2.6

5.3.2.9 *Visualisation of the pathway overview*

I have summarised the set of trigger-actions that I examined in the pathway analysis in figure 5.2. This figure is a schematic representation of the pathway of care for CHD through which an individual might move. A matrix is shown, with the clinical triggers shown across the top of the figure, and the clinical actions to the left. Where clinical trigger-actions combinations are indicated by NICE guidance and where there is sufficient data to address them, I have marked the matrix with a green tick. The coloured boxes represent the different regions of the pathway, as discussed above; the key to these is at the bottom of the figure. For example, from the figure one can see that an ACE inhibitor is indicated in those with stable angina and diabetes, but is not indicated in those with stable angina but no diabetes.

In chapter 9, I have made further use of this approach to summarising the pathway, with a view to aiding presentation of a complex set of results.

Figure 5.2: The pathway from the data perspective

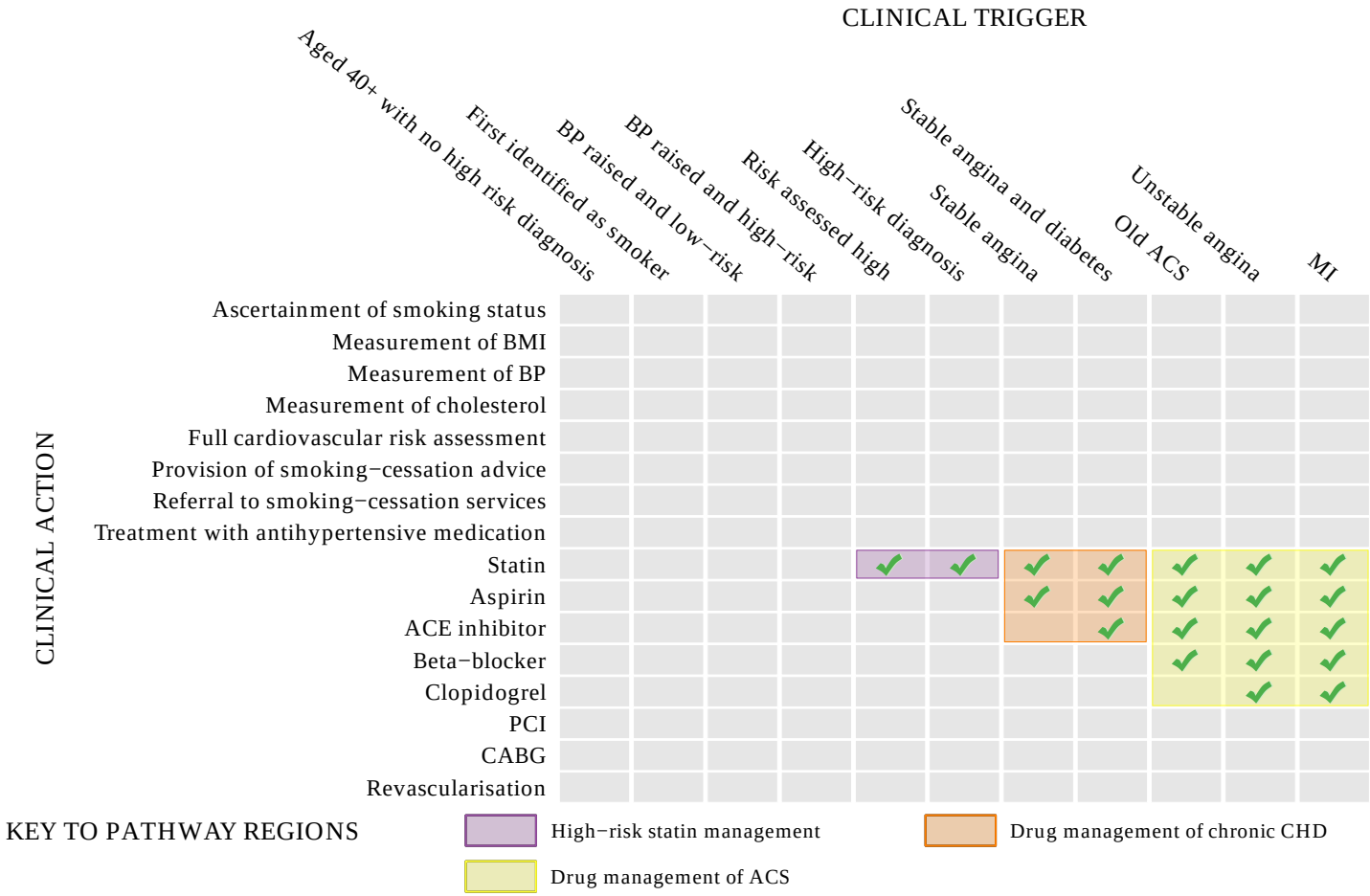
5.3.2.10 *Drug cessation clinical trigger-actions*

I wished to examine for how long drugs that were clinically indicated continued to be prescribed. I devised a measure for this, to be structured like the other trigger-action combinations. I designated the date of the first prescription as a clinical trigger in order to mark the start of the period I wished to measure. Obviously, the first prescription is also a clinical action, but I apply the term clinical trigger here in this restricted way in order to use the same method of analysis and nomenclature as for all the trigger-action combinations.

I looked from the time of the drug prescription being initiated to the last prescription, where this was defined as the point at least 56 days prior to the cohort censoring date for that individual. Thus, to obtain a last prescription date, which for drug cessation clinical trigger-actions counted as the action, I looked for a clear window of at least 56 days (28 days for the last prescription; 38 days clear) between the date of the last prescription and the cohort censoring point for the individual.

A schematic overview of the clinical trigger-actions related to drug cessation is shown in figure 5.3. Here, as before, the diagram represents a matrix of the possible clinical actions I might have considered; those examined are marked with a green tick. Once again, I have illustrated the main regions of the pathway. I did not look at drug cessation for antihypertensive medication, because I judged that doing so would be too difficult, given the permutations of drug treatments that might be used to treat the condition.

Figure 5.3: The pathway from the data perspective: points in the pathway at which drug cessation was examined



5.3.2.11 *Points not included in the the pathway*

Some points in the pathway of care for CHD met many of the criteria for inclusion, but ultimately were excluded from the analysis. This was because insufficient data were available in the routine data on individuals. In particular, I would have liked to examine differences in the medical management of cases of ACS during hospital admissions. These data are not available within the PEDW dataset. Likewise, information on cardiac rehabilitation following ACS was not available to support an adequate analysis.

5.3.3 *Pathway simplifications*

While attempting to address the pathway of care for CHD in the way outlined has advantages, I have made some assumptions and simplifications. In presenting an overview of the pathway, illustrated schematically in the previous section, I have made assumptions about the way in which individuals can move between clinical-trigger states and about what it means for an individual to be at any one place in the pathway at a given time.

When an individual activates a clinical trigger, I have defined them as being in a clinical-trigger state for that trigger from that time point until any stipulated event occurs to terminate the indication period for that clinical trigger. I have simplified the allowable states that an individual might occupy in the following ways:

- An individual's risk cannot return from high risk to low risk state; once an individual is assessed as being at high risk they remain high risk, regardless of subsequent risk assessments
- The clinical trigger 'risk assessed high' is superseded by the clinical trigger high-risk diagnosis and by CHD clinical triggers
- The clinical trigger 'high-risk diagnosis' was superseded by CHD clinical triggers. The list of codes used to define a 'high-risk diagnosis' clinical trigger does not include CHD, although CHD is a condition which indicates that an individual is a high risk: I have dealt in detail with CHD related clinical triggers separately, and to avoid duplication in the analysis, have left CHD codes out of the 'high-risk diagnosis' definition
- 'Stable angina' is superseded by 'stable angina and diabetes', as well as by clinical triggers for ACSs

- 'Stable angina and diabetes' is superseded by clinical triggers for ACSs
- 'Old MI' is superseded by 'unstable angina' and 'MI'. An individual cannot return to the 'old MI' indication state following clinical triggers for ACSs even if the relevant codes occur
- Each new ACS event initiates a new clinical trigger (for 'unstable angina' or 'MI' as appropriate)

Despite efforts to simplify the allowable clinical-trigger states, the pathway overview would still not place the individual at any one time at only one point in the pathway. While many of the indications are mutually exclusive – 'aged over 40 with no high risk diagnosis' and the high-risk clinical triggers or the CHD clinical triggers – others are not. For example, an individual may simultaneously trigger 'Aged over 40 with no high-risk diagnosis', 'First identified as smoker', and 'BP raised and low-risk'. Likewise, 'BP raised and high-risk' can trigger at the same time as 'Risk assessed high', 'High-risk diagnosis', and CHD clinical triggers. With each clinical trigger comes one or more clinical actions. Thus, any one individual, at any given time, is best conceived as having a specific *indication pattern* that might be represented by a selection of ticks in schematic overview (figure 5.2, rather than as being at a particular point in the pathway.

5.3.4 *Overview of programmatic implementation*

I implemented the detail of my approach to clinical-trigger actions and the CHD pathway in a C# program that I wrote to accomplish the task, which I refer to as the derived dataset generator. Its role was to take the cleaned data, generated from the process described in chapter 4, and to run algorithms based on the conceptual methods, details of the CHD pathway, and clinical trigger-action approach that I have outlined above. In subsequent sections, I describe the methods used to accomplish the following:

1. Determine the cohort dates of the individual
2. Extract appropriate clinical trigger-actions for each individual
3. Determine relevant covariates for each clinical trigger-action

I have left discussion of the methods used to analyse the data generated by this program to chapter 6.

The derived dataset generator examined the data for each individual in the dataset in turn, each time making available to its own internal processing algorithms all available:

- Demographic data
- PEDW data
- GP data
- Mortality data

The outputs of the programme were exported to four tables.

Complete set table This table contained one row for every individual who had any data in the original datasets, regardless of whether or not they were included in the final analysis. Keeping such a record was necessary, because in the extract provided to me information was given on many individuals who should not have been included in my dataset. This table contained fields related to the reasons that individuals were either excluded or included in the final analysis.

Individual table This table contained one row for every individual included in the final analysis. It contained fields related to demographic characteristics of the individual (age, sex, deprivation), mortality information (whether the individual died during the cohort period, date of death, cause of death, and related fields), information about individual's LSOA of residence at annual sampling points, and information about the GP practice with which the individual was registered at annual sampling points.

Trigger action table This table contained one row for every clinical trigger-action identified in the analysis. It contained fields relating to the clinical trigger type, clinical action type, action times and related variables, and covariate information at the clinical trigger date.

Risk assessment table This table contained one row for every time point at which a risk assessment could be updated on any individual in the final dataset. It contained fields for the most recent cardiovascular risks available at each time point, whether or not the individual was treated with

antihypertensive medications and statin at each time point, and the results of risk assessments using different risk assessment tools.

5.3.5 *Cohort*

On each individual I needed to determine the time period during which the individual had contributed data to the electronic cohort. I have illustrated the way in which this process was carried out in figure 5.4. For each individual I wrote algorithms to limit the period of observation in line with the available data. I assumed that the maximum observable period for each individual, which I termed the *cohort period*, ran from 1 January 2004 to 31 December 2010. I then checked to see if the individual had died and, if so, when. In the event that the individual had died before 1 January 2004 (something that was possible in my data because I had the lead-in period), I excluded the individual. If the individual had died, and that death took place on or before 31 December 2010, I changed the end date of the cohort period to the date of death and set a variable to register that the reason that the individual had left the cohort was that they had died.

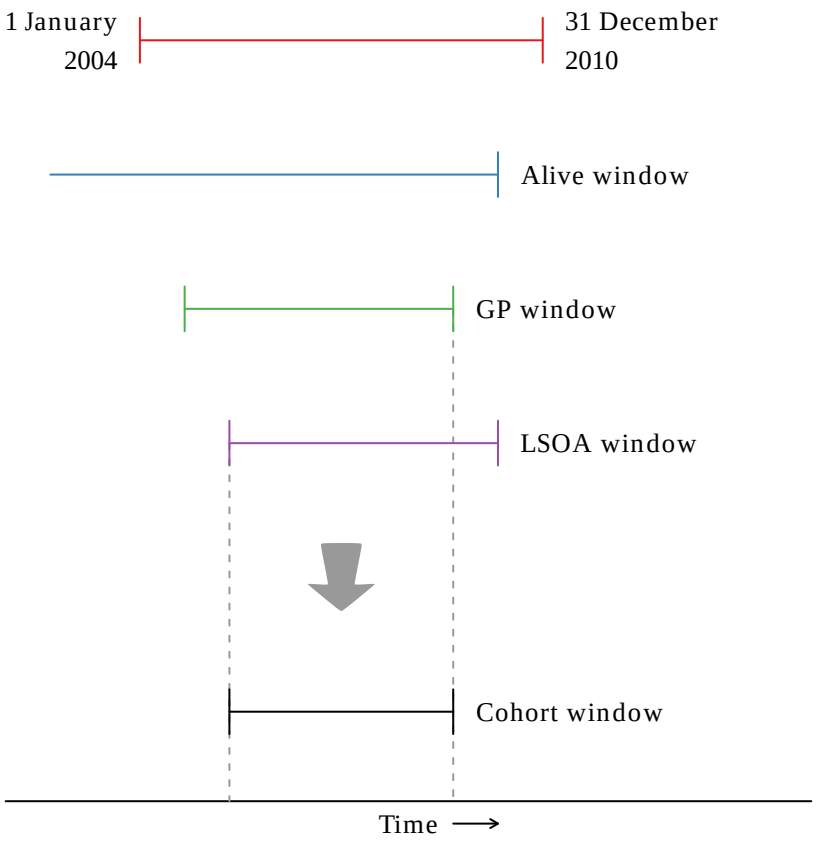
Similarly, I used the information on an individual's GP practice (available on 1 January each year from 2003 to 2010, as discussed in chapter 4) to determine whether an individual had been registered with a SAIL practice. Where necessary, I reset the cohort period start and end dates in line with the available data. As a simplifying assumption, I removed from the analysis individuals with discontinuous GP practice registrations within SAIL GP.

I also examined the time window during which an individual was resident in Wales (based on LSOA at annual time points). While the dates of registration with SAIL practices and LSOA dates were likely to be the same, there was no theoretical reason why this would always be the case. Therefore, I examined LSOA separately, using the approach outlined above for the GP window – this time to produce an LSOA window.

On the basis of these processes I was able to refine, for each individual, the cohort window, a period during which, as illustrated in figure 5.4, an individual was:

- Alive

Figure 5.4: Derivation of cohort window



- Registered with a SAIL GP (subject to the limitations of the annual-time-point approach)
- Resident in Wales (again subject to the limitations of the annual-time-point approach)

I used the cohort window thus derived in subsequent algorithms. For each individual, reclassified the end of the cohort period according to whether they reach the end of the study period or whether they were censored. Censoring occurred either because individuals died or because they left SAIL GP. Because the demography data were simplified, such that LSOA-of-residents and GP were available only at annual time points, some error was inevitably introduced to censoring times for some individuals.

At this point, I also excluded a small number of individuals from the final data where there was no valid date of birth or valid sex.

5.3.6 *Clinical trigger-actions*

In implementing the clinical trigger-actions approach I needed to develop the main algorithm which identified and processed clinical trigger-actions and also processed the covariates at the time of the clinical trigger. I discuss these separately below.

5.3.6.1 *Main algorithms*

Firstly, the main algorithms identified clinical triggers and their subsequent indication periods based on the coding definitions and rules described above. In order to do this, the programme examined each record for the individual, registering both codes that defined a clinical trigger and codes that indicated that the indication period for that trigger had been superseded. In the case of clopidogrel, the algorithm calculated the date 12 months following the clinical trigger and ended the indication period at that time.

Secondly, for each clinical trigger-action combination, the algorithm compiled a table of the relevant clinical actions, together with their dates of occurrence, to inform subsequent processing.

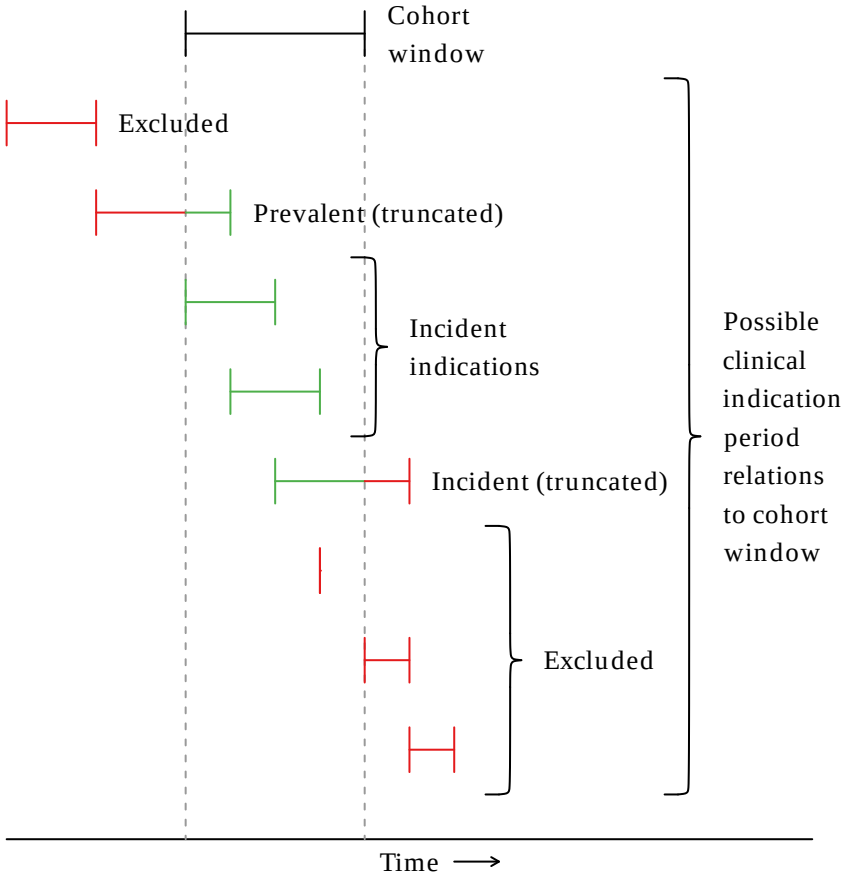
The above information (indication period, and table of actions) was, for each clinical trigger-action combination, passed to the main processing algorithm which then carried out the following:

1. Determined the relationship of the indication period to the cohort window

2. Determined the relationship of clinical actions to the indication period

I show a schematic representation of the first of these processes in figure 5.5. The processing is based on the relationships between the start and finish of the cohort window and the start and finish of the indication period. I illustrate a number of possibilities, and have noted how I handled them. In the event that both the start and end of the indication period occurred before the cohort window, I excluded the clinical trigger-action; where the indication period started before the cohort window but continued into it, I include the clinical trigger-action, but classify it as a *prevalent indication*; where the indication period started on or after the start of the cohort window, I included it, this time classified as a *incident indication*; where the indication period (whether a prevalent or incident indication) continued beyond the end of the cohort window, I truncated the indication period by setting its

Figure 5.5: Relations between the cohort window and the indication period



end date to the end date of the cohort window; where the start date for the indication period occurred after the end date of the cohort window, I excluded the clinical trigger-action.

When looking at drug cessation, I did not look at prevalent triggers, as all drug initiation clinical triggers were by definition incident. In other words, I did not look for or analyse the situation in which an individual had a clinical trigger requiring a drug prior to the initiation period of the cohort window and had begun treatment with the drug.

In examining the relationship between the indication period and the clinical actions, I sought a number of bits of information. Paramount amongst these was the time from the clinical trigger to the first clinical action (if one occurred during the indication period). For every clinical-trigger action I updated two bits of information: the *IsAction* variable, to indicate whether any actions occurred at all during the indication period and the *ClinicalTriggerActionLength* variable, based on the time from the clinical trigger dates to the first clinical action date, set

to the length of the indication period if no clinical action occurred. Where the clinical action was a drug, algorithms also calculated the proportion of the indication window that the individual could have taken the drug for, variable termed *DrugCoverageProportion*. I also coded variables for the number of clinical actions that occurred during the indication period, and for the achievement of the clinical action at various set times throughout the indication period (one week, one month, three months, six months, one year, and three years). When examining clinical trigger-actions related to drug cessation, I used an exactly analogous approach. Here, the clinical trigger was defined by the time point at which the first prescription for the medication occurred; the clinical action was defined by cessation times for the medication. In order to determine the cessation times, I looked for the last prescription occurring at least a defined time period before the cohort end date; the period chosen was 56 days, but I also employ different time periods in sensitivity analysis. The 56 is day figure allows for a three-month gap and three-month prescription to elapse.

Before discussing the ways in which the algorithms captured information on covariates, I detail some of the difficulties encountered in deciding how to handle certain eventualities.

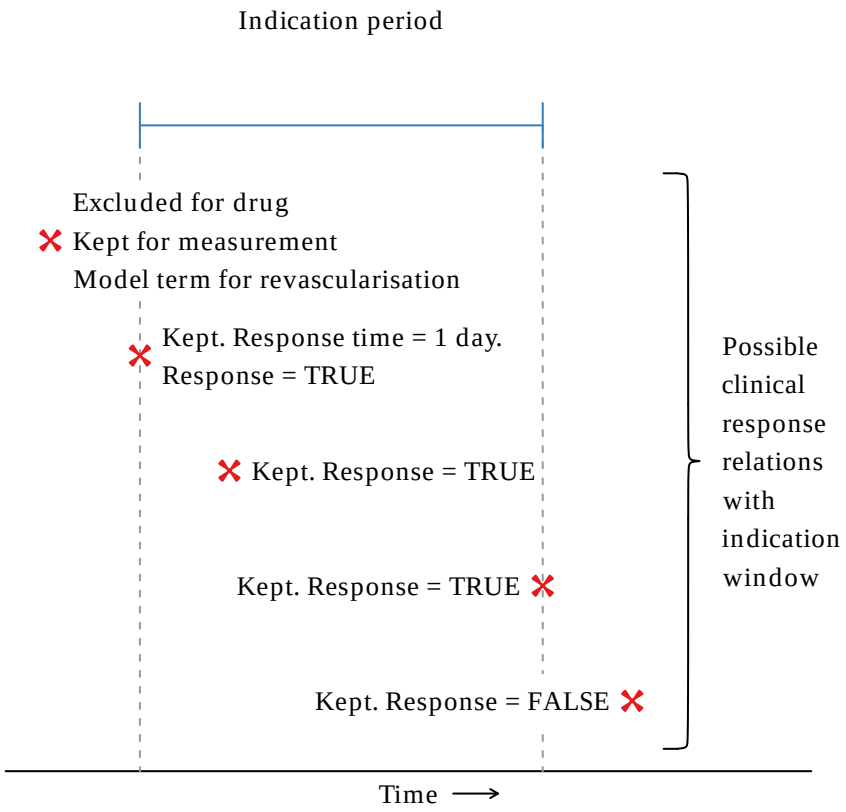
5.3.6.2 *Difficulties*

NICE guidance gives an involved set of definitions of hypertension. These do not naturally fit in with the clinical Read codes. I had to take reasonable steps to identify two situations[183]:

1. An individual with a high cardiovascular risk and a BP greater than 140 systolic
2. An individual with a unknown or low cardiovascular risk with a BP greater than 160 systolic

Available information from Read codes gave systolic blood pressure readings, hypertension diagnoses (where the criteria for the Read code are not known), and information on cardiovascular risk factors. In order to define clinical triggers for hypertension, I needed to decide which risk assessment tool to use, and how to define a raised blood pressure. I used the Framingham non-laboratory risk assessment tool in the primary analysis, but used the older Framingham tool in a sensitivity analysis. In order for an individual to classify as meeting the systolic blood pressure cut-offs, it required three consecutive readings

Figure 5.6: Indication period relations with clinical actions



above the threshold (140 or 160 systolic). I used the hypertension diagnostic codes as markers of blood pressure greater than 140.

Available codes within PEDW from the ICD-10 coding system allow for quite a disparate set of categorisations of CHD. The problem here is that some codes gave only quite general information, such as that an individual had unspecified coronary heart disease, or unspecified acute coronary syndrome; sometimes quite specific categorisation was possible, for example in classifying partial-thickness MI (NSTEMI). I simplified the classification to the following four categories:

> *Stable angina and chronic* CHD I included in this category codes for unspecified CHD, unspecified chronic CHD, stable angina, and also some non-specific codes relating to acute CHD where a definitive ACS could not be identified
>
> *Old* ACS I included in this category PEDW codes for old MI. I also used Read codes suggesting an ACS, where unable to identify a record of ACS from PEDW records
>
> *Unstable angina* I used unstable angina codes from PEDW to define this category
>
> MI I use codes for unspecified MI, NSTEMI, and STEMI to define this category. I also included codes for subsequent MI in this category

The exact codes used for these definitions are shown in appendix E.

A number of considerations motivated this approach. When considering some of the ICD-10 codes which appear in the acute section of the cardiovascular disease chapter, I decided that these codes, though suggestive of ACSs, were insufficient to definitively identify the condition. On the other hand, I did not wish to dismiss this information completely, and so classified these individuals as having CHD but not as having a ACS; I analysed the clinical trigger-actions for these individuals on this basis.

The 'old ACS' category would not be required in an ideal situation. In reality, indications arose within an individual's data that suggested that they had suffered an ACS previously, without the presence of the record of this event itself within the PEDW data. This either arose through the presence of an old MI code in PEDW or through the presence of ACS codes in GP data. While I could not rule out the possibility that these individuals had recently undergone ACSs and that codes had not appeared in the PEDW (either through the event occurring outside Wales, outside the NHS, or through missing data), I

wished to only examine clinical trigger-actions where data suggested they were relevant. Using the old MI category allowed me to look at trigger actions differently for these patients where the date of the ACS was unknown; in particular, I did not look at clopidogrel prescription in these patients.

Initially, I wanted to examine NSTEMI and STEMI separately. PEDW coding did not allow differentiating between the conditions: the majority of events were coded simply as unspecified MI. I settled upon the approach of using a catch-all category for MI.

ICD-10 codes make a distinction between MIs and subsequent MIs, where 'subsequent' implies that the event took place within 28 days of the previous one. The preliminary investigation of this situation suggested that in reality subsequent MI-codes were only preceded by MI-codes a small proportion of the time (about 7%). After considering the possibility of dropping these codes entirely, I settled on the approach of simply using them interchangeably with the non-subsequent variety of MI-code.

In general, the kinds of difficulties discussed here inevitably arise when using routine data. When confronted with them, I have tried to come up with a defensible approach, simplifying where possible, and making explicit what the approach has been.

5.3.7 *Covariates*

Above, I discussed the wish to adjust the analysis of clinical trigger-actions for important covariates that might confound the relationship between socio-economic deprivation and the delivery of healthcare interventions. Using a clinical trigger-action approach, I was faced with decisions about which covariates to include, at which time point I should ascertain the covariates, and how I should define them. In the next sections, I discuss how I addressed these issues. Which defer to chapter 6 discussion of how these covariates were used in statistical models: in this section my aim is to explain how these variables were actually obtained from the data.

To simplify implementation, I set up my algorithms within the derived dataset generated to extract all possible information on covariates, whether or not I would actually employ those covariates for the model for any given clinical trigger-action. The exception to this was that I was unable to extract variables relating to the hospital admission for those clinical triggers that were not based on such an admission.

5.3.7.1 *Time-point of capture*

For simplicity, I always extracted the latest available covariates at the date of the clinical trigger. While it is possible that variables might have changed between the clinical trigger date and any clinical action, in other words time-dependent covariates might have been driving any relationship between socio-economic deprivation and clinical provision, I did not take this approach because of the analytical demands that it would have made on an already demanding analysis.

I ascertained the latest available covariates: that meant that, for example,if a clinical trigger occurred on 1st January 2005, where there has been no BMI recorded since January 2004, I took that most recent value to be the value at the date of that clinical trigger. I set no time limit on the persistence of variables in this way.

5.3.7.2 *Demographic covariates*

For each clinical trigger-action, I recorded an individual's sex, storing the information in a variable related to it. For information on age, my algorithm calculated the age in years at the time of the clinical trigger, generated a variable for this value, and created variables based on it for the 10-year age group and 5-year age group of the individual. I used age as a categorical variable in this way to avoid the issues around checking assumptions of linearity. Clearly, this was a compromise, which involved potentially introducing some bias by collapsing to categories and under adjusting for age.

When looking at deprivation, I used WIMD 2005. For each clinical trigger, I identified the nearest LSOA in time. This was necessary because of the annualised time-points employed for LSOA data. The algorithm then used a lookup table to determine the deprivation quintile and decile of this LSOA.

5.3.7.3 *Supply-related covariates*

I wanted to adjust for some covariates relating to the healthcare supplier for the individual. For GP-related clinical trigger-actions, I looked at the practice at which the individual was registered at the time-point closest to the trigger date, and used the anonymised practice codes that SAIL analysts had provided.

Similarly, for ACS-related clinical triggers, I entered the hospital (provider site code), for the admission in which the ACS occurred. I extracted further information on the nature of the admission: emer-

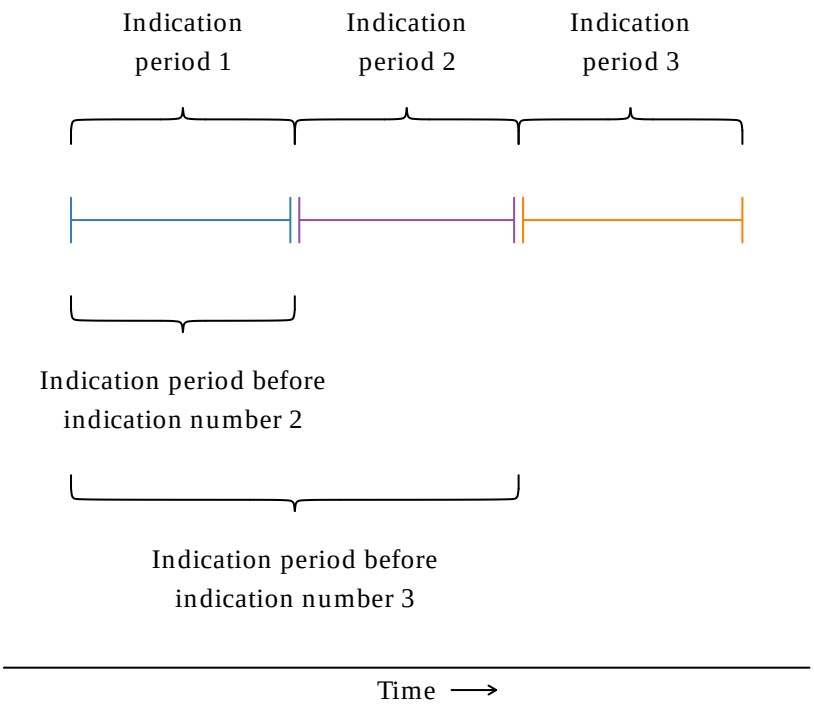
gency, elective or other admission; the specialty the individual was admitted under (cardiology; cardiothoracic surgery; medical specialties; or other). In addition, the algorithm created a variable for the type of hospital in which the admission took place: this was a binary variable, either *Cardiac centre*, if the admitting hospital was a tertiary centre for cardiac care, or *Other centre*, if it was not. I defined tertiary centres as University Hospital of Wales in Cardiff, Morriston Hospital in Swansea, and the Liverpool Heart and Chest Hospital.

5.3.7.4 *Pathway-history covariates*

Figure 5.2 shows that for a number of clinical actions, there are several different clinical triggers. Moreover, it is possible for an individual, at different times, to be in more than one trigger state. For example, the same individual might theoretically have started out with their cardiovascular risk assessed high, have a CVA – moving them to the clinical trigger 'high-risk diagnosis'; subsequently they might develop stable angina ('stable angina' clinical trigger), then diabetes ('stable angina and diabetes' clinical trigger), before having an episode of unstable angina for which they were admitted to hospital ('unstable angina' clinical trigger), followed by an MI ('MI' clinical trigger), with another MI a year later (initiating another 'MI' clinical trigger). For every one of these clinical triggers, statins would have been indicated. By the time of the last MI, that individual would have had six previous clinical triggers to initiate the statin; a statin might have been indicated for several years by that time. Intuitively, this situation is different from that in which an individual has their first MI.

I wished to allow for this kind of situation, without using a time-dependent covariates approach (alluded to above), as many analytical difficulties would result. Instead, I decided to program my algorithms to produce *pathway history variables*: for every clinical trigger action, two were created, the first numbering the clinical trigger; the second gave the time for which the clinical action had been indicated prior to this clinical trigger. I have illustrated the way these variables are derived in figure 5.7. Here, I have shown three clinical triggers and their subsequent indication periods, each of which is conceptualised as pertaining to the same clinical action. As a concrete example, this might represent an individual with stable angina (clinical trigger 1 – 'stable angina'), who developed diabetes (clinical trigger 2 – 'stable angina and diabetes'), who then had an MI (clinical trigger 3 – 'MI'). In each of these situations, guidelines recommend aspirin. The clinical

Figure 5.7: Derivation of pathway history variables



trigger actions are numbered according to chronological sequence. In addition, the algorithm calculates, for every clinical trigger, the time prior to that clinical trigger for which the clinical action in question has been indicated.

I felt when developing methods that this approach provided a more intuitive way of addressing the issue of prior pathway activity (compared say to time-dependent covariates), while still allowing appropriate adjustment for previous activity such that like-with-like comparisons of trigger-action times could be made between deprivation groups. I hoped to capture and allow for knock-on effects in the pathway by this means. Moreover, such an approach has a precedent in semi-Markov models, in which the time an individual has spent in a state is taken account of in calculating probabilities of state transition.[191]

5.3.7.5 *Previous-action covariates*

A further issue that arose with this approach occurred where clinical actions were observed prior to the clinical trigger period. I illustrate this schematically in figure 5.8. After thought, I handled this situation in three different ways, according to clinical action type.

1. For measurement-type clinical actions (measurement of BP, measurement of BMI, measurement of cholesterol, and a full cardiovascular risk assessment), I ignored previous clinical triggers

2. For drug-related clinical actions (treatment with antihypertensive medication, statin, aspirin, ACE inhibitor (including angiotensin II receptor antagonist), beta-blocker, and clopidogrel), I excluded clinical trigger-actions where the action had occurred prior to the clinical trigger date

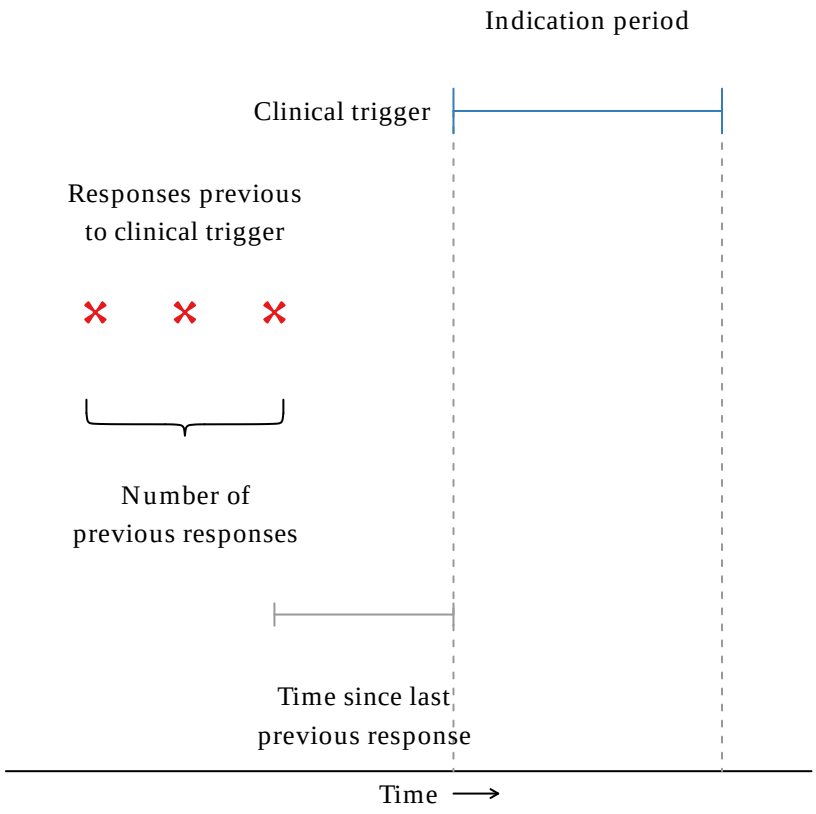
3. For revascularisation clinical actions (revascularisation, PCI, and CABG), I programmed my algorithms to generate a variable to determine the number of previous clinical actions of that type

I discuss in chapter 6, the way in which I used this variable for revascularisation clinical actions when modelling clinical trigger-actions with a time-to-event approach.

5.3.7.6 *Risk and risk factors*

A further set of covariates that I obtained via my algorithms centred around patient cardiovascular risk and risk factors. I obtained, at a

Figure 5.8: Derivation of variables relating to previous actions



time point as close as possible to the clinical trigger date, information on the following:

BP: I wrote an algorithm to classify an individual into one of the following four categories:

- No hypertension
- Undiagnosed hypertension
- Controlled hypertension
- Uncontrolled hypertension

The presence of hypertension was identified on the basis of systolic blood pressure measurement and Read codes for hypertension.

BMI I created a variable based on the most recent reading of BMI at the time of the clinical trigger, placing an individual in one of the following categories:

- Normal or underweight (BMI less than 25)
- Overweight (BMI 25 or more but less than 30)
- Obese (BMI more than 30)

CVD risk I determined cardiovascular risk from risk factors where possible, using the Framingham non-laboratory risk assessment tool. I used the following categories:

- Low risk (cardiovascular risk of less than 20 percent over 10 years)
- High risk (cardiovascular risk of 20 percent or more over 10 years)

In determining this information, I used the same approach as discussed above in section 5.3.2.3.

Smoking status I determined the last known smoking status of the individual on the clinical trigger date, using the approach outlined above in section 5.3.2.2. In doing so, I classified the individual at the trigger date as either a smoker or non-smoker.

Cholesterol:HDL ratio Using a similar approach, I identified the last known cholesterol:high-density lipoprotein (HDL) ratio prior to the clinical trigger date. In doing so, I used both Read codes for cholesterol:HDL and for cholesterol

and HDL separately (in which case I calculated the ratio). I categorised the cholesterol:HDL ratio as:

- Less than 4
- 4 or more

In chapter 6, I discuss the points in the pathway at which I used these covariates. In the implementation of algorithms, I did not limit the extent to which I captured covariates – they were ascertained regardless of whether I would subsequently use them for that clinical trigger-action.

5.3.7.7 *Comorbidity*

I also implemented algorithms to extract a number of important comorbidities for each individual, again at the time point of the clinical trigger. The variables were binary, indicating the presence or absence of the condition. I defined the following variables:

CHD I identified the presence of CHD using the presence of any CHD codes in either PEDW or GP data. The full set of codes used is shown in appendix E. Where none of these codes were present, I assumed that the individual did not have the disease

CVA or TIA I implemented the derivation of this variable in the same way as for CHD, but with a different set of codes, again shown in appendix E

Diabetes I again looked for PEDW and GP codes; the list is shown in appendix E

Other comorbidity I had planned to use the Charlson comorbidity score as a variable to indicate the presence of comorbidities. This score contains CHD, CVA, and diabetes in its scoring system. To avoid duplicating the effect of the presence of these diseases, I redefined a variable to indicate whether or not any Charlson comorbidities other than these three were present for the individual at the time of the clinical trigger. I categorised individuals either as having or not having other comorbidities on this basis. Codes used are shown in appendix E.[192] Though this approach simplified the analysis, collapsing the Charlson comorbidity score to a binary variable involved the loss

of some information and may have resulted in under adjustment and biasing of results. Further, in contrast to the derived binary variable, the Charlson score is an externally validated measure.

5.4 SUMMARY

In this chapter I have discussed the theoretical underpinnings of my methodological approach and have discussed in detail how I implemented algorithms to support this approach. The outputs from these algorithms were data tables suitable for the kind of analysis which would allow me to address the research question for this thesis. In the next chapter, I discuss in detail the nature of that analysis.

6 ANALYTICAL METHODS

6.1 INTRODUCTION

In this chapter, I describe the means by which I addressed the research question using the data tables generated by the processes described in previous chapters. In addition, I outline my methods of descriptive analysis, give details of sensitivity analyses performed to check the impact of major assumptions on the findings, and describe the checks that performed on processes to identify any errors that might have undermined the results.

I have covered this information in five sections:

1. Descriptive data
2. Main analysis of clinical trigger-actions
3. Pathway overview analysis, based on clinical trigger-actions
4. Sensitivity analysis and data checks
5. Software considerations

The aim throughout is to provide the reader with a coherent record of the way in which I performed the analytical processes.

6.2 DESCRIPTIVE DATA ANALYSIS

In presenting descriptive data I aimed to present information on inclusion and exclusion from the dataset, to convey to the reader the important characteristics of the study population, to provide simple summaries of service utilisation in the study population, to present summaries of cardiovascular risk within the study population, and to present an overview of the clinical trigger-actions identified for this population. Carrying out this analysis did not allow me to directly address the research questions, but rather served as a preliminary process. It did inform subsequent data analysis, help identify errors and inconsistencies in the data, and provide an overview of the dataset.

I prepared descriptive tables and figures in order to examine four important areas:

1. Exclusion from and inclusion in the final dataset
2. Population characteristics for key variables, including service utilisation
3. Population distribution of cardiovascular risk
4. Broad scoping of clinical-trigger actions for the study population

6.2.1 *Filtering of SAIL extraction*

I tabulated the number and proportion of individuals excluded from the dataset for different reasons (unrealistic date of birth, invalid sex, and discontinuous GP codes). An exclusion for a discontinuous GP code arose because of the simplifying assumption made: if an individual was registered with a SAIL-submitting practice with a gap in registration (likely to be the result of an individual moving out of SAIL GP, then back in again), I excluded such individuals. This considerably simplified my algorithms.

When presenting descriptive data, I defined annual cohorts, based on the first year of registration for each individual in the cohort. I prepared simple descriptive summaries of the number of individuals in each of these cohorts. As a simplifying assumption, in the main descriptive analysis I used the 2004 cohort; all analyses in subsequent chapters include all individuals contributing time during the cohort.

I presented summary information on the numbers of people leaving the 2004 cohort for different reasons (end of follow-up period, died, and left SAIL GP). Where the cause of an individual leaving the cohort was death, I analysed the numbers of deaths relating to different broad categories of cause.

6.2.2 *Population characteristics for key variables, including service utilisation*

I performed simple descriptive summaries of demographic variables for individuals in the 2004 cohort.

I examined the prevalences of major conditions (CHD, Stable angina, MI, CVA, Diabetes). In order to allow time for diagnostic codes to accrue, I assessed prevalences in 2008. I looked at the proportion of the population at a specified time point (1 January 2008) who had a record of the disease.

The coding definitions used to identify these diagnostic categories are shown in appendix E. I have discussed in section 6.2.4 the ways the prevalences so obtained were used to validate my data against comparable Welsh data. In addition to examining these diagnostic categories, I also summarised the 'other comorbidity' variable that I created based on the Charlson comorbidity index[192], discussed in the previous chapter. This was a binary variable indicating either that individual did or did not have Charlson comorbidities other than CHD, MI, CVA, or diabetes.

Because NHS-service use was the key focus of my thesis, I also examined simple descriptive summaries relating to this in my data. While the main analysis addresses this in far more detail (discussed in section 6.3,) I also prepared these overviews for descriptive purposes for hospital spells per individual for any cause, by deprivation quintile and for the numbers of GP records related to CVD, by deprivation quintile.

In performing this analysis, I looked at the 2004 cohort, and at the numbers of the above events between 1 January 2004 and 31 December 2010. Where individuals were not present for the entire period, I excluded them from these data summaries, as this made the analysis simpler to perform.

I also used the same approach to look at the mean numbers of measurements for key cardiovascular risk factors.

6.2.3 *Assessment of population cardiovascular risk*

I prepared summary information on the cardiovascular risk in the population. The *risk assessment* table that I created using the derived dataset generator program contained information on major cardiovascular risk factors available in my data, treatment with antihypertensive and statin medications, and calculated risks from risk assessment scores. I used this table to produce summaries of risk factor information and cardiovascular risk in the population.

I prepared histograms of population distributions of measured risk factors in the population. The algorithms used to create the summaries looked at the earliest available measurement or reading for an individual at a given age.

6.2.4 *Data validation*

I carried out a number of descriptive analyses in order to check the validity of our data. While I had no control over the set of data processes that resulted in the movement of data from clinical systems into SAIL, it was important to determine the extent to which these processes had properly functioned. I undertook two strands of data checking: the first was intended to demonstrate that our data had been correctly extracted; the second to check that the subsequent processing carried out produced results consistent with external sources.

In the first set of checks, I made comparisons between the data in my tables and compared them with expected volumes of data. I determined the number of individuals over 20 in 2004 (mid-year estimate) in Wales according to ONS census data. I then found the proportion of the Welsh population over 20 present in our dataset in the *demography* table. The logic of my checks was based on the assumption that the proportion of data in the other tables should reflect this proportion of data: thus, if I had 25% of individuals over 20 in Wales in our dataset, one would expect to have about the same percentage of mortality, PEDW, and GP data in my extract. I used the year 2004 for all comparisons.

While I performed checks in this way for the mortality, PEDW, and GP tables, for GP data, I was limited to looking at drug prescriptions, as this was the only data for which I had a good external data source against which to compare numbers (All Wales Prescribing Audit Report data, which gives information on the number of items dispensed – rather than prescriptions written by GPs); for the main groups of drugs in our data, I found the proportion of prescriptions for Welsh residents in 2004 that were present in our data.

This exercise demonstrated initial shortcomings in our data extract, which I were then able to rectify. The extract initially provided by SAIL had ≈44% of Welsh individuals in the demography table, ≈40% of deaths for Welsh individuals, ≈47% of Welsh PEDW episodes, and only ≈29% of drug prescriptions (the exact percentage varying slightly around this figure, depending on drug class). After identifying the causes of these problems, I received a corrected set of tables from SAIL – a proportion of ≈40% of Welsh data being present in each, suggesting that linkages had been correctly performed and that expected volumes of data were present in the underlying datasets in SAIL.

In the second set of checks, I performed a number of simple comparisons against prevalences estimates of clinical conditions in two Welsh datasets: the Welsh Health Survey (WHS) and Welsh QOF data.

First, I estimated point prevalences in the study population for 2005 and 2009, concentrating on major cardiovascular diagnoses – angina, CHD, diabetes, MI, and CVA (including TIA) – and on risk factors.

As comparison data sources, I used the WHS (for the years 2005 and 2009) and Welsh QOF data (again for the years 2005 and 2009).[193] The WHS is a bespoke survey in which self-report questionnaires are administered to a sample of Welsh residents;[193] QOF is based on data collated from primary care providers in Wales. I obtained, where possible, prevalences from these sources for CVDs, diabetes, and important cardiovascular risk factors, with which I compared prevalences from our data.

There was a systematic difference in the denominator populations when calculating the overall prevalence of conditions in the SAIL data compared to QOF: SAIL contained a denominator population of individuals aged over 20; QOF contained all age groups in the denominator. Therefore, I expected slightly higher prevalences in SAIL because I was looking at conditions and risk factors predominantly affecting older age groups (meaning that the numerator would be relatively unaffected).

The WHS contained a question on angina; Welsh QOF did not contain angina prevalence. I compared MI prevalence between our data and WHS for 2005 and 2009. Diabetes and CVA comparisons were possible against both QOF and WHS data, again for 2005 and 2009. Obesity and overweight/obesity prevalences were present in WHS data (for 2009). Smoking data comparisons were made with WHS (2005 and 2009) and with Welsh QOF data for 2009. When examining these data on risk factors, I also determined the proportion of individuals within the dataset for whom the risk factor status was known and on which the prevalence calculation was based.

When making comparisons for prevalence of hypertension, the situation was complicated by the lack of clarity about the definition of hypertension used in comparison data. Hypertension prevalence as recorded in QOF and from WHS were available in 2005 and 2009. I compared prevalences for different hypertension definitions from our data.

6.3 MAIN ANALYSIS OF CLINICAL TRIGGER-ACTIONS

6.3.1 *General principles*

In the previous chapter, I developed the idea of a pathway of clinical care, and described the make up of it. Clinical trigger-action combinations of interest arose at different points in the pathway. In my main analysis, I investigated these in detail.

The points of interest within the pathway that I identified were quite numerous (45 clinical trigger-actions for delivery of healthcare, as well as another 21 related to cessation of medications). Moreover, I wished to be capable of checking the main assumptions made, by performing sensitivity analysis by adjustment (processes that I have described in section 6.2.4). Each of the checks I might perform could require the analyses to be repeated at each point in the pathway. In this situation, I faced a potentially daunting range of analyses to perform. While limiting this to a smaller subset of the pathway was an option, I believed that this would undermine one of the key strengths of this study – my attempt to examine a comprehensive picture of the pathway of care for CHD. I settled on an alternative solution to the problem: I used an automated process.

Automation itself presented a number of challenges. It was difficult to produce code capable of carrying out each of the processes described below, including preparation of basic statistics, more complex models, and graphical output. More importantly, automating processes was a double-edged sword: it allowed me to cope with a large analytical volume, but I knew of the way in which an undiscriminating, algorithmic approach might be too crude to take account of important subtle differences at a point in the pathway – particularly when carrying out model-fitting, which can require an element of human judgement. I was therefore presented with the challenge of developing an automated process, whose finer points of variation could be altered by user specification.

I have described the architecture of my overall solution to these challenges below, involving R and SQL, a settings file in which I was able to specify details of the automated analysis, a variable-selection frame which the user modifies in order to specify model structures, and an automated approach to graphical output.

As for the main descriptive analysis, I took the approach of using embedded SQL code within R, allowing me to connect to the main

SAIL DB2 database, and thus to exploit the strengths of DB2 for manipulation of large datasets while carrying out the statistical and graphical analysis in R.

Throughout the analysis I handled clinical trigger-actions related to drug cessation separately. Likewise, I performed separate analyses for incident and prevalent clinical triggers. While for the most part I was interested in incident clinical triggers, for the clinical trigger based on age ('aged over 40 with no high risk diagnosis'), prevalent results were also important, and so I examined these as well. The derived datasets generator program produced three different clinical trigger-action tables: one based on the use of the Framingham non-laboratory risk assessment tool (which I used in the main analysis), one where algorithms employed the Framingham 1991 original risk assessment tool (instead of the non-laboratory risk assessment tool), and one where the Townsend index of deprivation was used (as opposed to WIMD 2005). I included analyses using the second and third of these tables in my checks on major assumptions, discussed in section 6.2.4.

The main analysis employed the principle of looking at the times from clinical triggers to clinical actions, and comparing these times across deprivation quintiles. When doing this, I wished to take account of important covariates with the potential to influence this relationship, and to look at supply-related variation from practice and hospital as random effects within the model. I also wanted to take account of missing data. In the next two sections discuss the principles I employed to address these requirements.

6.3.1.1 *Principles of frailty models*

The statistical problem with which I was presented in this work was to find an appropriate technique to examine survival times (or times-to-event), while at the same time taking account of the other requirements outlined above. The standard approach for survival analysis is to use the Cox proportional hazards model, a type of survival analysis that allows that censoring (exit of individuals from the cohort for reasons other than achievement of the outcome in question) be taken account of, while allowing that baseline hazard be left unspecified.[194] A standard Cox model has the form:

$$\lambda(t) = \lambda_0(t)e^{X\beta}$$

where $X\beta$ represents a vector of fixed effect; $\lambda(t)$ is the hazard function; $\lambda_0(t)$ is the baseline hazard function. A further requirement of my analysis was that I was able to examine effects from variation at practice and hospital level.[195] The Cox model can be extended to include random effects as well, using the following formula:

$$\lambda(t) = \lambda_0(t)e^{X\beta+Zb}$$

where β represents fixed effects parameters, Zb represents the random effects, and where b is assumed to have a Gaussian (normal) distribution.[196] This mixed effects or frailty model is a kind of cross-classified random effects model that allows modelling of times-to-event with additional examination of area-level effects, modelled as random variables.

A number of assumptions are implicit in the model's use: importantly, the assumption of proportionality – whereby instantaneous hazards for subgroups determined on the basis of each covariate are proportional over time. This is an assumption of convenience to allow estimation of a single summary effect for each covariate. This assumption can be tested (using residual diagnostics tests, often based on Schoenfeld residuals), though for tractability reasons I did not attempt to do this in this work. (I discussed this decision further in section 10.) A further important, though effectively untestable assumption, is that of 'independent censoring' – whereby censoring is non-informative and independent of outcome.

In order to quanitify the variation in survival times attributable to different model components, I considered for simplicity the transformed scale on which fixed and random effects act additively. On this scale, partitioning the variance attributable to different random effects is in principle straightforward, and is independent both of any modelled fixed effects and of the unknown baseline hazard function.

A mixed-effects Cox model can also be written

$$H(T) = \epsilon - X\beta - Zb$$

where β and b are the fixed and random parameters, respectively, corresponding to covariates X and Z. Here ϵ is assumed to have a particular extreme value distribution, and H is an unspecified increasing function that corresponds directly to the (likewise unspecified) baseline hazard. Assuming ϵ has the standard Gumbel (extreme value) distribution, its variance is $\pi^2/6$. In mixed effects models the random

I acknowledge the help and advice that I have had from statisticians in selecting, using, and describing the statistical methods outlined in this section

parameters b are often assumed to have a normal distribution, whose variance σ^2 is to be estimated. This variance can be compared to the residual $\pi^2/6$ in the usual fashion, forming a kind of intraclass correlation coefficient (ICC), for instance

$$\text{ICC} = \frac{\sigma^2}{\sigma^2 + \pi^2/6}$$

This ICC ranges from 0 to 1, with small values indicating that little variation is being explained by the random effects. In subsequent part of this work, I refer to this statistic as the ICC.

The models were implemented using the *coxme* in R, which allows for flexible specification of frailty models.

6.3.1.2 *Principles of multiple imputation*

Problems of missingness arose in our data for two different reasons: firstly, it is likely that some variables that I defined by the presence or absence of clinical codes were, on occasion, missing these codes when they should have been present – resulting in a measurement or misclassification error, which I did not try to address with statistical techniques.

The second type of missingness occurred when values that I knew were relevant for an individual (systolic BP, BMI, cholesterol:HDL ratio, smoking status, admission specialty, and admission type) were absent from an individual's data at a designated time. For these individuals, I used a multiple imputation technique. By doing so, I was assuming that imputing these values for these individuals at these times was meaningful. This assumption seems reasonable in this case, because, even if unmeasured, these individuals could in theory have had such values measured.

In using a multiple imputation technique, I was, when confronted by missing values, trying to express appropriate uncertainty about what those values were.[197] The overarching principle of multiple imputation is to build up a better picture of the things that you do not know, based on things that you do. Chained equations are iterative numerical method that can be used to converge on a valid distribution of missing variables, from which imputed values can then be sampled to generate a number of imputed datasets. These individual datasets are then analysed using standard methods, with pooling techniques used to synthesise results. In a situation where a likelihood analysis would be difficult because of missing covariates, multiple imputation

offers a convenient alternative. It assumes that data are 'missing-at-random' – an assumption that cannot be tested.[198] Other assumptions are also inherited from the underlying models used by the imputation process's model-fitting procedures.

When electing to employ multiple imputation, I was aware that its advantages in allowing appropriate account to be taken of uncertainty relating to missing values and the ability its minimise bias arising from missing data had to be balanced against its limitations: the introduction of additional assumptions, which may be violated; the introduction of additional complexity for those evaluating interpreting the study; the practical difficulties involved in carrying out the approach. Overall, I judged that, in this situation, the advantages outweighed the disadvantages.

6.3.2 *Analytical stages*

6.3.2.1 *Overview of analytical stages*

In overview, the stages of my analysis at each point in the pathway of care were:

1. Obtain descriptive summaries of the main variables
2. Obtain simple descriptive indications of the relationships of the main variables to the outcome (time to clinical action)
3. Create Kaplan-Meier plots for the times-to-event for each of the deprivation quintiles
4. Fit univariate frailty models, taking account of the practice of registration and where appropriate hospital at the time of the clinical trigger, to estimate differences between deprivation quintiles
5. Fit multivariate frailty models, again using practice and hospital at the time of the clinical trigger as random effects, this time also adding in age and sex at the clinical trigger as covariates
6. Fit multivariate frailty model, looking at practice and hospital as random effects, including all other available and appropriate covariates

6.3.2.2 *Clinical trigger-action descriptive data*

I prepared descriptive statistics relating to the clinical trigger-action at each stage of interest in the pathway. I extracted data from the main SAIL DB2 at each point, using an SQL query embedded within R that pulled out data based on the clinical trigger name and the clinical action name. The R function that performed this process, the *ExtractData* function, also performed a number of checks and updates on the data, including formatting variables to the correct data type and, where necessary, generating factor variables so that subsequent models would interpret the variables in the right way.

For each clinical trigger, I determined the number of those with the trigger and the number undergoing a clinical action within the indication period. I presented the numbers and percentages of clinical triggers in each category for each of the variables. I looked at the binary variables sex, smoking status, cholesterol:HDL >= 4, diabetes, CVA/TIA, previous ACS, other comorbidities, and, for clinical trigger-actions where the clinical trigger was MI or unstable angina, whether the admission was at a cardiac centre.

I looked at numbers and percentages for the other non-binary categorical variables. I categorised age at the date of the clinical trigger into five-year age bands, starting with the '35 to 39' category finishing with '85+'. Though there were younger age groups in our data, due to the very small numbers in these categories, I excluded them from my analysis in order to make presentation of data and statistical modelling easier. I looked at deprivation quintile using the WIMD 2005 index: 1 was the least deprived category; 5 the most.

I looked at BMI weight categories (normal or low, overweight, obese, and missing). I used my hypertension categories as created by the algorithms in the derived dataset generator: none, undiagnosed (undiag.), controlled (contr.), and uncontrolled (uncontr.). For MI and unstable angina clinical triggers I also examined categories for admission specialty: cardiology, other medical specialties (med. spec.), other specialties (other spec.), and missing. Likewise, for these I looked at admission type categories: elective, emergency, other, and missing.

I also examined descriptive data relating to my history variables, which were created by the derived dataset generator's algorithms, and which allowed me to take account in the models of previous states that the individual had been in and whether or not the individual had previously received the clinical action. The derivation of these

variables is discussed in section 5.3.7.4. I summarised these in the first instance using histograms, looking at the following variables:

- The indication numbers for the clinical trigger
- Indication days prior to this clinical trigger
- The number of previous clinical actions prior to this clinical trigger
- The number of days since the most recent previous clinical action

6.3.2.3 *Descriptive variable relationships with outcome*

I wished to examine the relationships between the main clinical trigger-action covariates and outcomes. In this context, the outcome was the time to the first clinical action. I calculated rates using a person-years-at-risk (PYAR) approach, expressed as the number of actions per person-year-at-risk. I calculated rates for each of the categories discussed above in section 6.3.2.2.

When looking at history variables and outcomes, I converted the history variables from discrete numerical to categorical variables. For each category for each of these variables, I calculated rates as described above.

6.3.2.4 *Kaplan-Meier plots*

I produced Kaplan-Meier plots for each clinical trigger-action. In these plots, the times to clinical action following a trigger are treated in terms of survival – here survival indicates 'not yet having had the clinical action', rather than true survival. The curves start at 100%, as initially no one has the clinical action. The steepness in decline of the curve indicates the rate at which clinical actions are being provided, taking into account censoring in the data. I presented separates curves for each of the five deprivation quintiles. I did this for each of the clinical trigger-actions of interest and for incident and prevalent clinical triggers.

In order to implement the production of Kaplan-Meier plots in R, I used functions *Surv* and *Survfit* from the *Survival* package. I wrote additional functions to allow me to generate the graphics themselves using the package *ggplot2*.

6.3.2.5 *Univariate modelling*

While also taking account of variations in practice and, where relevant, admitting hospital as random effects, I fitted frailty models with deprivation quintile as the only covariate, and produced HRs for each quintile; quintile 1 (the least deprived quintile) was the reference category. I determined 95% CIs for the HRs.

6.3.2.6 *Models with age and sex added*

I ran a similar set of models at each point in the pathway, this time with additional covariates in the model:

- Age-group in five-year age band at the clinical trigger date
- Sex

Again, I determined HRs, with 95% CIs. I calculated the ICC as described above. For the five-year age bands, I used the '50 to 54' age band as the reference category, because taking reference categories at extremes of the age range led to very large HRs that were difficult to interpret. I used 'Male' as the reference category for sex.

6.3.2.7 *'Complete models'*

I performed a further set of models at each point in the pathway, this time including every covariate for that particular clinical trigger-action that might be relevant. I considered the following covariates (in addition to deprivation quintile, five-year age band, and sex):

- Smoker/non-smoker
- BMI category
- Hypertension category
- Cholesterol:HDL category
- CVA/no CVA (CVA includes TIA)
- Other comorbidities/no other comorbidities
- Diabetes/no diabetes
- Indication number
- Indication years

- Previous action
- Admission method
- Admission specialty
- Cardiac centre
- Practice
- Hospital

For each of these, I determined whether they were potentially appropriate at each point in the pathway. I implemented the approach using a data object held within R, termed the *variable selection frame*. This allowed me to specify, for every point in the pathway, the relevant covariates. I wrote an R function to generate the model formulae (which are used in R to control inclusion of covariates in a model) based on the information in the *variable selection frame*. In specifying covariates, I had to keep, for example, the following considerations in mind: some covariates (admission method, hospital type, specialty) were only available for MI and unstable angina clinical triggers; I only used the 'previous action' covariate for revascularisation clinical actions; some clinical trigger-actions could not have an indication number greater than one or an indication years value other than zero; some clinical triggers ('aged over 40 with no high-risk diagnosis', 'BP raised and high-risk', and 'Risk assessed high') implied the absence of diabetes and CVA.

There is no universally agreed method for selecting variables to include in regression models, and frequently there is a large component of human judgement in the way models are selected: commentators describe model fitting as an art as well as a science. Additional but analogous complications arise in determining how variables ought to be included in the model, and in the selection of interaction terms between variables. In the context of a project in which a large number of models were envisaged with their performance controlled in an automated way, such a situation presented considerable difficulty. The requirement was for a process that made adequate adjustment of comparison between deprivation quintiles with respect to the outcome (times to provision of health care); I wished to account for potential confounders as far as was practicable, but I did not necessarily need to produce the most parsimonious models. As a result, I determined on an approach of minimising human input to model fitting (relying

on specification of covariates whose adjustment made clinical sense), rather than on producing the most statistically efficient models possible. This was a conscious trade-off: detailed human-guided model fitting at every point in the pathway would simply have been impractical; limiting my approach to much more circumscribed parts of the pathway of care would, in my view, have diluted or undermined one of the key strengths of my approach, namely its effort at comprehensiveness.

When producing models based on the available covariates at each point in the pathway, I did, at one stage, implement a systematic data-driven approach, based on the idea of producing models for all possible combinations of available variables, computing the Akaike information criterion (AIC) statistic for each of these, and choosing the model structure with the minimum value. Ultimately I discarded this approach, as the computational implications of it were quite onerous: for example, where 15 potential variables could be considered for the model using this approach, I needed to fit 2^{15}, or 32,768 models, models in order to find the optimal one. Moreover, this does not take account of any interaction terms that might be considered. I settled instead on a pragmatic selection of clinically-reasonable variables, and ignored interaction terms. To do this, I considered each model in turn, and looked at the possible covariates that might be employed. I ensured that I did not include variables that would be nonsensical for that particular model. For example, I did not include smoking status as a variable in 'First smoking' clinical triggers or hypertension category for the hypertension clinical triggers. At all times, I tried to keep in mind which variables would be clinically plausible as relevant for each of the models. I inputted the results of deliberations in the *variable selection frame* object, from which my analytical code was able to construct the required model.

Because I had excluded individuals from the dataset with a missing date of birth, LSOA, or sex, these data were complete for all clinical trigger-actions. As mentioned above, other variables appeared complete, because they were based on the presence or absence of clinical codes.

Missing data arose for some variables and I have discussed the measures used to address this issue in section 6.3.1.2. At each point in the pathway where data were missing, I imputed 5 datasets, performed separate analyses on each of these, and pooled the results. When imputing, I allowed all variables (including the outcome) other than

practice and hospital to contribute to the imputation. I imputed using the 'mice' function from the *MICE* package; I pooled data using the 'pool' function available within the *MICE* package in R; this function does not work automatically on the outputs from 'coxme' models; I therefore wrote functions to extract a variate-covariate matrix and table of coefficients to pass to this function. To pool the ICC, I took the mean of the ICCs for each of the imputed datasets.

Making the assumption of linearity for deprivation quintiles, I performed a simple linear regression model of log hazard ratios across quintiles to derive a slope index of inequality[199] for the provision of clinical actions for particular clinical triggers. I did so using the *lm* function in R. I assumed equal weighting for each of the quintiles, justified on the grounds that the estimated variances across the quintiles were very similar. I present these results in chapter 8.

6.3.2.8 *Presentation of models*

The analytical approach generated a large number of models. I wanted to ensure that these were presented in a consistent way, and in a manner that made it as easy as possible to recognize the point in the pathway. When presenting models, I have given HRs with 95% CI for each variable category. The reference category is always identified with the word 'Reference', with the HR set to 1. The indication years variable is modelled as a continuous variable. The HR here indicates the changing risk for each increase of one year in the variable. Other variables were handled as categorical.

6.4 PATHWAY OVERVIEW ANALYSIS

Because my interest was in the overall pattern of any healthcare inequity by deprivation, I wished to amalgamate these results in such a way as to make it possible to look across the pathway of care. Without doing so, I felt that the overall picture would be overwhelmed by detail.

To do this, I made comparisons between deprivation quintile 5 and deprivation quintile 1, using the HR and its p-value, as generated by the models described above. In other words, I reasoned that systematic healthcare inequity across the pathway would be likely to be manifested in a simple comparison between quintile 5 and quintile 1. Moreover, I thought that any general pattern in these comparisons would be most easily identified using a graphical summary.

I wrote R functions to store the outputs from frailty models in data objects within R, which I called the *results frames* – one of these was for the main analysis, the other for the drug cessation analysis. For each clinical trigger-action and for each model (univariate, age-sex-deprivation, complete model), I entered the quintile 5:quintile 1 HR and the p-value (as well as some other relevant model outputs) into the results frames.

I used a separate set of R functions to produce graphical summaries based on the data held within the result frames and on the pathway diagrams previously developed to show the points on the pathway that I was examining.

At each point, I wrote a function that examined the HR and p-value. Where the p-value was less than 0.05, I entered the HR in the pathway box relevant to that clinical trigger action; I shaded the box dark green if the hazard ratio suggested favourable provision of care in quintile 5; I shaded box dark red if the hazard ratio suggested favourable provision of care in quintile 1. Where the p-value was greater than or equal to 0.05, I shaded the box light green if the hazard ratio suggested favourable provision of care in quintile 5 (at a non-statistically significant level) and light red if the hazard ratio suggested favourable provision of care in quintile 1 (again at a nonstatistically significant level). Using this approach, I was able to generate graphical summaries of the pathway of care for different model types.

In presenting the results in overview, I employed the pathway diagram, which used a matrix approach to demonstrating the pathway of care. The approach throughout this chapter was based on using summary information from the models described in the preceding chapter and those contained in the appendix to give overviews of what was happening in the pathway as a whole. For each of these pathway overviews, I employed a consistent presentation system. I used a colour-coding system within the pathway-overview diagrams, with the four colours used indicating the following:

Dark red A statistically significant result for the hazard ratio comparing quintile 5 with quintile 1 which suggests that the hazard ratio favours quintile 1 in terms of provision of healthcare at that point in the pathway

Dark green A statistically significant result for the hazard ratio comparing quintile 5 with quintile 1 which suggests that the hazard ratio favours quintile 5 in terms of provi-

sion of healthcare at that point in the pathway

Orange A non-statistically significant result for the hazard ratio comparing quintile 5 with quintile 1 which provided limited evidence that the hazard ratio favours quintile 1 in terms of provision of healthcare at that point in the pathway

Light green A non-statistically significant result for the hazard ratio comparing quintile 5 with quintile 1 which suggest that the hazard ratio favours quintile 5 in terms of provision of healthcare at that point in the pathway

Statistical significance throughout was assessed at the 5% level. In addition, I wanted to look at the HRs themselves, as their size indicated the meaningfulness of any difference. Where results were statistically significant for the HR comparison between quintile 5 and quintile 1, I included the HR itself at the relevant point in the pathway (HR comparing quintile 5 to quintile 1, with quintile 1 as the reference category).

For the main overview analysis I generated the following summaries:

- Univariate frailty models for main clinical trigger-actions
- Univariate frailty models for drug cessation clinical trigger actions
- Frailty model for deprivation, age, and sex for main clinical trigger actions
- Frailty model for deprivation, age, and sex for drug cessation clinical trigger actions
- Frailty model using the complete set of available variables for main clinical trigger actions
- Frailty model using the complete set of available variables for drug cessation clinical actions

For each of these main overview analysis, I used the non-laboratory Framingham risk-assessment tool. I used incident definitions for clinical triggers. I included practice, and, where appropriate, hospital as random effects terms in the model.

6.5 SENSITIVITY ANALYSES

In the analytical processes outlined above, I made several assumptions. For example, in the main analysis I looked only at incident clinical triggers, I used a drug cessation definition based on an 56-day lapse, I used the Framingham non-laboratory risk assessment tool, and so on. I wished to check the sensitivity of the results to important assumptions. I did this at the level of the entire pathway, looking at the differences in graphical summaries across the pathway care when these assumptions were adjusted.The methods used in the sensitivity analyses were identical, being implemented with the same code, the only difference being the changes made to the underlying assumptions.

With respect to checking the effects of examining incident, as distinct from prevalent, clinical triggers, I was particularly interested in the effects on clinical trigger-actions in which the clinical trigger was 'aged 40 and over with no high-risk diagnosis'. Because of the way this clinical trigger was defined, individuals undergoing an incident clinical trigger during the period of observation would by definition always be in the five-year age-band '40 to 45'. In examining prevalent figures as well, I was also able to look at potential differences in measurement and risk assessment in older age groups.

The choice of risk assessment tool that defined high risk was an important assumption, because it not only affected the rate of clinical action ('full cardiovascular risk assessment'), but also affected the time-point at which some clinical triggers occurred ('BP raised and low-risk', 'BP raised and high-risk', and 'risk assessed high'). I therefore ascertained the effect of using a different risk assessment tool in defining clinical triggers and clinical actions, again with a view to determining whether such a change would affect my main conclusions.

6.6 SOFTWARE CONSIDERATIONS

I performed the analysis using the statistical software package R (version 2.13). This software was available within the SAIL Gateway – the remote access facility for the SAIL databank. This software has been widely used by researchers in statistics, epidemiology, and related fields. It is freely available, and comes with a number of user-contributed add-on packages. In performing my analysis, in addition to using the base packages that shipped with the main installation of R, I also used a number of these:

RODBC Used for connection from R to the SAIL DB2 databank

Survival; coxme Used for time-to-event analysis and Kaplan-Meier plots

MICE Used to perform multiple imputation with chained equations

ggplot2 Used for generating plots

grid; gridExtra Used for the generation of general graphical output (other than plots)

RColorBrewer; stringr Used for formatting colour and text output

Reshape2; plyr Used for manipulating data

While R was extremely useful for data manipulation, statistical analyses, and generation of graphical output, its use did present some difficulties, the main weakness being handling very large data tables – something with which I had to contend. With a view to using R in its areas of strength, while at the same time avoiding this weakness, I took the approach of extracting data as and when needed from the SAIL DB2 databank using a direct connection from R – something that is possible with the *RODBC* package. This allowed me to write SQL queries that I embedded in R code enabling me to take advantage of the superior capabilities of DB2 in manipulating large datasets while at the same time retaining the advantages of using R.

6.7 SUMMARY

In this chapter, I have detailed the methods performed my main analyses using the data tables generated from the processes described in the preceding two chapters. In the next three chapters, I present the findings from this analysis.

7

DATASET OVERVIEW AND DESCRIPTIVES

In this chapter, I have a number of specific objectives, each based around the presentation of descriptive statistics. Firstly, I provide an overview of our dataset; here I examine inclusion and exclusion in our cohort, as well as looking at entry into the cohort and at censoring events. I then discuss the distinction between observations of individuals in in this cohort and the actual derivation of clinical trigger-actions on these individuals.

In subsequent sections of this chapter, I present descriptive analyses of the characteristics of the individuals included in our cohort and characterisation of important covariates used in later models, including examination of risk factors and risk. I examine broad patterns of healthcare utilisation in different deprivation quintiles. I show the results of a simple validation of our data against external sources. In the last section of this chapter, I examine mortality in our data, particularly with respect to CHD mortality by quintile.

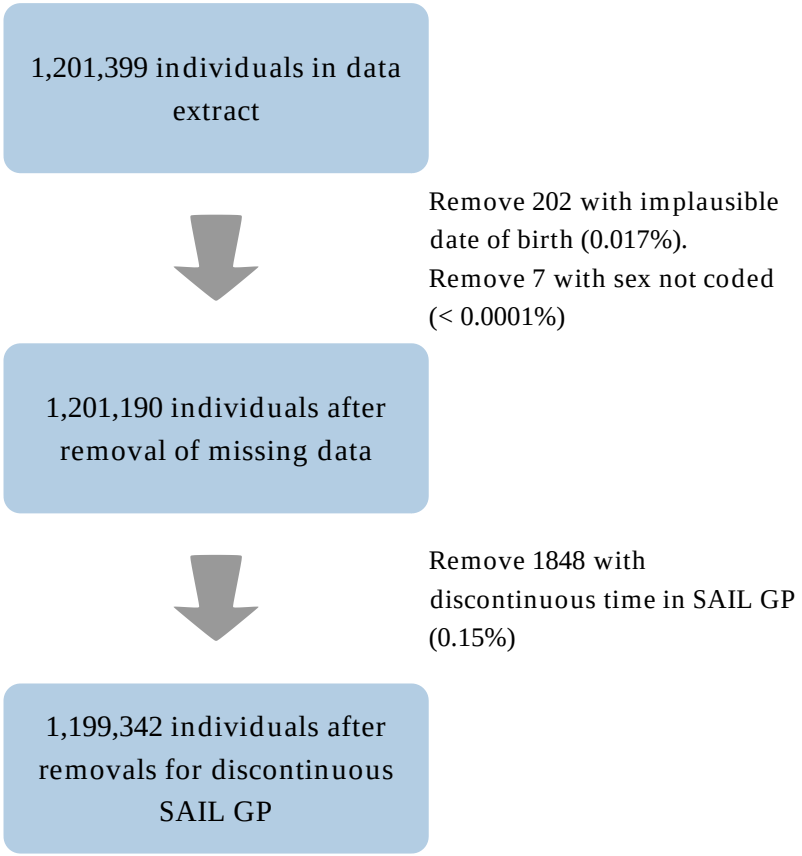
7.1 DATASET OVERVIEW

I make a basic distinction in my analysis between data relating to the cohort on whom it was possible to make observations, and the data on clinical trigger-actions identified by observing the individuals in that cohort. To make what follows readily comprehensible, I outline in this section the broad overview of the dataset, and seek to make clear this distinction.

In figure 7.1, I show schematically the means by which our dataset was filtered, using the algorithms to identify individuals in our cohort presented in chapter 5. I started with 1,201,399 eligible individuals in the extract. After removals for implausible date of birth, because sex was not coded, and because of discontinuous time in SAIL GP, there were 1,199,342 individuals left in the cohort (as summarised in figure 7.1).

Because of the annualised time-points simplification of underlying LSOA and practice data, individuals were constrained to enter our cohort on 1 January of a year between 2004 and 2010. The majority of individuals were present in 2004 (924,068), with a generally declining

Figure 7.1: Individuals excluded from the dataset



addition of individuals at annual time-points thereafter. (As time went on, the number of individuals moving into areas served by SAIL-submitting practices was drawn from a decreasing pool of individuals aged greater than 20 in 2011 – accounting for the decreasing numbers entering our cohort over time). In table 7.2, I show the number of

Table 7.1: Numbers of individuals who appear in the dataset from different starting years

Year	Number
2004 or earlier	924068
2005	57246
2006	48082
2007	47904
2008	54020
2009	43268
2010	24754
TOTAL	1199342

individuals ending their time in the cohort for different reasons. The majority, 964,940 (80.4%), reached the end of the designated follow-up period for the study (31 December 2010); a further 144,576 (12.5%) left SAIL GP (either because they left a SAIL-submitting practice, left a Wales LSOA, or both). There were 89,826 (7.4%) individuals in the cohort that died. By following through time the cohort of 1,199,342

Table 7.2: Number of individuals ending their time in the cohort for different reasons

Reason for end	Number
End of follow-up period	964940
Left SAIL GP	144576
Died	89826
TOTAL	1199342

individuals, using the algorithms described in chapter 5, I could identify clinical triggers relevant to my analysis of the pathway of care for CHD. I show the numbers of clinical triggers identified in table 7.3. For several of these clinical triggers I examined more than one clinical action – thus my analysis of later chapters actually takes account of more clinical trigger-actions than there are clinical triggers shown in

table 7.3. For example, in individuals with the clinical trigger 'MI', I looked at clinical actions 'Statin', 'Aspirin', 'ACE', and others.

In table 7.3, I show the numbers of incident clinical triggers (those arising during the period of observation) and prevalent clinical triggers (those already present at the start of the study – identifiable on the basis of lead-in data). Generally, there are more triggers related to primary prevention (clinical triggers in individuals who do not have CHD) than to established CHD. The balance between incident and prevalent triggers varies according to trigger: in particular, the 'Aged over 40 with no high risk diagnosis trigger' has many more prevalent triggers, because of the number of individuals already aged 40 or more at the time the study started. I present the detailed analysis of the clinical triggers shown in table 7.3 and the relevant clinical actions in chapters 8 and 9. Here the aim is to make clear that the existence of these clinical triggers was determined by observing the individuals in our cohort throughout the period of observation for each individual.

Table 7.3: Numbers of each different kind of clinical trigger (according to incident and prevalent definitions) for individuals in the final dataset

Clinical trigger	Number (incident)	Number (prevalent)
Aged over 40 with no high risk diagnosis	122486	491886
First identified a smoker	96422	238181
BP raised and low-risk	14478	14531
BP raised and high-risk	106520	85282
Risk assessed high	120472	102903
High-risk diagnosis	47338	59063
Stable angina	19039	30014
Stable angina and diabetes	8988	7492
Old ACS	4288	19198
Unstable angina	13954	4988
MI	20542	6468
TOTAL	574527	1060006

7.2 POPULATION CHARACTERISTICS FOR KEY VARIABLES

In this section, I present descriptive results in three main areas: demographic characteristics, prevalences of major conditions and risk factors, and simple measures of health care utilisation. For simplicity, for the first and last of these I have looked only at individuals present in the dataset from 2004 onwards.

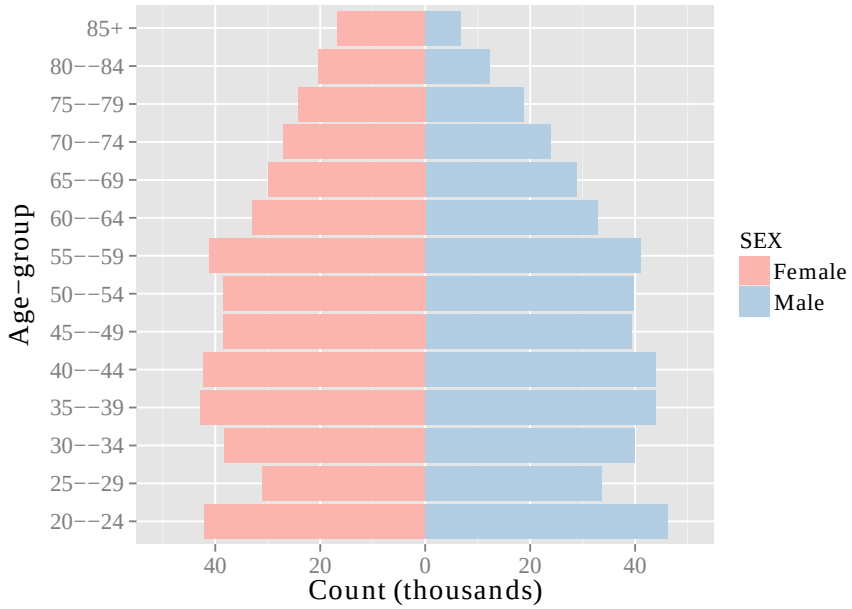
7.2.1 *Demography*

Table 7.4: Population of the 2004 cohort by age and sex

Age	Male	(%)	Female	(%)	Person	(%)
<20	3325	0.70	3896	0.80	7221	0.80
20–24	46289	10.20	42062	9.00	88351	9.60
25–29	33661	7.40	30993	6.60	64654	7.00
30–34	39920	8.80	38282	8.10	78202	8.50
35–39	43839	9.60	42778	9.10	86617	9.40
40–44	43844	9.60	42267	9.00	86111	9.30
45–49	39298	8.60	38522	8.20	77820	8.40
50–54	39709	8.70	38560	8.20	78269	8.50
55–59	41107	9.00	41051	8.70	82158	8.90
60–64	32913	7.20	33027	7.00	65940	7.10
65–69	28867	6.40	29963	6.40	58830	6.40
70–74	23942	5.30	27030	5.80	50972	5.50
75–79	18690	4.10	24236	5.20	42926	4.60
80–84	12261	2.70	20307	4.30	32568	3.50
85+	6677	1.50	16752	3.60	23429	2.50
All ages	454342	100.00	469726	100.00	924068	100.00

I show the age and sex distribution of individuals present in our final dataset from 2004 onwards in table 7.4. I present the same information graphically in figure 7.2, in the form of a population pyramid. Ages were shown in five-year age bands. Though our cohort looked at individuals aged 20 and over, some individuals were younger than this in 2004, but they would turn 20 before 2011, thus allowing them to contribute time towards the study later. In all, 924,068 individuals were present in the dataset by 2004.

Figure 7.2: Population pyramid showing age and sex breakdown for individuals in the 2004 cohort



In table 7.5, I present similar information to that shown in table 7.4, but this time data related to the whole of Wales from mid-2004 (based on mid-year population estimates from ONS). In our cohort, I had slightly higher proportions of individuals in the younger age bands (20–24, 25–29, 30–34, 35–39) compared to Wales as a whole. For example, 9.6% of individuals were in the 20–24 age band in our SAIL cohort, compared to 8.4% for Wales. As a result, the SAIL cohort contained a slightly smaller proportion of individuals in the age bands 40–44 and over.

In table 7.6, I show the numbers of individuals in each of the WIMD 2005 deprivation quintiles. Here, as throughout, quintile 1 was the least deprived quintile; quintile 5 the most. Fewest individuals appeared in quintile 5 (171,428). Quintile 3 contained the most individuals, with 212,059. Quintile 1 had the second largest number of individuals, with 197,491, followed by quintiles 4 and 2 with 172,995 and 170,095 individuals respectively. In table 7.6, I have also shown the total numbers in the Welsh population in each of the WIMD 2005 deprivation quintiles according to estimates for 2004. The highest proportion of individuals are from quintile 3 (35.3%), falling to a minimum in quintile 2 (28.4 latex percent). It should be noted that these figures represent the proportion of the population in each quintile in the total population of Wales – proportions of the Welsh population

Table 7.5: Mid-year estimates for the population of Wales for the year 2004, by five-year age band, and sex

Age	Male	(%)	Female	(%)	Person	(%)
20–24	93833	8.80	92999	8.00	186832	8.40
25–29	79121	7.40	79331	6.80	158452	7.10
30–34	91465	8.60	96209	8.30	187674	8.40
35–39	103582	9.70	108570	9.30	212152	9.50
40–44	103928	9.80	108364	9.30	212292	9.50
45–49	94205	8.80	97525	8.40	191730	8.60
50–54	94134	8.80	96993	8.30	191127	8.60
55–59	101256	9.50	103670	8.90	204926	9.20
60–64	81992	7.70	84548	7.30	166540	7.50
65–69	70416	6.60	74689	6.40	145105	6.50
70–74	57903	5.40	67229	5.80	125132	5.60
75–79	45084	4.20	60034	5.20	105118	4.70
80–84	30615	2.90	51152	4.40	81767	3.70
85+	16942	1.60	42272	3.60	59214	2.70
All ages	1064476	100.00	1163585	100.00	2228061	100.00

Table 7.6: The number of individuals in each of the WIMD quintiles in the 2004 cohort (quintile 1 is least deprived)

Quintile	Number	Number in Wales	Proportion
1	197491	590392	33.5
2	170095	598291	28.4
3	212059	599943	35.3
4	172995	584487	29.6
5	171428	570350	30.0
TOTAL	924068		

aged 20 and over would obviously be higher. The overrepresentation from individuals in quintile 3 is a reflection of the lack of geographical representativeness of the sample with respect to Wales overall, discussed further below, and shown in table 7.7. These numbers were broken down into population pyramids, shown in figure 7.3; again, individuals aged less than 20 were not included as this was a very small group. Arguably, the more deprived quintiles had a more classic 'pyramidal' shape, with a high proportion of individuals in the younger age groups and a steeper drop-off in numbers with increasing age, leaving a smaller proportion of individuals in the older age groups; similarly, the less deprived quintiles maintained more of the bulge in population in middle-aged age bands.

It was known that different local authority populations were differentially represented in the SAIL databank. In table 7.7, I show the numbers of individuals in the final dataset from each of the local authority areas in Wales. Swansea local authority area contains the most individuals (172,628), followed by Neath Port Talbot (102,160), and Carmarthenshire (88,636). Each of these local authorities had over ten times as many individuals in the dataset as the two local authorities with fewest individuals – Monmouthshire (1898) and Denbighshire (5097). Other local authorities had intermediate numbers of individuals in the dataset.

Figure 7.3: Population pyramids showing age and sex breakdown for individuals in the 2004 cohort by quintile

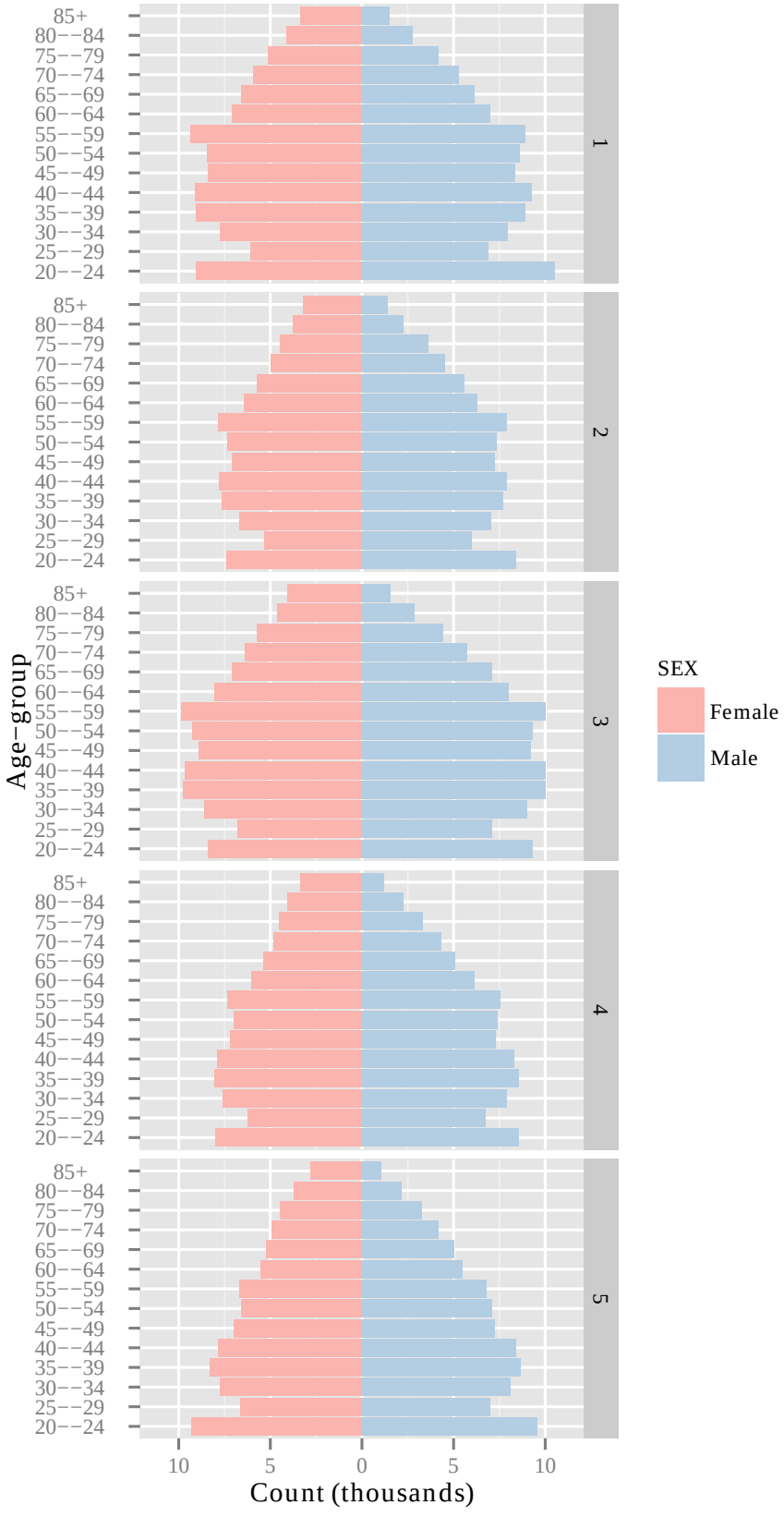


Table 7.7: Number of individuals in the 2004 cohort, by local authority

Local authority	Number in SAIL	Number in ONS	Percentage in SAIL
Swansea	172628	228176	75.70
Neath Port Talbot	102160	317099	32.20
Carmarthenshire	88636	137144	64.60
Cardiff	85158	177487	48.00
Bridgend	79719	131947	60.40
Caerphilly	47566	172361	27.60
The Vale of Glamorgan	47236	75775	62.30
Ceredigion	41917	122101	34.30
Isle of Anglesey	31526	118721	26.60
Gwynedd	30928	233971	13.20
Pembrokeshire	28311	116428	24.30
Conwy	26426	112272	23.50
Powys	23805	68753	34.60
Rhondda Cynon Taff	23061	129568	17.80
Newport	21818	90516	24.10
Torfaen	18176	139316	13.00
Flintshire	13870	149681	9.30
Wrexham	13135	129005	10.20
Merthyr Tydfil	11144	69242	16.10
Blaenau Gwent	9853	56020	17.60
Denbighshire	5097	94010	5.40
Monmouthshire	1898	87829	2.20
TOTAL	924068	2957422	31.20

In the same table, I also show the number of individuals resident in each Welsh local authority as indicated by population estimates for the year 2004. I have also indicated the percentage of this population present in our cohort for that year. The local authorities with the greatest proportion of individuals within our cohort were concentrated in south-west Wales: Swansea (75.7%), Bridgend (60.4%), and Carmarthenshire (64.6%). Coverage in Denbighshire and Monmouthshire was lowest, at 5.4% and 2.2% respectively. While the 2004 cohort represented 31.2% of the Welsh population overall, at local authority level coverage was disproportionately higher in south-west Wales.

7.2.2 *Covariates overview*

In this section, I present an overview of the clinical covariates used in subsequent chapters in order to attain insight into their broad distribution within the general population. In the below tables the time point for both the numerator and the denominator was 1 January 2008, a time close to the midpoint of the designated observation period. For each of the main covariates, I present simple point prevalences (for categorical variables) or means (for continuous variables).

In addition, I include in the current section a more in-depth description of the distributions of major cardiovascular risk factors in our study population, based on information in the risk assessment table, with a view to informing subsequent discussion of the drivers of any inequity in CHD outcomes. Because the presentation of risk factor results was not the main focus of my analysis, I have limited what I present. For most risk factors (BMI, systolic blood pressure, and cholesterol:HDL ratio) and for assessed cardiovascular risk, I have chosen to look at one age band only (60–64). Doing so simplified the presentation and allowed me to disregard differences in the age-structure of the different quintile populations as drivers of difference. Moreover, the patterns for this age-band were reproduced, in broad terms, for other age-bands. I decided in favour of this approach, as opposed to an approach using adjustment, to avoid the possibility that in-depth analysis here would distract from the main analysis for the project.

7.2.2.1 *CHD and comorbidities*

In table 7.8, I show the numbers of individuals with CHD of any type (including previous ACS) by quintile. While the absolute number

of individuals with CHD was highest in quintile 3 (16,000), taking account of the different denominator populations, the unadjusted point prevalence was highest in quintile 5 (7.72%), with a declining prevalence as deprivation decreased, falling to 5.96% in quintile 1. The overall prevalence of CHD in the cohort was 6.91%. In table 7.9, I show

Table 7.8: Point prevalence of CHD in 2008, by quintile

Quintile	Number	Denominator	Prevalence (percent)
1	12946	217354	5.96
2	12248	185688	6.60
3	16000	229861	6.96
4	14049	188608	7.45
5	14343	185891	7.72
All quintiles	69586	1007402	6.91

prevalence of CHD by age and quintile in 2008, from which table it is clear that prevalence increases steeply from age 50 onwards; prevalence is higher in more deprived quintiles, with relative differences quite marked in the middle age-groups (for example prevalence is double in quintile 5 compared to quintile 1 in the 50 to 59 age-group).

Table 7.9: Point prevalence (%) of CHD in 2008, by age-group and quintile

Age-group	1	2	3	4	5
20–24	<0.05	<0.05	<0.05	0.1	<0.05
25–29	0.1	0.1	0.1	0.1	0.1
30–34	0.1	0.1	0.2	0.2	0.2
35–39	0.2	0.2	0.3	0.3	0.6
40–44	0.5	0.5	0.7	1	1.2
45–49	1.1	1.4	1.6	2.2	3
50–54	2.4	2.7	3.2	4.7	5.5
55–59	4.5	4.9	5.5	7.1	9.1
60–64	7.4	8.8	9.5	11.9	13.6
65–69	12.3	13.5	15.3	17.9	19.1
70–74	17.5	19.6	20.4	22.4	24.3
75–79	22.6	24.3	24.8	27.1	27.6
80–84	26.4	27.3	27	29.7	30.7
85+	27.9	29.2	28.9	29.2	30.1

I show in table 7.10 numbers and prevalences for individuals with a previous ACS. Here, a similar pattern emerged: the highest prevalence was in quintile 5 (3.62%), declining with decreasing deprivation to a minimum in quintile 1 (2.71%). Overall, 3.15% of individuals within the cohort had had an ACS.

Table 7.10: Point prevalence of previous acute coronary syndrome in 2008, by quintile

Quintile	Number	Denominator	Prevalence (percent)
1	5887	217354	2.71
2	5398	185688	2.91
3	7286	229861	3.17
4	6485	188608	3.44
5	6724	185891	3.62
All quintiles	31780	1007402	3.15

Prevalence by age-group and quintile is shown in table 7.11. As with CHD overall, prevalence rises steeply from the middle age-groups onwards; again prevalences are more than double in quintile 5 compared to 1 in some middle age-groups.

Table 7.11: Point prevalence (%) of previous acute coronary syndrome in 2008, by age-group and quintile

Age-group	1	2	3	4	5
20–24	<0.05	<0.05	<0.05	<0.05	<0.05
25–29	<0.05	<0.05	<0.05	<0.05	<0.05
30–34	0.1	0.1	0.1	0.1	0.1
35–39	0.1	0.1	0.2	0.1	0.3
40–44	0.3	0.3	0.3	0.6	0.6
45–49	0.6	0.6	0.8	1.1	1.5
50–54	1.2	1.3	1.5	2.3	2.8
55–59	2.1	2.3	2.7	3.5	4.4
60–64	3.4	3.7	4.5	5.3	6.2
65–69	5.2	5.7	6.7	7.9	8.7
70–74	8.2	8.7	9.2	10.3	11.5
75–79	10.3	10.4	11.3	12.5	12.7
80–84	12.1	12.7	12.3	13.5	14.4
85+	12.3	12.8	13	13.3	13.6

In table 7.12, I present figures for the number and prevalence of CVA/TIA in the SAIL cohort. Again, prevalence declined with decreasing deprivation: in quintile 5 prevalence was 3.16%, declining to 2.75% in quintile 1. Overall prevalence was 2.98%. From table 7.13, the

Table 7.12: Point prevalence of previous CVA/TIA in 2008, by quintile

Quintile	Number	Denominator	Prevalence (percent)
1	5980	217354	2.75
2	5389	185688	2.90
3	6942	229861	3.02
4	5824	188608	3.09
5	5880	185891	3.16
All quintiles	30015	1007402	2.98

relationship of CVA with age and increasing deprivation emerges – similar to the pattern seen for CHD. Again, relative prevalences are substantial when comparing quintile 5 and quintile 1 in the middle age-groups.

Table 7.13: Point prevalence (%) of CVA in 2008, by age-group and quintile

Age-group	1	2	3	4	5
20–24	<0.05	<0.05	<0.05	0.1	0.1
25–29	<0.05	0.1	0.1	0.1	0.1
30–34	0.1	0.1	0.1	0.2	0.2
35–39	0.1	0.2	0.2	0.2	0.3
40–44	0.2	0.3	0.3	0.4	0.5
45–49	0.4	0.5	0.6	0.8	0.9
50–54	0.8	1	1.1	1.3	1.8
55–59	1.5	1.5	1.7	2.2	2.8
60–64	2.6	2.8	2.9	3.4	4.7
65–69	4.5	4.8	5.4	5.9	6.9
70–74	7	7.5	8.2	9	9.2
75–79	11.1	10.5	11.1	12	12.5
80–84	14.5	14.4	14.4	15.3	15.7
85+	18.7	19.7	19.1	18.3	17

Table 7.14 shows corresponding figures for diabetes in the study population. A similar, though more pronounced gradient in preval-

ence was seen. While the overall prevalence was 6.48%, in quintile 5 there were 7.71% of individuals with diabetes; in quintile 1, the figure was 5.31%. Figure 7.15 illustrates that diabetes prevalence is

Table 7.14: Point prevalence of diabetes in 2008, by quintile

Quintile	Number	Denominator	Prevalence (percent)
1	11534	217354	5.31
2	11020	185688	5.93
3	15059	229861	6.55
4	13289	188608	7.05
5	14333	185891	7.71
All quintiles	65235	1007402	6.48

generally increase with age, though do decline in the older age-groups, presumably relating either to cohort effects from changing prevalences or differential survival aamong diabetics.More deprived quintiles have higher prevalences.

Table 7.15: Point prevalence (%) of diabetes in 2008, by age-group and quintile

Age-group	1	2	3	4	5
20–24	0.6	0.5	0.7	0.7	0.7
25–29	0.7	0.9	0.9	1.1	1.1
30–34	0.8	1	1.3	1.2	1.6
35–39	1.3	1.5	1.9	1.9	2.5
40–44	1.8	2.2	2.7	3.1	4
45–49	2.8	3.3	3.7	4.5	5.3
50–54	4.2	5.1	5.4	6.7	8.3
55–59	6	6.6	7.2	8.6	10.7
60–64	8	8.6	10.1	12.1	14
65–69	10.9	12.1	13.6	15.6	17.6
70–74	14.4	15.5	16.3	18	21.2
75–79	14.9	16.4	18	20.2	21
80–84	14.4	16.3	15.8	17.7	17.9
85+	12.6	13.2	13.3	14.3	14.7

The prevalences of individuals in different quintiles with 'other comorbidities' shown in table 7.16, were based on the proportion

of individuals in the cohort with comorbidities from the Charlson comorbidity index, excluding those presented above. The prevalence of other comorbidities was highest in quintile 5 (11.85%). Prevalence overall of these other comorbidities was 9.88%. From figure 7.17, it is

Table 7.16: Point prevalence of 'other Charlson comorbidities' in 2008, by quintile

Quintile	Number	Denominator	Prevalence (percent)
1	17646	217354	8.12
2	16734	185688	9.01
3	22667	229861	9.86
4	20503	188608	10.87
5	22030	185891	11.85
All quintiles	99580	1007402	9.88

clear that the prevalence of having other Charlson comorbidities rises with age, again with higher prevalences with increasing deprivation in all age-groups.

Table 7.17: Point prevalence (%) of other Charlson comorbidities in 2008, by age-group and quintile

Age-group	1	2	3	4	5
20–24	2.1	2.6	3.5	3.9	4.4
25–29	3	3.3	4.1	4.1	5.2
30–34	3.4	3.5	4.1	4.8	5.2
35–39	3.4	3.7	4.2	5.1	5.7
40–44	3.6	4.2	4.7	5.8	6.4
45–49	4.1	4.8	5.2	6.4	8
50–54	5.5	6.3	7	8.6	10.6
55–59	7.3	8.2	8.8	10.9	13.2
60–64	9.9	10.7	12.2	14.1	16.5
65–69	13	14.6	16.6	18.6	21.3
70–74	17.1	18.4	19.8	22.8	25
75–79	21.4	23.2	25.1	27.5	28.7
80–84	25.9	28	27.2	31.3	33.1
85+	28.2	30.4	31	33	34.4

7.2.2.2 *Risk factors*

In table 7.18, I present the prevalence of smokers in those whose smoking status was known, by quintile in 2008. I also show the percentage of the cohort on which a smoking status was known. The prevalence of smoking varied markedly between deprivation quintiles: in quintile 5, the prevalence was 32.76%; this declined as deprivation decreased to 14.45% in quintile 1. Overall smoking prevalence in the cohort was 22.31%. The percentage of individuals on whom a smoking status was known (and on which the prevalence figures were based) varied little. The highest proportion known was in quintile 3, at 92.83%; the lowest was in quintile 5, at 92.18%.

Table 7.18: Percentage of individuals in the final dataset with a known smoking status and the percentage of those individuals that smoked by quintile at the beginning of 2008

Quintile	Percent smokers	Percent known
1	14.45	92.63
2	18.20	92.31
3	21.49	92.83
4	26.13	92.69
5	32.76	92.18
All quintiles	22.31	92.55

Table 7.19 shows the smoking prevalence by age-group and quintile. Two patterns were seen. First, in line with table 7.18, prevalence rates of smoking were higher in more deprived quintiles. For example, for all age-groups, the smoking prevalence in quintile 5 was approximately double that in quintile 1. Second, smoking prevalence was highest in young and young middle-aged age-groups for all quintiles, with a general decline with increasing age thereafter. In quintile 1, the peak prevalence was in the 25–29 age-group (21.1%); in quintile 3, it was in the 20–24 age-group (30.7%); in other quintiles (4, and 5), the peak prevalence was in an older age-group – 40–44. The highest smoking prevalence was in individuals from the 40–44 age-group for quintile 5 (46.9%). The lowest prevalence was in the 85+ age-group quintile 1.

Table 7.20 shows mean BMI by quintile (here not adjusted for age), and the percentage of individuals on whom a BMI measurement was known. Mean BMI in the general population was highest in quintile 5, at 27.68, followed by quintile 4 at 27.65. In the less deprived quintiles,

Table 7.19: Percentage of individuals with a known smoking status who smoke, by quintile and age-group, from 2004 to 2010

Age-group	1	2	3	4	5
20–24	19.80	24.60	30.70	34.60	42.20
25–29	21.10	25.40	29.40	34.20	40.70
30–34	19.30	23.80	29.10	34.70	41.90
35–39	18.90	23.90	29.80	36.70	44.90
40–44	19.00	24.70	29.90	37.50	46.90
45–49	18.60	24.40	30.10	36.60	46.40
50–54	18.40	23.60	28.50	35.10	44.00
55–59	16.60	20.80	25.10	31.40	39.70
60–64	14.90	18.10	21.50	27.30	34.90
65–69	12.60	15.30	17.80	22.20	30.20
70–74	10.00	12.80	14.10	18.20	24.60
75–79	8.70	10.10	11.80	14.70	20.20
80–84	7.10	7.90	10.10	11.30	14.60
85+	4.80	5.10	6.30	6.90	9.50

mean BMI was lower: 26.33 in quintile 1, and 26.84 in quintile 2. The mean BMI overall was 27.13. Figure 7.21 shows the mean BMI by

Table 7.20: Mean BMI and the percentage of individuals on whom a BMI was known by quintile for 2008

Quintile	Mean BMI	Percentage known
1	26.33	78.46
2	26.84	78.84
3	27.24	79.73
4	27.65	79.10
5	27.68	79.04
All quintiles	27.13	79.05

age and quintile. Broadly, patterns showing increased BMI in more deprived quintiles, with BMIs generally highest in the 50s and early 60s.

In the two figures 7.4 and 7.5, I present the distributions of BMI for men and women from the 60–64 age-band respectively. The distributions for the five different deprivation quintiles are shown, with the

Table 7.21: Mean BMI in 2008, by age-group and quintile

Age-group	1	2	3	4	5
20–24	23.6	24	24.5	25.2	25.3
25–29	24.5	25	25.5	25.8	26.1
30–34	25.3	25.8	26.3	26.8	26.8
35–39	26	26.7	27.1	27.6	27.7
40–44	26.5	27	27.4	28	28.1
45–49	26.8	27.4	27.8	28.5	28.6
50–54	27.3	27.8	28.1	28.8	28.9
55–59	27.5	27.9	28.1	28.9	29
60–64	27.5	27.9	28.3	28.8	28.9
65–69	27.3	27.8	28.2	28.6	28.6
70–74	27.1	27.7	27.9	28.4	28.1
75–79	26.7	27.1	27.4	27.5	27.5
80–84	25.8	26.5	26.4	26.6	26.5
85+	24.7	25.2	25.2	25.5	25.4

least deprived quintile (1) at the top and the most deprived quintile (5) at the bottom. The blue vertical lines mark the mean for each distribution, also shown by the blue annotations.

In each quintile, the distributions are slightly left skewed, with a longer tail to the right of individuals with high and very high BMIs. The means in women show a fairly clear pattern of increasing BMI with increasing deprivation from a low in the least deprived quintile at 27.6 to a high in the most deprived quintile at 29.1. In men, while the pattern is broadly similar, with increasing mean BMI from quintile 1 (28.1) to quintile 4 (28.6), the BMI in quintile 5 (28.4) is the same as that in quintile 3. The differences between quintiles are less pronounced than for women.

In figures 7.4 and 7.5, apparent artifactual peaks in the distribution occur at BMI 56. This occurred because individuals with a BMI with categorical BMIs greater than 55 ('high BMI') were assigned a BMI of 56.

Figure 7.4: Distribution of BMI in men aged 60–64, by deprivation quintile, with population mean for quintile

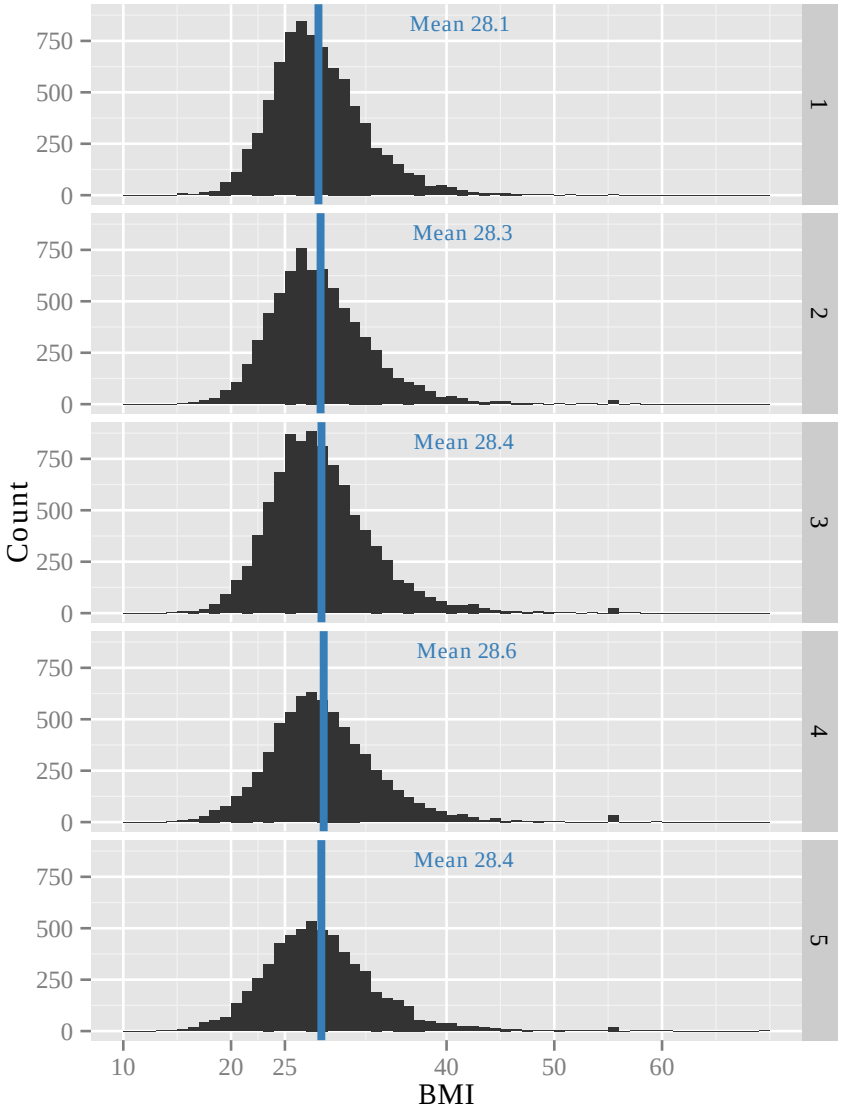
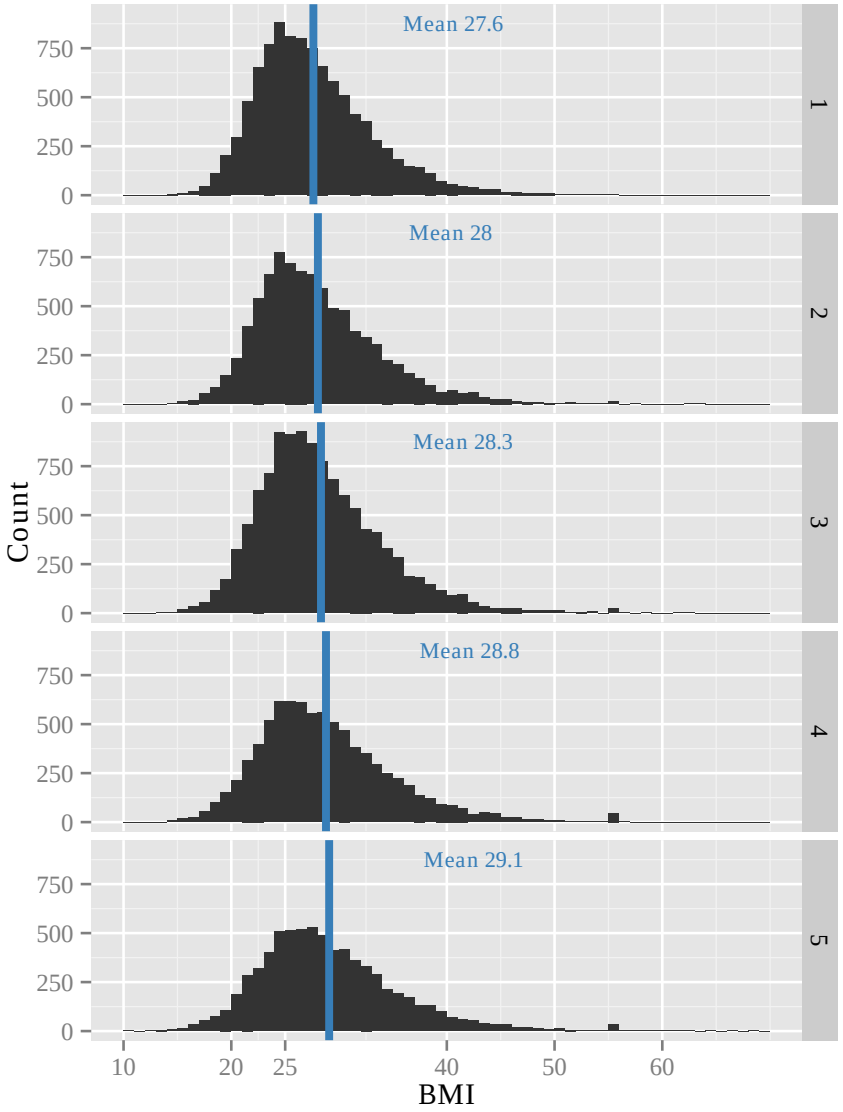
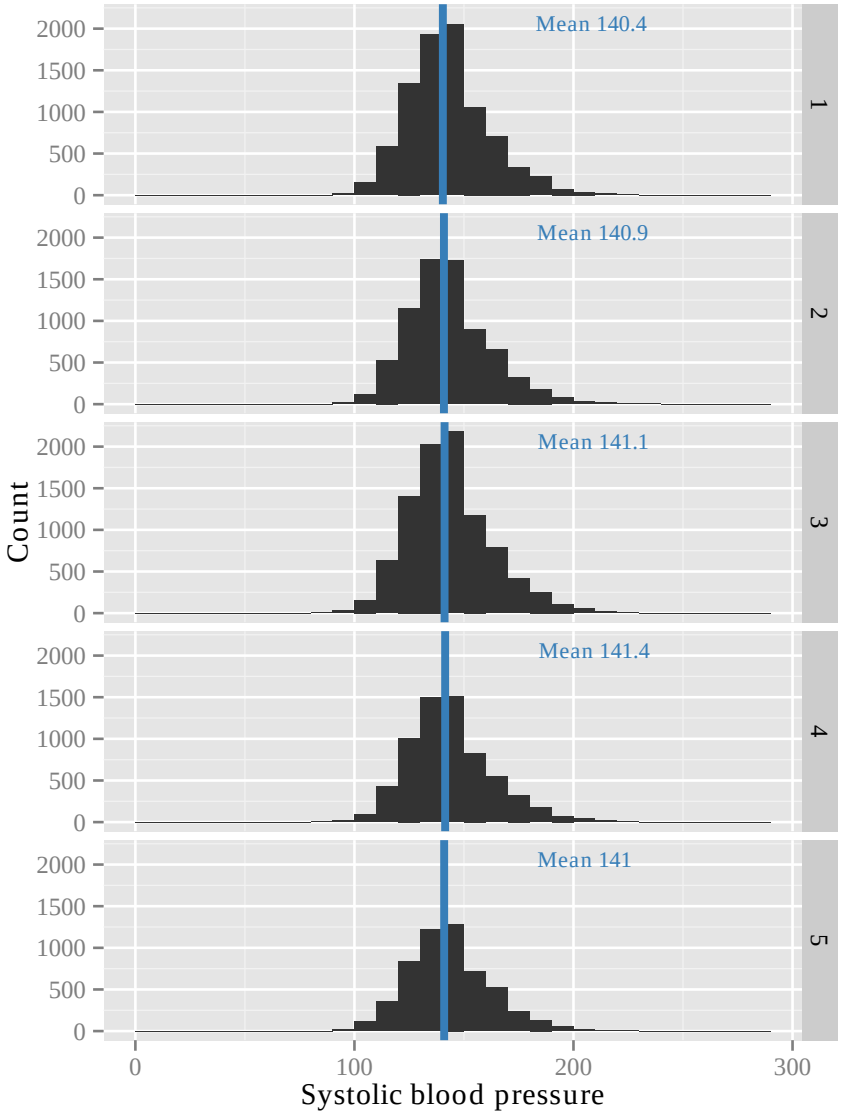


Figure 7.5: Distribution of BMI in women aged 60–64, by deprivation quintile, with population mean for quintile



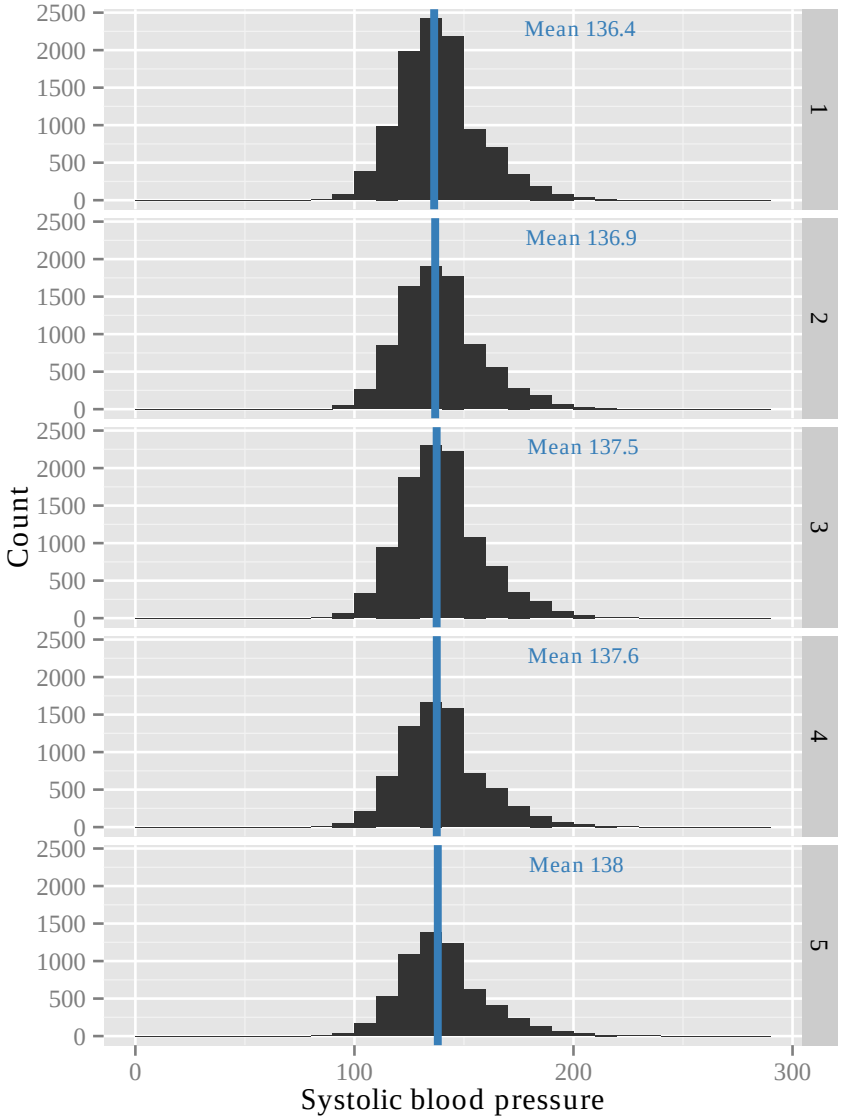
In figure 7.6, I present the distributions of systolic BP in untreated men aged 60 to 64, by deprivation quintile. While the distributions are similar in form, there is a small difference in means between quintiles. The pattern broadly appears to reflect increased mean systolic blood pressure (SBP) with increasing deprivation, with quintile 5 an exception – mean SBP here being lower than quintile 3.

Figure 7.6: Distribution of systolic blood pressure in untreated men aged 60–64, by quintile, with population mean for quintile



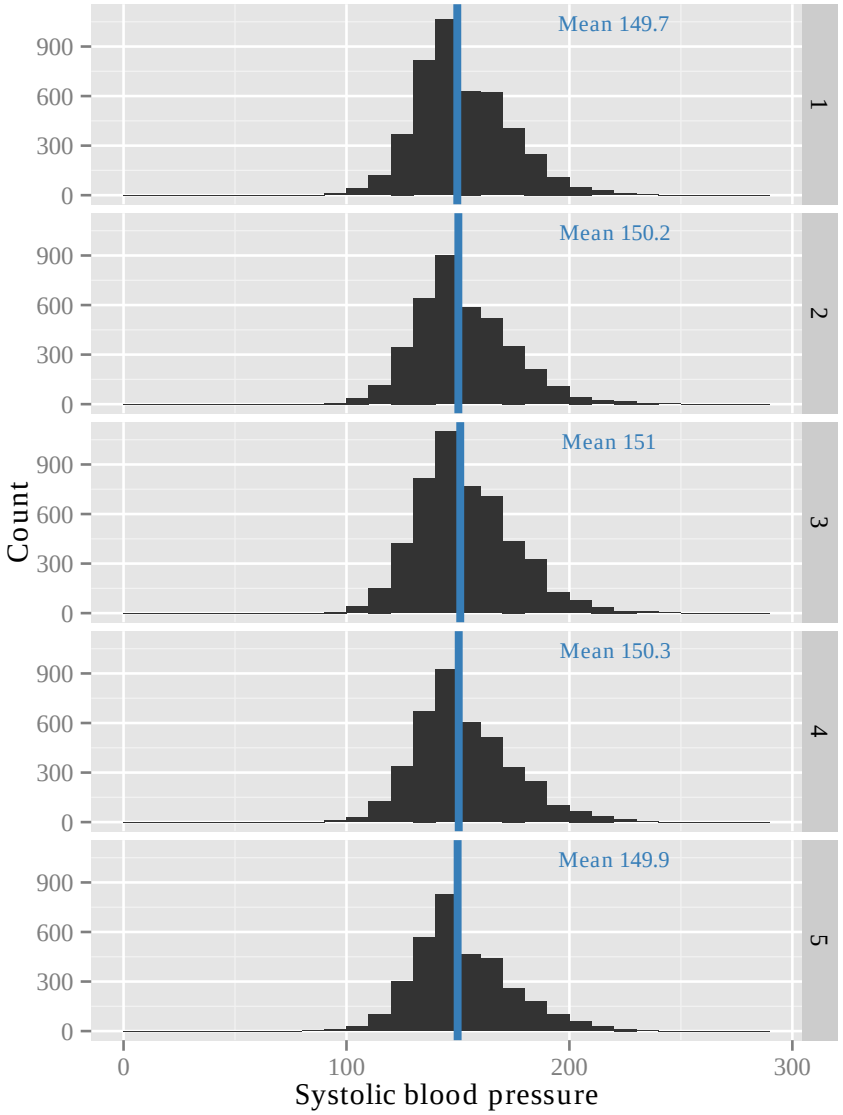
When mean SBP for untreated women in the same age-group is considered (figure 7.7), it is seen that mean SBP is lower in every quintile than for the corresponding quintile in men, by three or four mmHg. Here the pattern across quintiles is more consistent with a monotonic increase in mean SBP with increasing deprivation.

Figure 7.7: Distribution of systolic blood pressure in untreated women aged 60–64, by quintile, with population mean for quintile



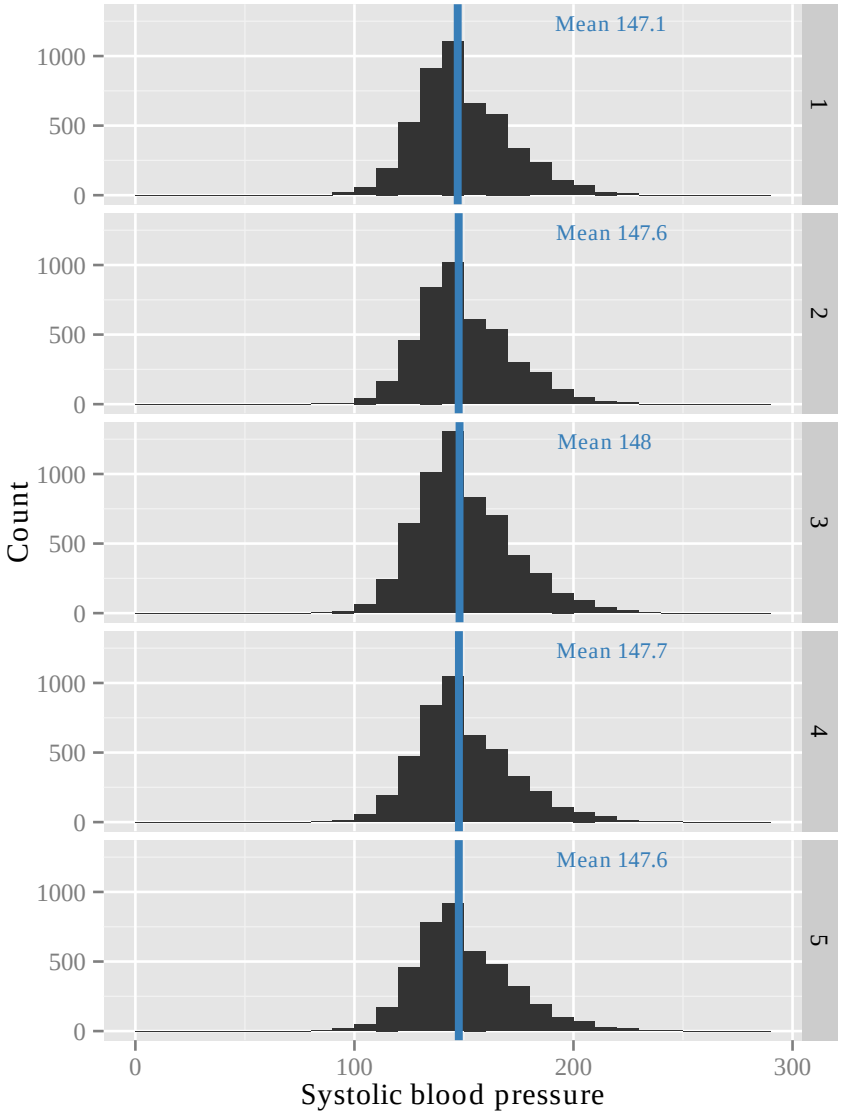
The distributions and means of SBP in treated men aged 60 to 64 are shown in figure 7.8. Here mean SBP peaks in deprivation quintile 3 at 151, declining from there as deprivation decreases or increases. In each quintile, SBP in treated individuals is roughly 10 mmHg higher than in the corresponding untreated population.

Figure 7.8: Distribution of systolic blood pressure in treated men aged 60–64, by quintile, with population mean for quintile



When considering the distributions and means of SBP in treated women, the pattern of means by deprivation is equivalent to that seen in men, with the highest mean SBP in quintile 3, again falling away as deprivation increases and decreases. The differences are not large (one or two mmHg). As with men, the treated group has a mean SBP approximately 10 mmHg higher than in the corresponding untreated group.

Figure 7.9: Distribution of systolic blood pressure in treated women aged 60–64, by quintile, with population mean for quintile



I show mean cholesterol:HDL ratios by quintile in table 7.22. The percentages known here are lower, 31.8% overall, with a low of 27.24% in quintile 1. Thus, the mean values are based on a small proportion of the cohort. The mean cholesterol:HDL ratio did not vary greatly between quintiles when the population was considered as a whole, unadjusted for age. Figure 7.23 shows mean cholesterol:HDL ratio by

Table 7.22: Mean cholesterol:HDL ratio and the percentage of individuals on whom a cholesterol:HDL ratio was known by quintile for 2008

Quintile	Mean cholesterol:HDL	Percentage known
1	3.63	27.24
2	3.66	32.83
3	3.70	34.31
4	3.67	33.13
5	3.72	31.70
All quintiles	3.68	31.81

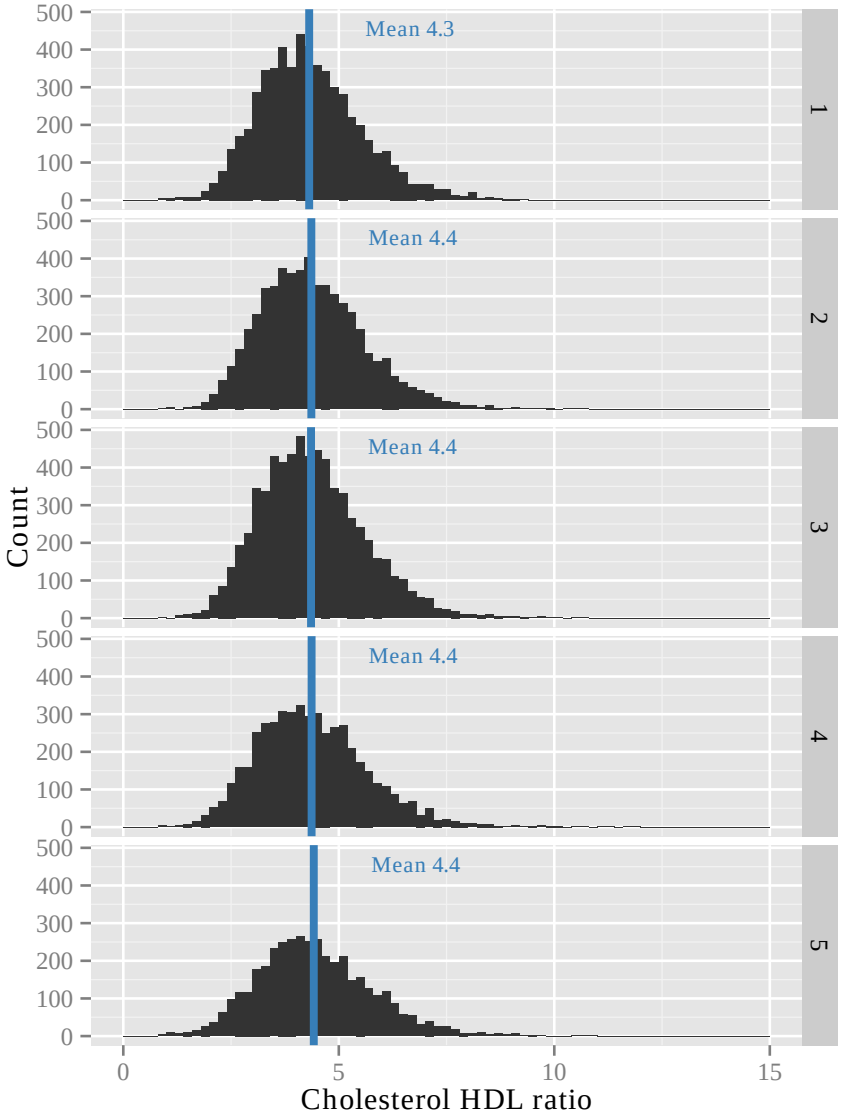
age and quintile. Patterns here are less clear-cut, with ratios peaking in the 40s. In these age-groups, mean ratios are higher in more deprived quintiles; in older age-groups ratios peak in quintile 3.

Table 7.23: Mean cholesterol:HDL ratio in 2008, by age-group and quintile

Age-group	1	2	3	4	5
20–24	3.4	3.31	3.43	3.49	3.56
25–29	3.5	3.52	3.58	3.69	3.72
30–34	3.7	3.78	3.91	3.89	3.94
35–39	3.87	3.93	3.99	4.02	4.07
40–44	3.94	3.94	4.02	4.08	4.08
45–49	3.91	3.94	3.98	3.99	4.07
50–54	3.89	3.92	3.94	3.93	3.96
55–59	3.8	3.82	3.86	3.83	3.87
60–64	3.68	3.7	3.74	3.69	3.75
65–69	3.58	3.6	3.59	3.56	3.58
70–74	3.46	3.48	3.49	3.43	3.46
75–79	3.34	3.39	3.4	3.34	3.35
80–84	3.26	3.33	3.35	3.24	3.22
85+	3.23	3.33	3.34	3.23	3.22

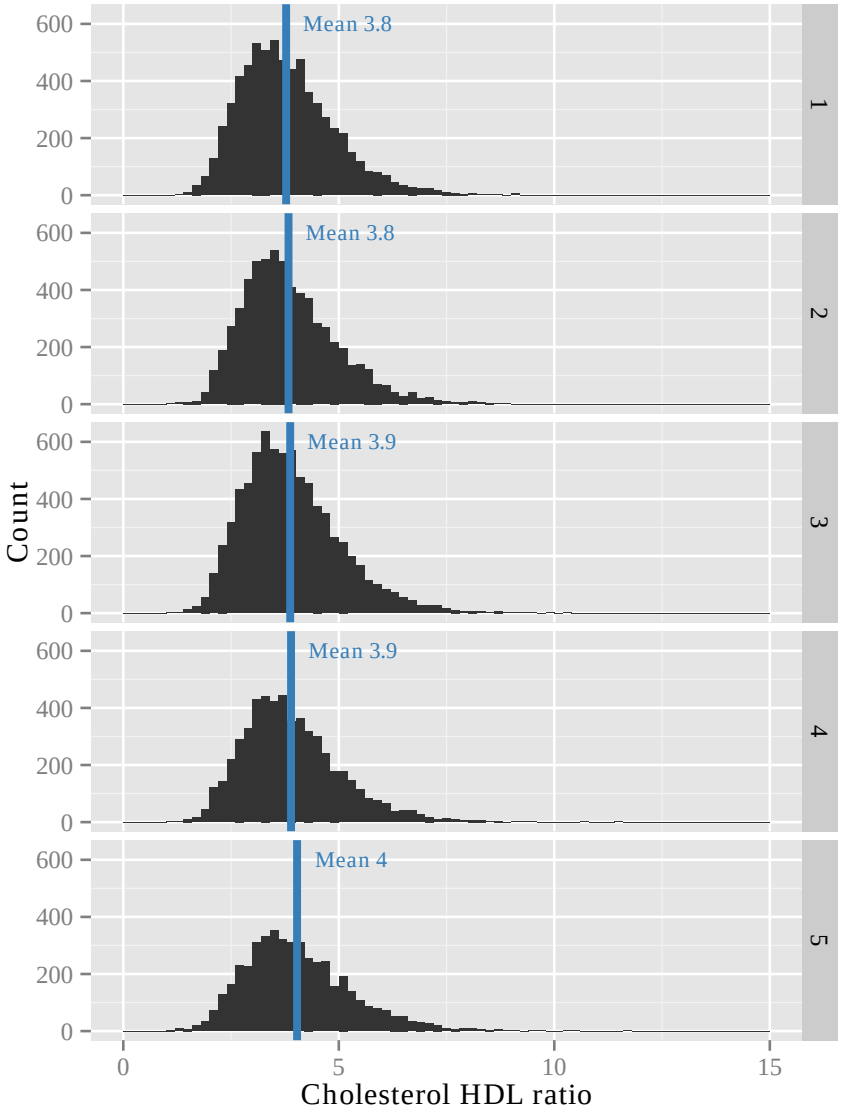
In figure 7.10, I present distributions of cholesterol:HDL ratio in men in the 60 to 64 age-group who are not treated with statins. The mean cholesterol:HDL is unvarying across the quintiles, excepting a slightly lower value in quintile 1.

Figure 7.10: Distribution of cholesterol:HDL in untreated men aged 60–64, by quintile, with population mean for quintile



For untreated women in the same age-group, the mean cholesterol:HDL was slightly lower for corresponding quintiles. A pattern of increasing mean cholesterol:HDL with increased deprivation was present, though differences were not large.

Figure 7.11: Distribution of cholesterol:HDL in untreated women aged 60–64, by quintile, with population mean for quintile



Where possible, based on available data, I calculated assessed cardiovascular risk using the Framingham non-laboratory risk assessment tool. I show the mean values for this assessed risk in table 7.24, together with the percentage of individuals on whom such a risk could be calculated. Because they are unadjusted, these figures provide only a crude estimate of cardiovascular risk in the general population in the study. Overall mean risk was highest in quintile 3, with risk then decreasing and increasing with decreasing deprivation.

Table 7.24: Mean cardiovascular risk and the percentage of individuals on whom a cardiovascular risk was known by quintile for 2008

Quintile	Mean cardiovascular risk	Percentage known
1	0.156	61.76
2	0.162	61.40
3	0.165	64.39
4	0.161	64.09
5	0.16	63.42
All quintiles	0.161	63.04

Age is the most important risk factor for CHD and CVD more generally – and this is reflected in table 7.25 – older age-groups have higher risk. In general, cardiovascular risk increases with increasing deprivation.

For men aged 60 to 64, the distributions of risk (based on the Framingham non-laboratory risk-assessment tool) and population means for each quintile are shown in figure 7.12. Here, a clear pattern emerges, with mean risk increasing with increasing deprivation, with a low of 0.247 in the least deprived quintile rising to 0.287 in the most.

Figure 7.12: Distribution of cardiovascular risk measured using the Framingham non-laboratory risk assessment tool in men aged 60–64, by quintile, with population mean for quintile

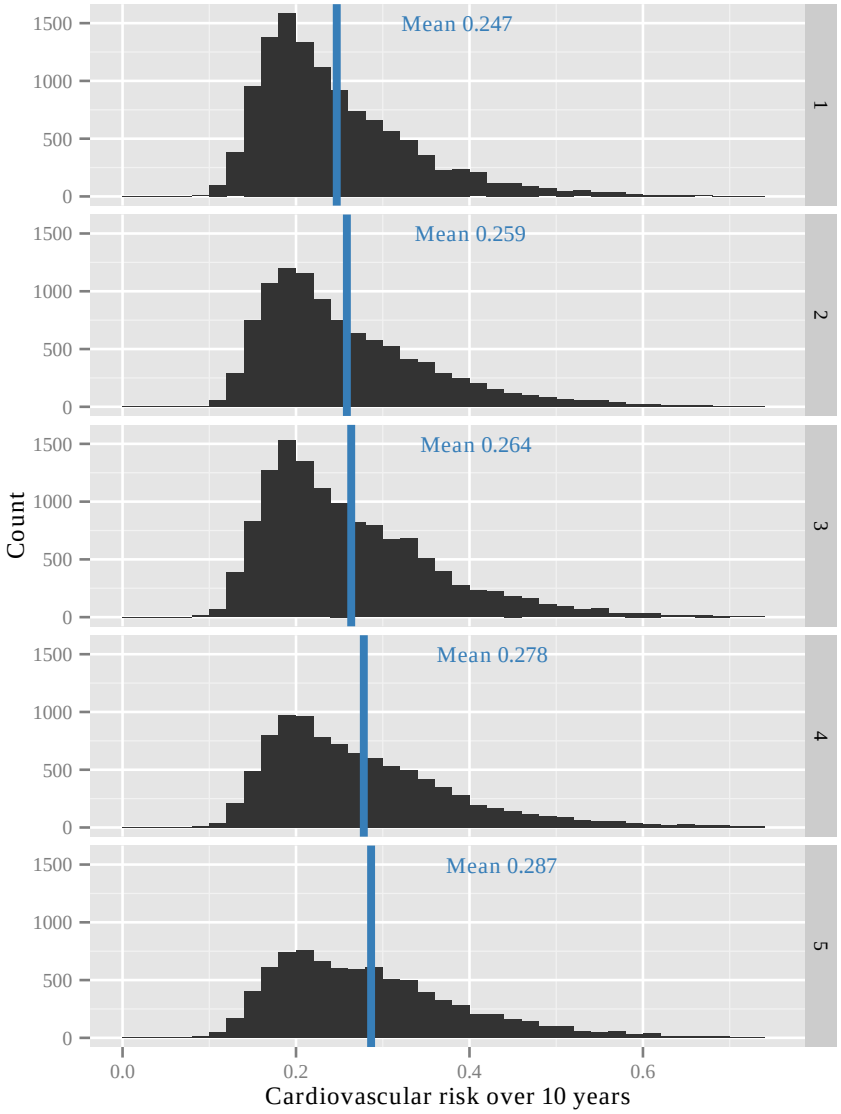
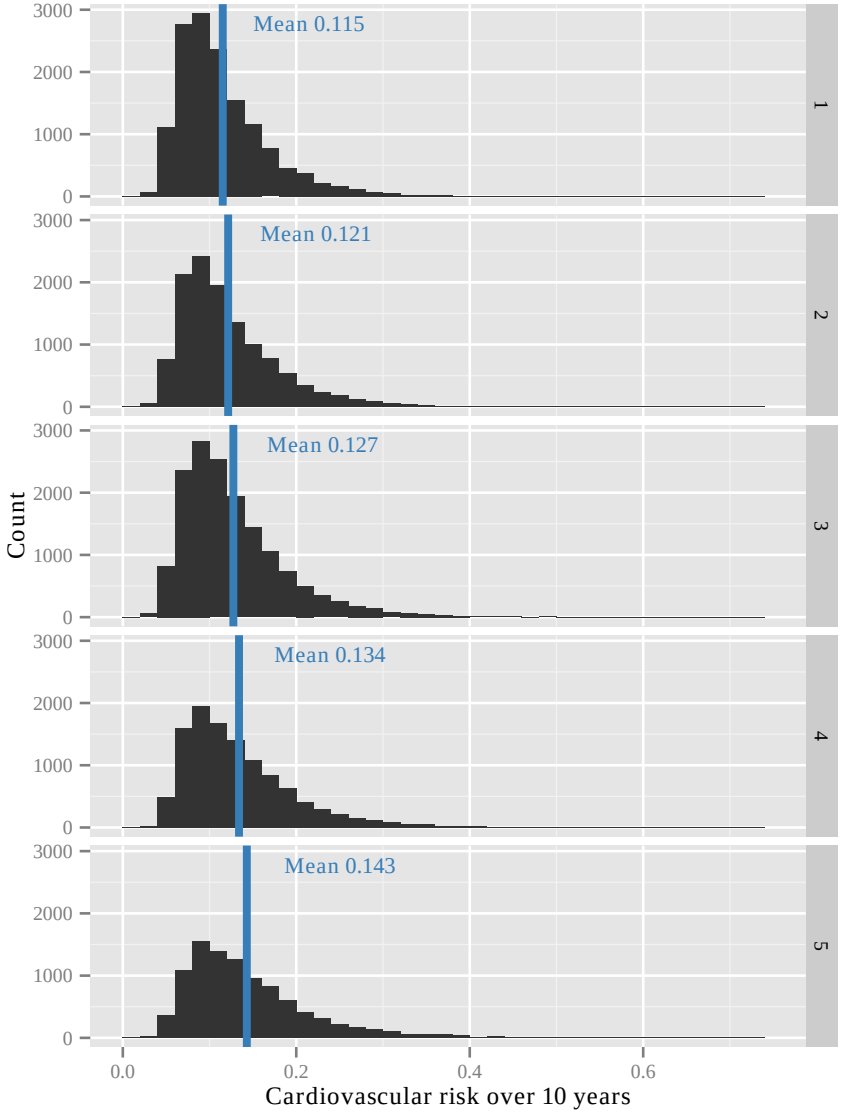


Table 7.25: Mean cardiovascular risk (%), using Framingham nonlaboratory assessment tool in 2008, by age-group and quintile

Age-group	1	2	3	4	5
20–24	0.6	0.6	0.7	0.7	0.7
25–29	1.1	1.2	1.2	1.3	1.3
30–34	1.9	2.1	2.2	2.3	2.5
35–39	3.1	3.4	3.6	3.8	4.1
40–44	4.9	5.3	5.6	6	6.4
45–49	7.4	8	8.3	9	9.6
50–54	10.8	11.5	12	12.6	13.5
55–59	14.8	15.3	16.1	17.1	18.1
60–64	19	19.8	20.7	21.6	22.7
65–69	23.7	24.5	25.6	26.4	27.1
70–74	28.5	29.5	30.7	30.8	31.3
75–79	33.2	34	34.6	34.5	35.3
80–84	36.8	37.3	37.6	37.4	37.7
85+	39.5	39.3	39.9	38.8	39.3

A similar pattern occurred for women aged 60 to 64, as shown in figure 7.13, though here risk was lower throughout (roughly half the mean value for men) – sex being an important component of cardiovascular risk models.

Figure 7.13: Distribution of cardiovascular risk measured using the Framingham non-laboratory risk assessment tool in women aged 60–64, by quintile, with population mean for quintile



7.2.3 *Healthcare utilisation*

I looked at simple measures of health care utilisation, making comparisons of mean levels between deprivation quintiles. For this simple analysis, I looked at measurements of important risk factors in primary care, total numbers of cardiovascular-related GP records, and total numbers of hospital admissions of all types for all causes. I looked across the whole time period of the study.

Table 7.26: Mean hospital admissions and CVD-related GP contacts during the study period, by quintile

Quintile	Admissions (all causes)	GP contacts (CVD-only)
1	2.88	131.46
2	3.02	145.5
3	3.17	152.95
4	3.45	154.26
5	3.67	159.45
All quintiles	3.23	148.44

In figure 7.26, I show the mean number of spells in hospital (admissions) for each of the different deprivation quintiles for the 2004 cohort. For these individuals, those in deprivation quintile 5 had on average 3.67 admissions to hospital during the study period. As the deprivation level of the quintiles decreased, the mean number of admissions decreased, falling to 2.88 in quintile 1 (the least deprived cohort). When looking at the mean number of GP records (table 7.26) of episodes or contacts relating to cardiovascular disease (including measurements, readings, symptoms, treatments, and diagnoses), a similar pattern emerged, with higher average numbers of GP contacts in the most deprived quintile (159.5 on average during the study period), falling as deprivation levels decreased to 131.5 in the least deprived quintile.Figure 7.27 shows mean hospital admissions through the study period by age-group and quintile. Mean admissions are higher in older age-groups (peaking in the 80–84 age-group), with general increases with increasing deprivation.

I present the mean number of BMI measurements in table 7.28. Quintile 5 had on average 5.9 measurements during the study period. The mean number of measurements declined as deprivation declined for the quintile, reducing to 4.5 in the least deprived quintile.

Table 7.27: Mean number of hospital admissions throughout the study period, by age-group and quintile

Age-group	1	2	3	4	5
20–24	1.7	1.9	2.3	2.7	3.2
25–29	2.2	2.3	2.5	2.7	3
30–34	2.2	2.2	2.3	2.4	2.5
35–39	1.8	1.9	2	2.1	2.3
40–44	1.7	1.9	1.9	2.1	2.4
45–49	1.9	2.1	2.1	2.4	2.5
50–54	2.3	2.3	2.4	2.8	3
55–59	2.6	2.6	2.9	3.2	3.5
60–64	3.2	3.3	3.4	3.9	4
65–69	4	3.9	3.9	4.3	4.4
70–74	4.5	4.5	4.5	4.7	4.8
75–79	4.7	4.8	4.6	5	5.1
80–84	4.8	4.9	4.8	5	5.4
85+	4.4	4.8	4.7	4.9	4.6

Table 7.28: Mean numbers of measurements and readings performed in general practice during the study period, by quintile

Quintile	BMI	Systolic BP	Cholesterol
1	4.54	15.16	3.69
2	4.98	15.33	3.85
3	5.39	15.68	3.96
4	5.56	15.77	3.87
5	5.9	15.37	3.82
All quintiles	5.26	15.46	3.84

For blood pressure (shown in table 7.28) the picture was different. The highest mean number of measurements was in quintile 4, at 15.77, the lowest number of measurements was in quintile 1, at 15.16. Mean measurements of cholesterol (table 7.28) were highest in quintile 3, at 3.96, second highest in quintile 4 at 3.87, and lowest in quintile 1 at 3.69. In table 7.29, we see the mean number of contacts with GP services for CHD-related activity. Mean numbers of contacts are highest in those in their 70s; as with admissions, mean numbers increase with increasing deprivation.

Table 7.29: Mean number of contacts with primary care related to cardiovascular disease throughout the study period, by age-group and quintile

Age-group	1	2	3	4	5
20–24	30.8	32.9	36	38.1	38.4
25–29	36.4	38.9	42	45	46.5
30–34	44.1	47.1	51	53.6	56.9
35–39	53.3	59.1	64.5	69.2	76
40–44	67.3	74.1	84.6	93.4	104.4
45–49	96.6	108.1	120.4	135.1	151.8
50–54	133.9	149.5	156.4	179.7	203.9
55–59	177.2	200.5	216.8	238.3	263.9
60–64	238.7	265.5	282.3	306	324.3
65–69	299.3	332.3	342.2	351.9	379.5
70–74	342	375	379.1	388.6	403.3
75–79	347.3	389	379.1	386.4	401.4
80–84	343.4	349.2	353.5	353	356
85+	268.7	294.6	281.6	284	279.8

7.3 DATA VALIDATION

In table 7.30, I have summarised the prevalences of angina, CHD, diabetes, MI, and CVA/TIA from different data sources and different time-points. Table 7.30 shows angina prevalence in the years 2005 and 2009 in SAIL and in the WHS, but angina prevalence was not available in QOF. Angina prevalence changed in both data sources: in SAIL from 4.53% in 2005 to 4.62% in 2009; in the WHS from 5.0% in 2005 to 4.0% 2009. Both time-points had a higher prevalence estimate for

Table 7.30: Prevalences of major diagnoses by data source and by year

Diagnosis	Data source	Year	Prevalence (%)
Angina	SAIL	2005	4.53
Angina	WHS	2005	5.00
Angina	SAIL	2009	4.62
Angina	WHS	2009	4.00
CHD	QOF (Wales)	2005	4.30
CHD	SAIL	2005	6.74
CHD	QOF (Wales)	2009	4.20
CHD	SAIL	2009	6.93
Diabetes	QOF (Wales)	2005	3.90
Diabetes	SAIL	2005	5.51
Diabetes	WHS	2005	5.00
Diabetes	QOF (Wales)	2009	4.60
Diabetes	SAIL	2009	6.79
Diabetes	WHS	2009	6.00
MI	SAIL	2005	3.02
MI	WHS	2005	5.00
MI	SAIL	2009	3.18
MI	WHS	2009	4.00
Stroke/TIA	QOF (Wales)	2005	1.80
Stroke/TIA	SAIL	2005	2.90
Stroke/TIA	WHS	2005	3.00
Stroke/TIA	QOF (Wales)	2009	2.00
Stroke/TIA	SAIL	2009	3.01
Stroke/TIA	WHS	2009	3.00

angina from the WHS. Prevalence of CHD was available from QOF and from SAIL (table 7.30). Prevalence in SAIL was 6.74% in 2005 and 6.93% in 2009. Prevalence was lower in QOF at 4.3% in 2005, falling to 4.2% in 2009. Diabetes prevalence was available from all three sources (table 7.30). In 2005, diabetes prevalence was 3.9% in QOF, 5.51% in SAIL, and 5.0% in WHS. In 2009, the diabetes prevalence had risen in each data source: to 4.6% in QOF, to 6.79% in SAIL, and to 6.0% in the WHS.

Prevalences of previous MI were present in SAIL and in the WHS. Contrasting patterns were observed for the two data sources over time. In SAIL, MI prevalence rose from 3.02% in 2005 to 3.18% in 2009. For the WHS, prevalence of MI fell from 5.0% in 2005 to 4.0% in 2009. Importantly, these two sources of information arrived at these estimates in entirely different ways: the WHS relied on asking a subset of the Welsh population whether they had ever had the condition; the SAIL dataset used hospital data recorded in PEDW relating to admissions during which an MI occurred.

For both SAIL and QOF the prevalence of CVA/TIA increased between 2005 and 2009 (table 7.30). For SAIL, the rise was from 2.90% to 3.01%; for QOF, the rise was from 1.8% to 2.0%. The prevalence in the WHS was the same for the two time-points at 3.0%.

Overall, prevalences between the data sources were broadly comparable. Where prevalences were available from both SAIL and QOF, prevalences were higher in SAIL. This pattern had been anticipated due to the differences in denominators. In addition, the more inclusive approach to labelling CHD taken in this thesis compared to QOF business rules is also likely to explain some of the difference seen. In comparisons between SAIL and the WHS, prevalences in the WHS were higher, except for diabetes where prevalences were higher in SAIL.

Table 7.31: Prevalences of smoking, obesity and overweight/obesity by data source and by year. The 'percentage known' shows the percentage of individuals in the SAIL data on whom a reading is available

Risk factor	Data source	Year	Prevalence (%)	Percentage known
Obesity	SAIL	2005	22.73	68.6
Obesity	SAIL	2009	26.45	77
Obesity	WHS	2009	21.00	
Overweight/obesity	SAIL	2005	58.78	68.6
Overweight/obesity	SAIL	2009	61.84	77
Overweight/obesity	WHS	2009	57.00	
Smoking	SAIL	2005	26.21	80.8
Smoking	WHS	2005	28.00	
Smoking	QOF (Wales)	2009	19.10	
Smoking	SAIL	2009	23.92	90.5
Smoking	WHS	2009	24.00	

I also looked at the prevalences of some important cardiovascular risk factors in different data sources, to allow comparison: obesity; overweight/obesity; smoking; and hypertension. I have summarised these preferences in table 7.31, and for hypertension in table 7.32. In 2005, the prevalence of obesity in SAIL was 22.73% and this figure had risen to 26.45% by 2009. Prevalence from the WHS was available from 2009 only and was 21.0%.

A similar pattern was observed with prevalence of overweight/obesity. This is a prevalence including individuals who are either overweight or obese, including everybody with a BMI of 25 or over. Here the prevalence in SAIL was 58.78% in 2005 rising to 61.84% by 2009; the prevalence from the WHS from 2009 was 57.0%.

Smoking prevalence was available from SAIL and from the WHS for 2005. SAIL prevalence at this time was 26.21%; in the WHS the prevalence was 28.0%. In 2009, QOF data were also available on smoking prevalence, at 19.1%; smoking prevalence in SAIL had fallen to 23.92%; in the WHS, prevalence had fallen to 24.0%.

Prevalences of risk factors in SAIL were based only on a proportion of the total population of the cohort, because for many individuals their status with respect to these risk factors was unknown. Moreover, the individuals on whom these risk factors are ascertained are not randomly selected from the population of the cohort.

In table 7.32, I have summarised a number of prevalences of hypertension for different diagnostic criteria. I have listed prevalences of hypertension, as included in QOF and WHS. In 2005, the QOF prevalence of hypertension was 12.7% rising to 14.9% by 2009. The equivalent prevalences from the WHS were 19.0% in 2005 and 20.0% and 2009.

Table 7.32: Prevalences of hypertension and related measures by data source and by year. The 'percentage known' shows the percentage of individuals in the SAIL data on whom a reading/diagnosis is available

Risk factor	Data source	Year	Prevalence (%)	Percentage known
Hypertension	QOF (Wales)	2005	12.70	
Hypertension	QOF (Wales)	2009	14.90	
Hypertension	WHS	2005	19.00	
Hypertension	WHS	2009	20.00	
3 consecutive BPs $>$ 160 in low-risk person	SAIL	2005	1.45	
3 consecutive BPs $>$ 160 in low-risk person	SAIL	2009	1.18	
3 consecutive BPs $>$ 140 in high-risk person	SAIL	2005	10.30	
3 consecutive BPs $>$ 140 in high-risk person	SAIL	2009	13.60	
Mean systolic BP $>$ 140	SAIL	2005	37.73	51.2
Mean systolic BP $>$ 140	SAIL	2009	29.70	63.2
Mean systolic BP $>$ 160	SAIL	2005	7.97	50.9
Mean systolic BP $>$ 160	SAIL	2009	4.31	62.7

For the SAIL data, I had to determine what hypertension actually constituted. I have cited prevalences in 2005 and 2009 in the SAIL dataset using different definitions in table 7.32. In the first two definitions, I followed NICE guidance and looked at the prevalence of individuals with three consecutive systolic BP measurements greater than 140 in an individual known to be at high risk of CVD; the prevalence of individuals meeting this definition was 10.3% in 2005 and 13.6% in 2009. I also considered individuals with three consecutive systolic BP measurements greater than 160 who were at low-risk of CVD; here the prevalence was 1.45% in 2005 and 1.18% in 2009. For comparison, I also looked at a simpler definition, looking at individuals with mean systolic BPs greater than a designated threshold (140 or 160) from three readings. Using the 140 threshold, 37.7% of individuals met this definition in 2005 falling to 29.7% by 2009; with the 160 threshold, 7.97% of individuals met this definition in 2005 falling to 4.31% by 2009.

There was a substantial difference between the prevalences of hypertension using different criteria. While the prevalences from QOF and the WHS were comparable, this was not the case for the definitions used to ascertain prevalence in SAIL, which found either substantially lower or substantially higher estimates than the comparison data sources.

7.4 MORTALITY

In this section I describe the causes of death by broad category for individuals in our cohort, and have looked at mortality by deprivation quintile in relation to CHD. One of the key underlying assumptions of this thesis was that the mortality rate from CHD was higher in more deprived groups, a pattern which has been observed in numerous studies. I use this section to present descriptive data that allowed me to test the validity of this assumption. In table 7.33, I show the numbers of deaths by different broad categories of cause for individuals in our cohort. In 67,529 individuals, death was from non-cardiovascular-related causes. Of the remainder, 15,339 individuals had a cause of death relating to CHD, representing 17.1% of deaths where the cause was known. An additional 1708 deaths (1.9% of deaths) were recorded as due to heart failure; CVA accounted for a further 5248 deaths (5.84% of deaths). Taking CHD, heart failure, and CVA together to constitute CVD deaths, CVD accounted for 24.8% of all deaths (22,295 deaths in

Table 7.33: Breakdown of the broad categories of cause of death for the individuals in the 2004 cohort who died

Cause of death	Number
Other	67529
CHD	15339
Stroke	5248
Heart failure	1708
Unknown	2
TOTAL	89826

all). The codes used to assign deaths to the different categories shown in figure 7.33 are shown in appendix E.

In table 7.34, I show the death rate from CHD for the different deprivation quintiles, per thousand person-years at risk within our cohort.

The rate of death from CHD was highest in quintile 5, 2.68, with a declining trend as deprivation declined through the quintiles to 1.77. I

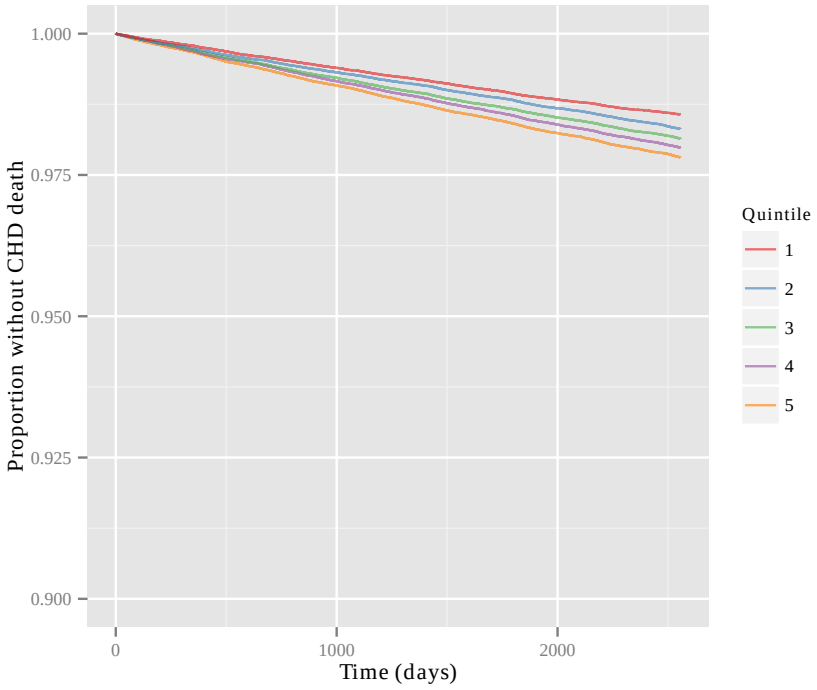
Table 7.34: Number of CHD deaths per 1000 person-years-at-risk, by quintile

Quintile	PYAR (1000s)	CHD deaths	CHD deaths per PYAR
1	1452	2576	1.77
2	1233	2605	2.11
3	1536	3647	2.37
4	1261	3172	2.51
5	1249	3345	2.68

illustrate the same pattern in figure 7.14. This is a Kaplan-Meier plot showing the patterns of mortality from CHD over time. In this figure, the Y-axis ends at 0.9 as the majority of individuals in the dataset did not die from CHD during the study period. The lines in figure 7.14 are coloured by quintile. The pattern shown suggests that, with increased deprivation, a higher proportion of individuals are dying from CHD.

In table 7.35, I present the results of a Cox proportional hazard model of death from CHD, showing the HRs with CIs for the different quintiles. Again, the pattern of increased risk of death with increased deprivation was shown. Using quintile 1 as the reference category with HR 1, the HR for quintile 5 was 1.54 (95% CI: 1.46; 1.62), suggesting

Figure 7.14: Kaplan-Meier plot of death from CHD by quintile



an increased risk of death of 54% in this quintile. When compared to quintile 1 other quintiles (2, 3, and 4) had an increased risk of death from CHD, the size of the HR declining as deprivation declined. I

Table 7.35: Hazard ratios for coronary heart disease death by quintile

Quintile	Hazard ratio	95% CI
Quintile 1	1	Reference
Quintile 2	1.17	1.11; 1.24
Quintile 3	1.3	1.24; 1.37
Quintile 4	1.41	1.34; 1.49
Quintile 5	1.54	1.46; 1.62

show a similar set of figures in table 7.36, though this time the HRs shown are adjusted for age and sex (these being obvious confounders of the relationship). Doing so has the effect of increasing the HRs in quintiles 4 and 5 – from 1.41 to 1.50 and from 1.54 to 1.72 respectively. In quintiles 2 and 3 the HRs changed slightly when the adjustment was made – from 1.17 to 1.16 in quintile 2 and from 1.30 to 1.32 in quintile 3. Overall, our results suggested that rates of death from CHD

Table 7.36: Hazard ratios for coronary heart disease death by quintile, adjusted for age and sex

Quintile	Hazard ratio	95% CI
Quintile 1	1	Reference
Quintile 2	1.16	1.1; 1.23
Quintile 3	1.32	1.26; 1.39
Quintile 4	1.5	1.42; 1.58
Quintile 5	1.72	1.63; 1.81

were related to deprivation, with increased rates of death in more deprived quintiles.

7.5 SUMMARY

In this chapter, I have given an overview of our dataset, specifically concentrating on the characteristics of the individuals on whom I set out to identify clinical triggers. I have described our dataset, looking at the demographic characteristics of the cohort as of 1 January 2004; I have presented prevalences for important covariates; I have summarised healthcare utilisation by deprivation quintile throughout our study. I have presented results from a simple validation of our dataset against prevalence estimates from external sources. Because of the importance of mortality from CHD by deprivation quintile as an underlying assumption for this work, I have presented results on CHD mortality differences between quintiles – to demonstrate that this starting point, incorporated into the rationale for this work in chapter 1, was justified based on patterns in our data.

Summarising the results from this chapter, I have found that

- Utilisation of healthcare in broad terms appears to be higher with increasing deprivation
- Risk profiles are often worse as deprivation increases, especially for smoking
- Mortality from CHD is higher with increasing deprivation

Although, following from the arguments in our rationale in chapter 1, healthcare inequity might explain some of the differences in outcome CHD mortality between deprivation groups reported in this chapter, the risk profiles presented here indicate that more deprived groups have worse risk factor profiles (particularly in relation to smoking, where prevalences in the most deprived are approximately double those in the least deprived quintile). In other words, purely on this (well-documented) basis, one can argue that it is not necessary to invoke healthcare inequity to explain differences in outcome. Taken with the findings of chapter 3, where I found quite equivocal evidence in the literature for the existence of healthcare inequity for CHD, I turn to our detailed analysis of clinical trigger-actions having established (partly in this chapter, partly on the basis of previous work reviewed in chapter 3) that the case for healthcare inequity in the NHS for CHD is fairly weak and is very likely unnecessary to explain observed differences in outcome. Further, the simple summaries of healthcare utilisation presented here suggest that, in broad terms,

deprived groups have more contacts (admissions, CHD-related measurements) with healthcare services.

In the next two chapters, I present analysis of clinical trigger-actions themselves. Firstly, I examine some exemplar analyses from selected points in the pathway of care for CHD; secondly, in chapter 9, I present an overview of our pathway analysis.

8

SELECTED PATHWAY RESULTS

In the previous chapter, I presented an overview of our data using a descriptive approach. In this chapter I report detailed results at two points on the pathway of care for CHD in order to explain and illustrate how results will be presented throughout this thesis. Because of the large volume of results it would have been impractical to present them all in the main text at this level of detail at every point in the pathway. An overview of all results appears in the next chapter, and further detailed results appear in appendix D.

The two pathway points I chose to focus on in this chapter are statin prescribing in individuals whose risk is assessed as high, and PCI for individuals who have had an MI. I did not choose these points because of the specific nature of their results or because their analysis was somehow different: I performed the same analysis as that presented in this chapter at every point in the pathway of care for CHD. I hope that focusing on statins in high-risk individuals will be of interest to the reader because the subject is topical at the time of writing; revascularisation with PCI was chosen as a contrast, because it is quite a different kind of activity to which different considerations apply. Thus, the aim here is to give maximally informative examples of the way my analysis was performed.

In presenting the results I have adhered to a consistent framework, also employed in the further results presented in the appendix. To aid with orientation in such a large amount of information, I have tried to make clear the point in the pathway the reader is looking at by using a frame coloured according to the area of the pathway, with a schematic overview of the pathway highlighting both the current point and the broad area of the pathway concerned.

Throughout, I have used single quotes in the titles of figures to indicate the names of the clinical trigger and clinical action; the name of the clinical trigger comes first. I present a hierarchy of results for each pathway point. I start with descriptive summaries of the clinical trigger-actions, by looking at the main covariates at the clinical trigger date, and at the history variables discussed in chapter 5. I then present summaries of the 'survival times' for that clinical trigger-action, using a Kaplan-Meier plot with separate curves for each deprivation quintile.

Next I present the hierarchy of models looking at clinical trigger-action times across quintiles. I present a univariate model looking only at HRs across quintiles, including practice (and where appropriate hospital of admission) as a random effects terms in the model. Secondly, I have included a model that adjusts in addition for the age-group and sex of the individual at the clinical-trigger date. Thirdly, I have looked at a model that in addition contains other plausible and relevant covariates, again containing random effects terms for practice (and hospital if necessary).

8.1 STATIN PRESCRIPTION IN INDIVIDUALS ASSESSED AS BEING HIGH RISK

I have considered first the clinical trigger-action in which an individual is determined as being at high cardiovascular risk (through risk assessment but not through having a 'high risk diagnosis') and thus, in line with NICE guidance, potentially able to benefit from a statin. The algorithms identified 120,459 individuals for whom this clinical trigger arose during the observation period of our study (1 January 2004 to 31 December 2010), and in whom I looked for prescription of statins following the date of this clinical trigger. Of those individuals with a cardiovascular risk that could be assessed as high, 33,226 went on to receive a statin. The clinical-trigger period was terminated in the event that an individual developed a 'high risk diagnosis'.

In figure 8.1, I have presented the breakdown of categorical variables at the clinical trigger date. A clear majority of individuals were men, 71,483 in all, representing 59.3%; this is consistent with the higher cardiovascular risk at a given age found in men compared to women. The percentage of smokers was 32.2% (38,788 individuals) at the clinical trigger date. That there was no missing data for smoking was expected: individuals could only be assessed as having high cardiovascular risk if a smoking status had been available by the clinical trigger date. The comparatively high smoking prevalence (32.2%), reflects its importance in the risk-assessment tool that designated the individuals as being at high risk. The high proportion of missing data for the cholesterol:HDL ratio (60.9%) is a reflection of the fact that this variable is not required for the Framingham non-laboratory risk assessment tool that I used in my main analysis. Similarly, none of the individuals were in any of the other diagnostic categories examined (diabetes, CVA/TIA, CHD, and previous ACS), because such indi-

viduals were considered separately in the 'high-risk diagnosis' clinical trigger.

Age is the dominant variable in the Framingham non-laboratory risk-assessment tool. In line with this, the largest number of individuals designated at high risk were in the 60 to 64 age-band (24,377 representing 20.2% of those with this trigger), and the figure was also high in the neighbouring age-bands. Younger and older age groups contained fewer individuals with this clinical trigger: the former because their risk was genuinely low; the latter because individuals had either already become high risk in an earlier age group or because they had a 'high-risk diagnosis' to disqualify them from this trigger. Thus, the age distribution seen is in line with expectations.

Deprivation quintile 3 was overrepresented in our entire dataset, and this was reflected in the numbers for this clinical trigger. For that quintile, 29,010 individuals had this trigger, representing 24.0% of the total. The number was lowest in quintile 5, at 21,947, representing 18.2% of the total.

The risk assessment I used included BMI as one of its variables, and so none of the individuals with this clinical trigger had a missing value for BMI. Overall more than 70% of these individuals were either overweight or obese at the time of the clinical trigger. Similarly, only 64,735 individuals (53.8%) did not have hypertension, 14,649 (12.2%) had undiagnosed hypertension, 23,025 (19.1%) had controlled hypertension, and 18,032 (15.0%) had uncontrolled hypertension.

In figure 8.2, I have shown crude rates, expressed as the number of clinical actions per-person-year-at-risk with the clinical trigger, in this case the number of individuals starting treatment with a statin during the time in which they have fulfilled the trigger 'risk assessed high'. The rate per PYAR in women was 0.123; in men 0.091. The rate in smokers was 0.091, compared to 0.11 in non-smokers. In those with a cholesterol:HDL ratio greater than 4, the rate was 0.199, compared to 0.165 in those whose ratio was less. The rate was slightly higher in those with other Charlson comorbidities, at 0.107 compared to 0.104 in those without.

In these presentations of crude rates, I have not presented CIs around my estimates or made formal comparisons: the significance of these relationships is dealt with in detail later, with the employment of appropriate statistical techniques

With respect to age, the rates at which individuals received statins were lower at the extremes of age, particularly for the older age bands: the 85+ age-band had a rate of 0.041 and the '80 to 85' age-band had a rate of 0.060; this compared to a maximum rate in the '65 to 69' age-band where the rate was 0.122.

Figure 8.1: Descriptive variables for the clinical trigger-action 'risk assessed high' and 'statin'

Frequencies of categorical variables for 'risk assessed high' and 'statin'. Incident clinical trigger (triggers = 120459; actions = 33226)

Number of clinical triggers for binary variables

Variable	Yes	(%)	No	(%)	Missing	(%)
Female	48976	(40.7)	71483	(59.3)	0	(0)
Smoker	38788	(32.2)	81671	(67.8)	0	(0)
Chol:HDL >= 4	23079	(19.2)	23961	(19.9)	73419	(60.9)
Diabetes	0	(0)	120459	(100)	0	(0)
CVA / TIA	0	(0)	120459	(100)	0	(0)
CHD	0	(0)	120459	(100)	0	(0)
Previous ACS	0	(0)	120459	(100)	0	(0)
Other comorbidities	11695	(9.7)	108764	(90.3)	0	(0)

Number of clinical triggers by age

Age	n	(%)
35 to 39	325	(0.3)
40 to 44	1884	(1.6)
45 to 49	8105	(6.7)
50 to 54	15185	(12.6)
55 to 59	21163	(17.6)
60 to 64	24377	(20.2)
65 to 69	18400	(15.3)
70 to 74	12955	(10.8)
75 to 79	8893	(7.4)
80 to 84	5550	(4.6)
85+	3622	(3)

Number of clinical triggers by BMI

BMI	n	(%)
Normal or low	35094	(29.1)
Overweight	48710	(40.4)
Obese	36655	(30.4)
Missing	0	(0)

Number of clinical triggers by hypertension category

Hypertension	n	(%)
None	64753	(53.8)
Undiag.	14649	(12.2)
Contr.	23025	(19.1)
Uncontr.	18032	(15)

Number of clinical triggers by quintile

Quintile	n	(%)
1	24868	(20.6)
2	21775	(18.1)
3	29010	(24.1)
4	22859	(19)
5	21947	(18.2)

Rates of provision of statins were lower in quintiles 3 and 4 than in other quintiles.

BMI categories showed a higher rate of provision in overweight individuals (rate 0.11) and obese individuals (rate 0.117), as compared to individuals with normal or low BMI, where the rate was 0.083. For hypertension categories, the rate of provision was lowest in individuals with no hypertension (0.071), rising to 0.105 in individuals with undiagnosed hypertension, to 0.151 in individuals with uncontrolled hypertension, and was highest in individuals with controlled hypertension at 0.178.

Overall, these results, which are a starting point for my analysis, suggest that overweight and obese individuals, those with hypertensive disease, and those with a raised cholesterol:HDL ratio were more likely to have received treatment, perhaps reflecting a situation where treatment was being initiated on the basis of risk factors considered separately, rather than on overall cardiovascular risk. Women and those from the mid part of the age range were more likely to receive treatment.

In figure 8.3, I present the distributions of the derived history variables. By my definition, the 'risk assessed high' clinical trigger would always be the first indication, given that it was always superseded by clinical triggers relating to high-risk or cardiovascular diagnoses. The distribution in the first of the figures, showing the counts for the different indication numbers, was therefore expected. Likewise, all individuals were expected to have zero days of previous indication prior to the clinical trigger date, confirmed in the second graphic (histogram showing indication days prior to this clinical trigger). The following graphic shows the distribution of the number of times individuals had received a statin prior to the clinical trigger date, the vast majority never having received a statin. For those individuals who did, I show the distribution of times since that previous statin in the fourth graphic in figure 8.3 (histogram of days since the most recent prior clinical action). The distribution is right-skewed, most individuals having received this treatment within the last 50 days.

In figure 8.4, I show results relating to these same derived variables relating to patient history, this time including rates of provision of a statin (expressed as years-per-person-year-at-risk). Only one category is present for the indication number and indication periods (for reasons given above). The number of previous clinical actions was zero for 105,301 individuals (in other words, these individuals had never

Figure 8.2: Relations between categorical variables and times to provision of statin in those with the clinical trigger 'risk assessed high'

Categorical variables relationships with outcome for 'risk assessed high' and 'statin'. Incident clinical trigger (triggers = 120459; actions = 33226)

Rates (n per PYAR) for binary variables

Variable	Yes	No	Missing
Female	0.123	0.091	--
Smoker	0.091	0.11	--
Chol:HDL >= 4	0.199	0.165	0.071
Diabetes	--	0.104	--
CVA / TIA	--	0.104	--
CHD	--	0.104	--
Previous ACS	--	0.104	--
Other comorbidities	0.107	0.104	--

Rates (n per PYAR) by age

Age−group	Rate
35 to 39	0.107
40 to 44	0.1
45 to 49	0.089
50 to 54	0.094
55 to 59	0.107
60 to 64	0.119
65 to 69	0.122
70 to 74	0.116
75 to 79	0.085
80 to 84	0.06
85+	0.041

Rates (n per PYAR) by BMI

BMI	Rate
Normal or low	0.083
Overweight	0.11
Obese	0.117
Missing	--

Rates (n per PYAR) by hypertension category

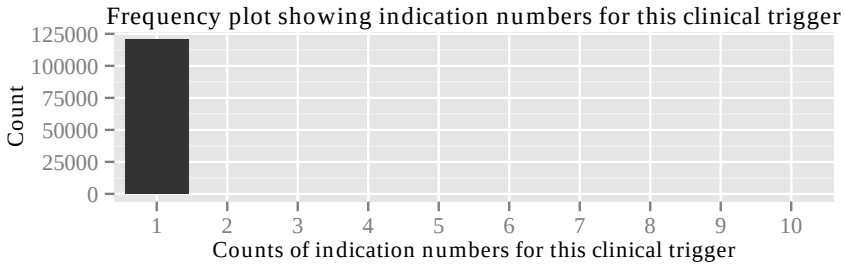
Hypertension	Rate
Contr.	0.178
Uncontr.	0.151
None	0.071
Undiag.	0.105

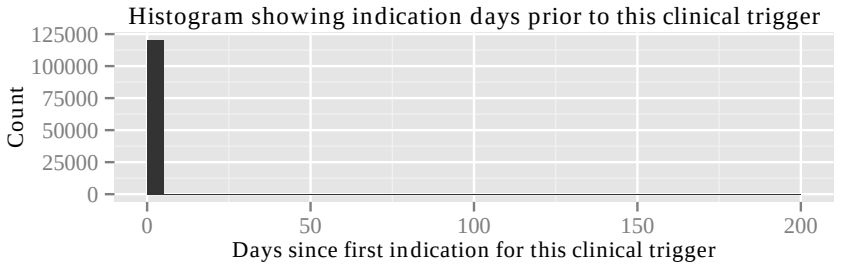
Rates (n per PYAR) by quintile

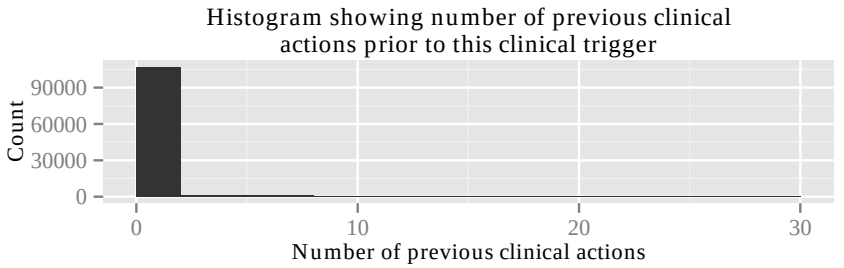
Quintile	Rate
1	0.104
2	0.105
3	0.103
4	0.103
5	0.105

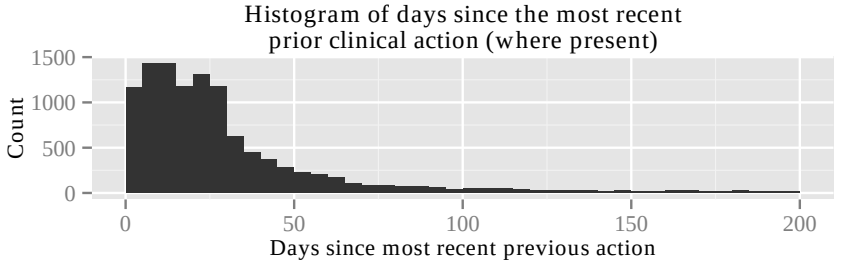
Figure 8.3: Frequencies of derived variables relating to an individual's history within the pathway for the clinical trigger 'risk assessed high' and 'statin'

Frequencies of derived variables relating to patient history for 'risk assessed high' and 'statin'. Incident clinical trigger (triggers = 120459; actions = 33226)









had a statin at the time of the clinical trigger). There were 11,029 individuals who had five or more previous statin prescriptions. Smaller numbers had had between one and four prescriptions. The rate of subsequent provision in those with five or more prescriptions was 3.287, compared to 0.066 in those who had had no previous statin: this is consistent with this group representing individuals already being treated with the drug. In subsequent analysis, I have only included the 105,301 individuals with no previous statin prescription. Similarly, those individuals who had their most recent statin prescription within one year of the trigger date (shown in last table in figure 8.4), had a higher rate of subsequent prescription for the drug (3.465) compared to 0.066 in those who had not previously received it.

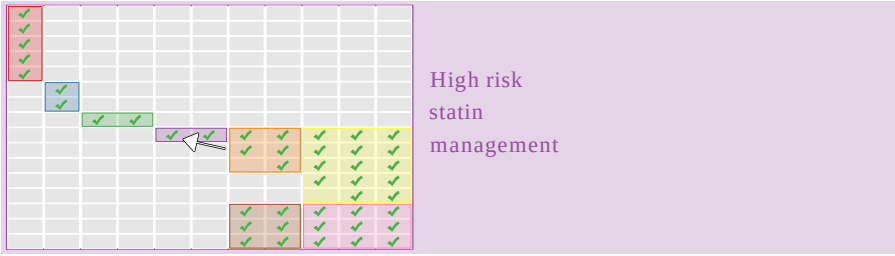
In figure 8.5, I show a Kaplan-Meier plot of the prescription of statins in individuals assessed to be at high risk, for each of the five deprivation quintiles. At time 0 the proportion of individuals who have not had a statin is 1; this figure declines with time, as an increasing proportion of individuals are treated. In all quintiles, there was an initial quite steep decline, accounting for about 10 to 15% of individuals receiving the drug. Thereafter, a more gradual decline persisted through the rest of the observation period. Clear differences between the quintiles were not apparent.

In figure 8.6 I present findings from a univariate mixed-effects model (frailty model) looking at HRs for deprivation quintiles, with quintile 1 as the reference category, and showing 95% CIs. The ICC for practices is also shown, which gives an indication of the proportion of the variability in the outcome that can be explained by taking account of practice-level variability as a random-effect term.

When performing this and subsequent analyses using frailty models to look at this clinical trigger-action, I included 105,301 individuals (those individuals who I had identified from the descriptive analysis as having had no previous statin prescription). Of these individuals 33,226 began a statin during the time-period in which it was indicated due to their being high risk on risk assessment.

HRs did not vary significantly across deprivation quintiles. While they were very slightly higher in the other quintiles as compared to the reference category, for example at 1.01 in quintile 2, the CIs for these estimates all crossed one, suggesting that the differences were not statistically significant. Further, the estimated HRs suggested only a very modest difference between quintiles in their hazard for receiving a statin (one or two percent). The ICC of 0.090 indicated

Figure 8.4: History variables and rates of provision for clinical trigger 'risk assessed high' and the clinical action 'statin'



Variable relationships with outcome for derived variables relating to patient history for 'risk assessed high' and 'statin'. Incident clinical trigger (triggers = 120459; actions = 33226)

Number and rate for different indication numbers

Indication number	Number	Rate
1	120459	0.104
2	0	--
3	0	--
4	0	--
5 or more	0	--

Number and rate for different total indication periods

Indication time (years)	Number	Rate
<= 1	120459	0.104
>1 and <=2	0	--
>2 and <=3	0	--
>3 and <=4	0	--
>4 and <=5	0	--
>5	0	--

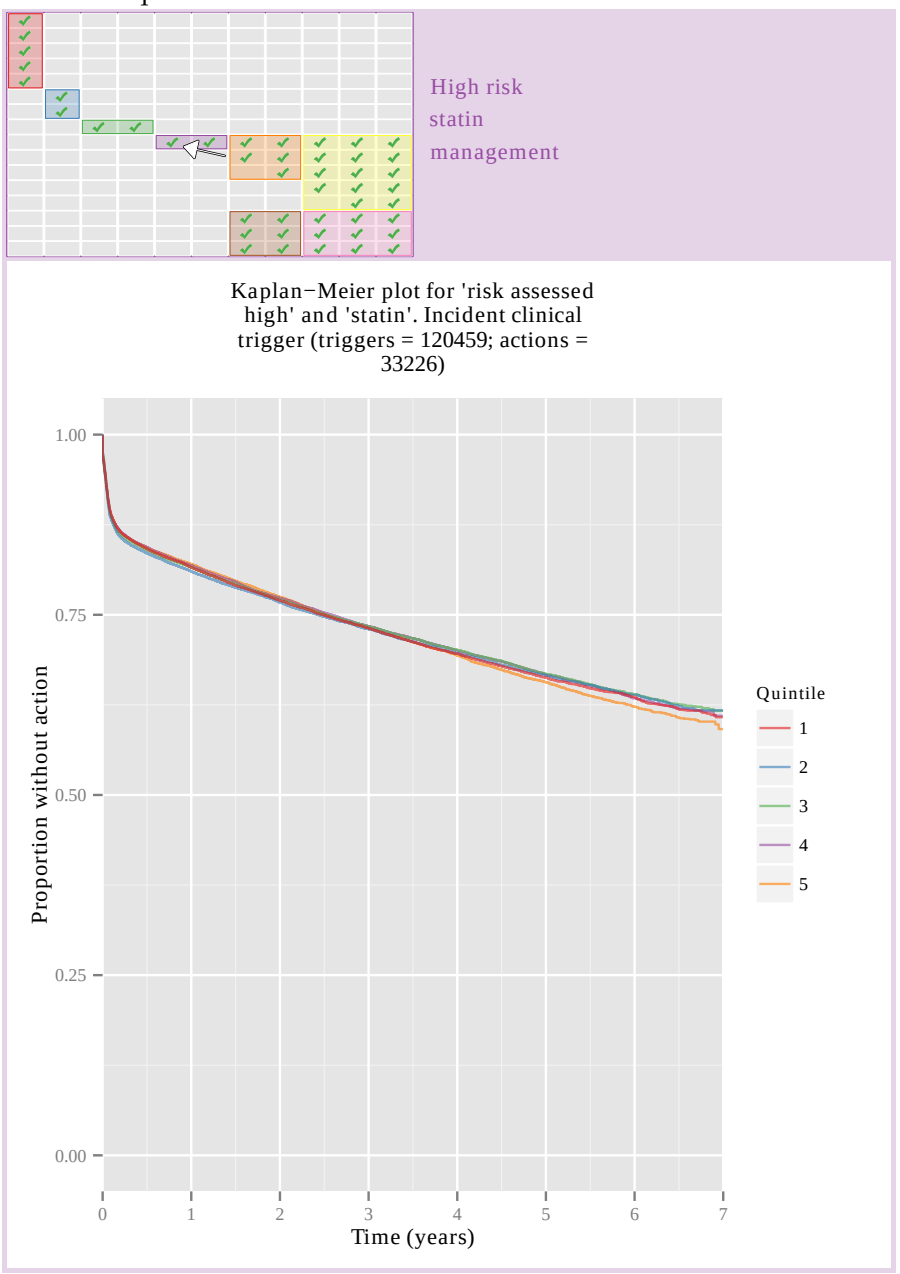
Number and rate for different numbers of previous actions

Responses	Number	Rate
0	105301	0.066
1	1887	0.385
2	970	0.488
3	663	0.618
4	609	0.943
5 or more	11029	3.287

Number and rate for different times since most recent prior action

Time since action (years)	Number	Rate
Not applicable	105301	0.066
<= 1	12525	3.465
>1 and <=2	870	0.236
>2 and <=3	585	0.179
>3 and <=4	424	0.18
>4 and <=5	260	0.189
>5	494	0.185

Figure 8.5: Kaplan-Meier plot showing the proportion of individuals who had not received a statin prescription by time and by deprivation quintile



that approximately 9% of the observed variation was explicable on the basis of practice-level variation.

In the next stage of the modelling, I added the variables age and sex as covariates, retaining the deprivation quintile variable, and again including practice as a random-effect term. The HRs and CIs for this model are shown in figure 8.7. In presenting HRs for age-bands, I took the '50 to 54' age-band as the reference category, in order to avoid using an extreme age-band for comparison. Importantly, no evidence emerged from this model of significant differences across deprivation quintiles in provision of statins to these patients. The HRs were close to 1 for quintiles 2 through to 5, and even small differences (HR 1.01 in quintile 2 and 0.98 in quintile 4) were not significant.

Older age categories were less likely to receive a statin based purely on risk. In the '75 to 79' age-band the HR was 0.65 (95% CIs 0.60; 0.70); for the '80 to 84' age-band the hazard ratio was 0.44 (95% CIs 0.40; 0.48); in the '85+' age-band it was 0.27 (95% CIs 0.31; 0.39). Other age bands were significantly more likely to receive the treatment than the reference category: '55 to 59' age-band, with HR 1.13 (95% CIs 1.08; 1.19); '60 to 64', with HR 1.13 (95% CIs 1.08; 1.19); and '65 to 69', with HR 1.10 (95% CIs 1.04; 1.16). The model suggested that women were also significantly more likely to receive the treatment, with a HR of 1.35 (95% CIs 1.31; 1.39), having adjusted for deprivation quintile and age. The proportion of the variation in outcome related to practice-level variation increased slightly, as compared to the univariate model, to 0.093.

Thus, on the basis of this further modelling, which allowed adjustment of the comparison across deprivation quintiles for age and sex, no evidence of a significant difference emerged in initiation of statin prescription between deprivation quintiles.

The final model used to examine this clinical trigger action, whose results are shown in figure 8.8, took the same approach as before, but with some additional variables (smoking status, BMI, hypertension category, cholesterol:HDL, and other comorbidities). Again, no significant differences existed in the quintile comparison. The HRs rose slightly in quintiles 3, 4, and 5. The HR was highest in quintile 5, 1.01 (95% CI 0.96; 1.07); it was 1.00 (95% CI 0.95; 1.06) in quintiles 1,2,3 and 4. A similar age-related pattern emerged to that seen in the age-sex-adjusted model. As a result of additional adjustments in this model, the HR in the '45 to 49' age-band was 0.89 (95% CI 0.83; 0.96); there was also a significant difference in the '70 to 74' age-band, with

Figure 8.6: Univariate mixed-effect model for the clinical trigger ‘risk assessed high’ and the clinical action ‘statin’ by deprivation quintiles and null model

Mixed−effects model for 'risk assessed high' and 'statin'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.01	(0.96; 1.06)
Quintile 3	0.99	(0.94; 1.04)
Quintile 4	0.98	(0.93; 1.03)
Quintile 5	1.00	(0.94; 1.05)

Number of clinical triggers 105301; Number of clinical actions 20661. ICC for practice = 0.09

Figure 8.7: Multivariate mixed-effect model for the clinical trigger 'risk assessed high' and clinical action 'statin' for deprivation quintiles, adjusted for age and sex

Mixed−effects model for 'risk assessed high' and 'statin'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.01	(0.96; 1.06)
Quintile 3	0.99	(0.95; 1.04)
Quintile 4	0.98	(0.93; 1.03)
Quintile 5	0.99	(0.94; 1.04)
Age 35 to 39	1.07	(0.81; 1.43)
Age 40 to 44	1.13	(1.00; 1.27)
Age 45 to 49	0.96	(0.90; 1.03)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.13	(1.08; 1.19)
Age 60 to 64	1.13	(1.08; 1.19)
Age 65 to 69	1.10	(1.04; 1.16)
Age 70 to 74	0.97	(0.92; 1.03)
Age 75 to 79	0.65	(0.60; 0.70)
Age 80 to 84	0.44	(0.40; 0.48)
Age 85+	0.27	(0.23; 0.31)
Male	1	(Reference)
Female	1.35	(1.31; 1.39)

Number of clinical triggers 105301; Number of clinical actions 20661. ICC for practice = 0.093

a HR of 1.18 (95% CI 1.10; 1.27). Likewise, the pattern seen earlier, whereby women were more likely to receive a statin in this group persisted in this model, with a HR 1.29 (95% CI 1.24; 1.33).

Of the other variables included, it was notable that obese individuals were less likely to receive a statin then those of low or normal weight, HR 0.92 (95% CI 0.88; 0.96). Those with controlled hypertension – HR 1.81 (95% CI 1.74; 1.88), uncontrolled hypertension – HR 1.80 (95% CI 1.72; 1.88), and undiagnosed hypertension – HR 1.43 (95% CI 1.37; 1.50) were all significantly more likely to receive a statin than those with no hypertension, adjusting for the other variables shown. Likewise, individuals with a cholesterol:HDL ratio greater than or equal to 4 were over twice as likely to receive a statin, with HR 2.37 (95% CI 2.30; 2.44). Those with Charlson comorbidities (other than high cardiovascular risk comorbidities) were significantly less likely to receive treatment, with HR 0.90 (95% CI 0.86; 0.96).

I estimated a slope index of inequality across the hazard ratios of deprivation for the 'fully adjusted model'. The estimated regression coefficient for the log hazard ratio was 0.0019, with a p value of 0.561, suggesting no significant slope across quintiles in the hazard of receiving a statin.

Summarising, the overall pattern that emerged from these findings for this clinical trigger-action was as follows:

- A fairly small proportion of individuals received the intervention
- Women in this group were more likely to receive a statin
- Older age groups with less likely to receive a statin
- Individuals with hypertension or raised cholesterol:HDL ratio were more likely to receive a statin in this group, though individuals who smoked were not
- Approximately 9% of the variation seen in times to receiving a statin related to variation at practice level
- There was no difference between deprivation quintiles in times to receiving a statin
- Their work to clear phases in the Kaplan-Meier plot, with an initial fairly rapid achievement of the clinical action, followed by subsequent slower population uptake. I discuss this pattern further in chapter 10, where I also consider results from other points in the pathway

Figure 8.8: Multivariate mixed-effect model for the clinical trigger 'risk assessed high' and clinical action 'statin' for deprivation quintiles, adjusted for age, sex, and other variables

Mixed−effects model for 'risk assessed high' and 'statin'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.01	(0.96; 1.06)
Quintile 3	0.99	(0.94; 1.04)
Quintile 4	1.01	(0.96; 1.06)
Quintile 5	1.01	(0.95; 1.07)
Age 35 to 39	0.77	(0.58; 1.03)
Age 40 to 44	0.94	(0.84; 1.06)
Age 45 to 49	0.90	(0.84; 0.96)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.20	(1.14; 1.26)
Age 60 to 64	1.30	(1.24; 1.37)
Age 65 to 69	1.31	(1.24; 1.39)
Age 70 to 74	1.19	(1.12; 1.27)
Age 75 to 79	0.82	(0.75; 0.88)
Age 80 to 84	0.56	(0.51; 0.62)
Age 85+	0.34	(0.29; 0.40)
Male	1	(Reference)
Female	1.28	(1.24; 1.32)
Non−smoker	1	(Reference)
Smoker	1.00	(0.96; 1.03)
BMI low / norm.	1	(Reference)
Overweight	1.05	(1.01; 1.09)
Obese	0.92	(0.88; 0.96)
No hyp.	1	(Reference)
Hyp. contr.	1.80	(1.73; 1.88)
Hyp. uncontr.	1.79	(1.71; 1.87)
Untreat. hyp.	1.43	(1.36; 1.49)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	2.35	(2.21; 2.51)
No oth. co.	1	(Reference)
Other co.	0.90	(0.85; 0.95)

Number of clinical triggers 105301; Number of clinical actions 20661. ICC for practice = 0.089. Missing values imputed using MICE.

8.2 PCI IN INDIVIDUALS WITH MI

In figure 8.9, I show descriptive summaries for the main categorical variables for the clinical trigger-action 'MI' and 'PCI'. I identified 20,467 MIs in our dataset for which I investigated times to provision of PCI. In 5118 cases, the MI was followed by a PCI. The majority of individuals having an MI in our dataset were men (12,371, representing 60.4%); a majority of individuals were non-smokers (14,677, representing 71.7%), with 4722 (23.1%) smokers – 943 (5.2 %) had missing smoking data. A majority had a cholesterol:HDL ratio less than 4 (7029, representing 34.3%); there were 4867 (23.8%) individuals with a cholesterol:HDL ratio greater than or equal to 4; this value was missing for 8571 of the MIs, representing 41.9%. By definition, every MI occurred in an individual who had CHD or an ACS. Of the MIs examined, 9586 (46.8%) occurred in individuals with other Charlson comorbidities at the time of the event. Of all the MIs, 3031 (14.8%) were treated in a cardiac centre.

The majority of MIs occurred in older age groups, despite the smaller overall populations there, reflecting the powerful effect of age as a risk factor for CHD. Thus, 3778 (18.5%) of the events occurred in those in the '85+' age-band, 3120 (15.2%) in the '80 to 84' age-band, and 2927 (14.3%) in the '75 to 79' age-band. Over half of the events occurred in those aged 70 and over.

A smaller proportion of events occurred in the less deprived quintiles than in the more deprived. There were 3528 (17.2%) events in quintile 1, compared to 4788 (23.4%) in quintile 3 and 4294 (21.0%) in quintile 5. Particularly with respect to quintile 3, this is partly a reflection of the over-representation of this quintile in the study population.

Of those MIs that occurred, 6567 (32.1%) occurred in overweight individuals and 4638 (22.7%) in obese individuals; for 3213 (15.7%) of the events that occurred the BMI value was missing. When looking at events in relation to hypertension category, I found that the majority occurred in individuals with controlled hypertension – 10,587 (51.7%), perhaps reflecting the older age of these individuals. Uncontrolled hypertension was present in individuals with an MI in 2835 cases (13.9%), while 6302 (30.8%) did not have hypertension.

I also looked at the specialty and type of the admission (emergency or elective) relating to the MI that was the clinical trigger. A large majority of the admissions had either cardiology, 8207 (40.1%), or

another medical specialty, 10676 (52.2%), as the clinical specialty; Most of the admissions were emergency admissions, 16523 (80.7%).

In figure 8.10, I show the crude rates of provision of PCI after MI in the same way as for the earlier clinical trigger-action ('risk assessed high' and 'statin'). The rate was higher in men, at 0.280 compared to 0.152 in women; it was higher in smokers at 0.378, compared to 0.191 in non-smokers, and 0.138 in those whose smoking status was unknown; it was higher in those with a raised cholesterol:HDL ratio, at 0.340, compared to 0.181 in those where it was not raised, and 0.209 in those where it was unknown. The crude rate of provision was lower in diabetics (0.174 compared to 0.243 for non–diabetics), in those who have had a previous CVA/TIA (0.97, compared to 0.243 in those who have not), and in those with other Charlson comorbidities (0.157 compared to 0.277 in those without). Crude rates were also higher in those treated in a cardiac centre (0.312 compared to 0.211 in a non-cardiac centre).

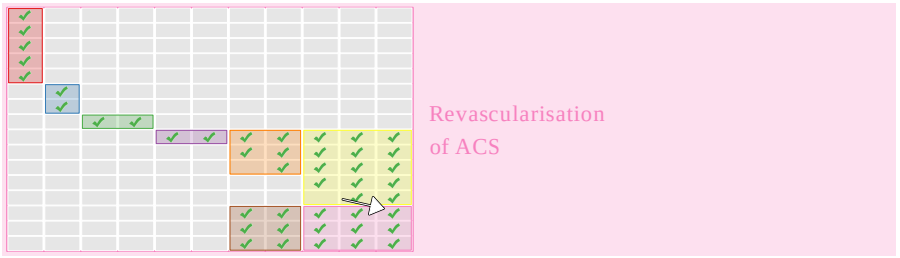
Overall, crude rates of provision of PCI seem higher in those with risk factors that are not also comorbidities (male sex, smoking, and raised cholesterol:HDL ratio) and lower in those with comorbidities (some of which are also risk factors) – diabetes, CVA/TIA, and other Charlson comorbidities. Provision was more likely in those treated at cardiac centres.

Younger age groups had higher crude rates of provision of PCI following MI. The highest rate was in the '40 to 44' age-band, 0.55, falling consistently as age increased to 0.31 for the '65 to 69' age-band and at a minimum of 0.031 in the '85+' age-band. In view of the known pattern, whereby more deprived individuals tend to have ACSs at a younger age, this decreasing rate with age highlighted the importance of adjusting for this variable in further analyses.

Following MIs in an individual with normal or low BMI, the rate of provision of PCI was 0.19. Where the individual was overweight the rate was higher (0.253) and similarly it was higher if the person was obese (0.276). Those with no hypertension had a rate of provision of PCI of 0.281; in those with undiagnosed hypertension the rate was 0.289. Rates were lower in those with diagnosed hypertension, whether it be controlled (0.188) or uncontrolled (0.227).

Where the admission relating to MI was under the cardiology specialty, rates were substantially higher, 0.495, as compared to 0.111 in other medical specialties. The rate in other specialties were 0.021. For admission type, the rate was highest in the 'other' category, at 0.366,

Figure 8.9: Descriptive variables for the clinical trigger-action 'MI' and 'PCI'



Frequencies of categorical variables for 'MI' and 'PCI'. Incident clinical trigger (triggers = 20467; actions = 5118)

Number of clinical triggers for binary variables

Variable	Yes	(%)	No	(%)	Missing	(%)
Female	8096	(39.6)	12371	(60.4)	0	(0)
Smoker	4722	(23.1)	14677	(71.7)	1068	(5.2)
Chol:HDL >= 4	4867	(23.8)	7029	(34.3)	8571	(41.9)
Diabetes	4871	(23.8)	15596	(76.2)	0	(0)
CVA / TIA	3278	(16)	17189	(84)	0	(0)
CHD	20467	(100)	0	(0)	0	(0)
Previous ACS	20467	(100)	0	(0)	0	(0)
Other comorbidities	9586	(46.8)	10881	(53.2)	0	(0)
Cardiac centre	3031	(14.8)	17436	(85.2)	0	(0)

Number of clinical triggers by age

Age	n	(%)
35 to 39	198	(1)
40 to 44	408	(2)
45 to 49	668	(3.3)
50 to 54	1136	(5.6)
55 to 59	1436	(7)
60 to 64	1954	(9.5)
65 to 69	2211	(10.8)
70 to 74	2631	(12.9)
75 to 79	2927	(14.3)
80 to 84	3120	(15.2)
85+	3778	(18.5)

Number of clinical triggers by BMI

BMI	n	(%)
Normal or low	6049	(29.6)
Overweight	6567	(32.1)
Obese	4638	(22.7)
Missing	3213	(15.7)

Number of clinical triggers by hypertension category

Hypertension	n	(%)
None	6302	(30.8)
Undiag.	743	(3.6)
Contr.	10587	(51.7)
Uncontr.	2835	(13.9)

Number of clinical triggers by quintile

Quintile	n	(%)
1	3528	(17.2)
2	3584	(17.5)
3	4788	(23.4)
4	4273	(20.9)
5	4294	(21)

Number of clinical triggers by admission specialty

Specialty	n	(%)
Cardiology	8207	(40.1)
Med. spec.	10676	(52.2)
Other spec.	1578	(7.7)
Missing	6	(0)

Number of clinical triggers by admission type

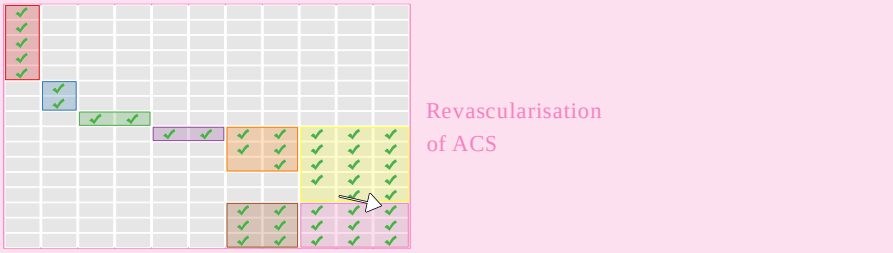
Admission type	n	(%)
Elective	622	(3)
Emergency	16523	(80.7)
Other	3294	(16.1)
Missing	28	(0.1)

followed by the emergency category at 0.208. Rates were lowest for those with an elective admission as 0.072.

In figure 8.11, I present the distributions of the derived history variables for this clinical trigger-action. In the first figure I show the distribution of indication numbers. Where the MI was the first indication that the individual had for PCI, the indication number was 1. In some cases individuals had had previous periods in which they had stable angina or an ACS, meaning that the MI in question was not their first indication for PCI. In figure 8.12, I have illustrated the variable shown in this distribution as a categorical variable, with numbers and rates for each category – in the first figure 'Number and rate for different indication numbers'. The great majority of individuals having an MI had an indication number of 1 (10,697 individuals), 2 (6165 individuals), or 3 (2225 individuals). There were 603 individuals for whom the indication number was five or more (meaning that prior to this MI the individual had had at least four other previous indications for PCI). The provision rate was highest in those for whom this was the first indication, at 0.248; where the second indication, the rate was 0.231; the rate was lowest in those for whom this was the fourth indication, at 0.152.

Similarly in figure 8.11, I show, in the second graphic, the number of indication days prior to the MI event under investigation. To give an example, were it the case that one year prior to that event the individual had had another MI (for which PCI would also have been indicated), that individual would register 365 days prior to this clinical trigger (assuming that no other indication events prior to that complicated the picture). From the distribution, it was clear that there was a peak at zero prior indication days, reflecting the individuals for whom this was indication number 1 (who by definition have no previous indication days). The distribution of prior indication days is otherwise very heavily right skewed, shown more clearly in the second graphic of figure 8.12. There were 14,302 individuals with prior indication periods less than or equal to one year; also 3920 MIs occurred in individuals who had already had prior indications for the procedure for over five years. The crude rate of provision was highest in those with prior indication times less than one year, at 0.258; longer prior indication times had lower provision rates for example for those with prior indication times more than three years and less than or equal to four years, the rate was 0.170; in those with prior indication times greater than five years the rate was 0.139.

Figure 8.10: Relations between categorical variables and times to provision of PCI in those with the clinical trigger 'MI'



Categorical variables relationships with outcome for 'MI' and 'PCI'.
Incident clinical trigger (triggers = 20467; actions = 5118)

Rates (n per PYAR) for binary variables

Variable	Yes	No	Missing
Female	0.152	0.28	--
Smoker	0.378	0.191	0.138
Chol:HDL >= 4	0.34	0.181	0.209
Diabetes	0.174	0.243	--
CVA / TIA	0.097	0.25	--
CHD	0.228	--	--
Previous ACS	0.228	--	--
Other comorbidities	0.157	0.277	--
Cardiac centre	0.312	0.211	--

Rates (n per PYAR) by age

Age−group	Rate
35 to 39	0.368
40 to 44	0.55
45 to 49	0.502
50 to 54	0.512
55 to 59	0.411
60 to 64	0.375
65 to 69	0.31
70 to 74	0.199
75 to 79	0.136
80 to 84	0.074
85+	0.031

Rates (n per PYAR) by quintile

Quintile	Rate
1	0.243
2	0.213
3	0.231
4	0.217
5	0.236

Rates (n per PYAR) by BMI

BMI	Rate
Normal or low	0.19
Overweight	0.253
Obese	0.276
Missing	0.178

Rates (n per PYAR) by hypertension category

Hypertension	Rate
Contr.	0.188
Uncontr.	0.227
None	0.281
Undiag.	0.289

Rates (n per PYAR) by admission specialty

Specialty	Rate
Cardiology	0.495
Med. spec.	0.111
Other spec.	0.021
Missing	0

Rates (n per PYAR) by admission type

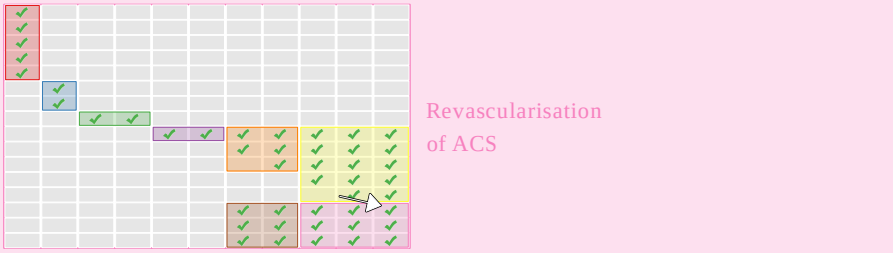
Admission type	Rate
Elective	0.072
Emergency	0.208
Other	0.366
Missing	0.273

The third graphic of figure 8.11, shows the distribution of clinical actions prior to the date of this clinical trigger. In this context, this meant how many PCIs the individual with the MI had previously undergone. The majority had never had a previous PCI; from the third graphic in figure 8.12, it can be seen that this was 19,458 of the MIs, compared to 892 for which there had been one previous PCI, 96 for whom there had been two, and small numbers for whom there had been at least three. The provision rate was highest in those with two previous PCIs, 0.594. This compares with a rate of 0.226 in those with no previous PCI.

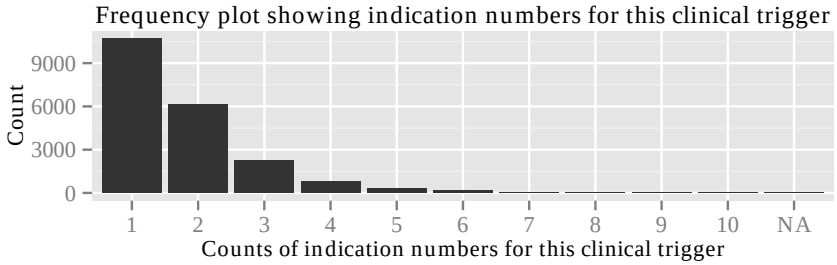
The final graphic in figure 8.11, shows how many days had elapsed since the most recent previous clinical action (PCI in this case). Thus, had an individual with an MI had a PCI most recently 100 days prior to that MI, this variable would be 100. There is arguably some concentration in the distribution in the 0 to 10 days time period, perhaps reflecting a tendency to instability of the coronary endothelium for a period following PCI. In the final graphic in figure 8.12, it is seen that the 19,458 individuals who had never had a previous PCI had a rate of 0.226, higher than those individuals who had had a previous PCI as recently as the last year (with a rate of 0.117), but had lower rates than individuals who had had previous PCIs longer ago than that (the numbers in these categories were quite small). For example, the 58 individuals who had had a PCI between four and five years previously had a rate of 1.224.

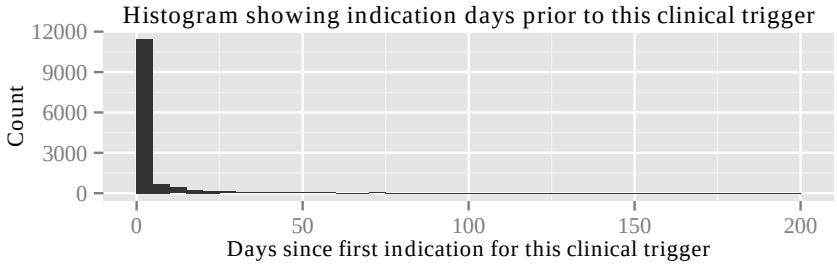
In figure 8.13, I show a Kaplan-Meier plot for this clinical trigger-action. In this figure, all individuals (the proportion of one) started out at time zero having not had a PCI; this proportion was adjusted as individuals underwent the procedure over time, taking account of the number of individuals censored. A clear feature of the graphic is that there is a near vertical decline subsequent to time zero, indicating that a percentage of individuals between 25 and 30% underwent a PCI very soon after the MI in question – presumably relating to the provision of primary PCI. It is important to emphasise that there is an apparent contradiction here with the 80% 'Emergency' figures presented in figure 8.9 in relation to admission type; in fact this difference is explained by the fact that the 80% 'Emergency' figure relates to the original MI (the clinical trigger), rather than to the PCI (the clinical action). No difference was evident in this initial decline between deprivation quintiles. Subsequently, a slower rate of receiving PCIs occurred to the end of the observation period. During this period,

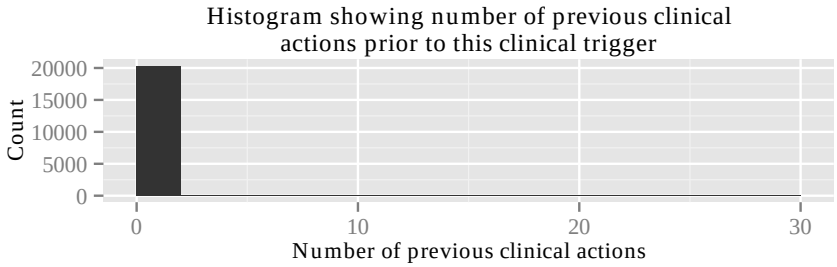
Figure 8.11: History variables for clinical trigger 'MI' and the clinical action 'PCI'



Frequencies of derived variables relating to patient history for 'MI' and 'PCI'. Incident clinical trigger (triggers = 20467; actions = 5118)







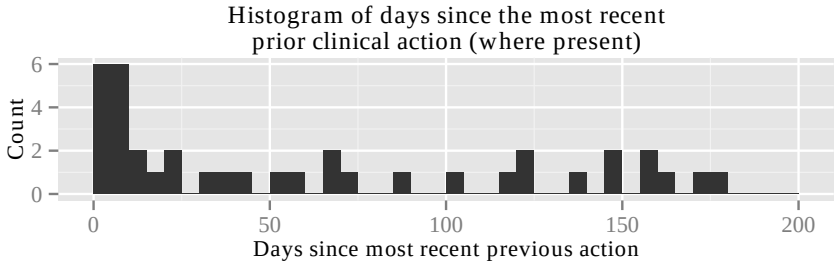
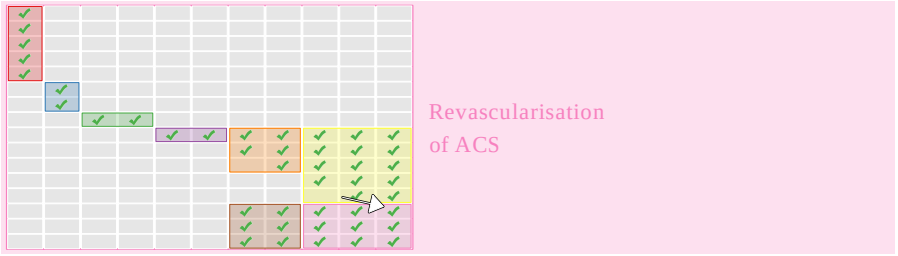


Figure 8.12: History variables and rates of provision for clinical trigger 'MI' and the clinical action 'PCI'



Variable relationships with outcome for derived variables relating to patient history for 'MI' and 'PCI'. Incident clinical trigger (triggers = 20467; actions = 5118)

Number and rate for different indication numbers

Indication number	Number	Rate
1	10697	0.248
2	6165	0.231
3	2225	0.159
4	777	0.152
5 or more	603	0.177

Number and rate for different total indication periods

Indication time (years)	Number	Rate
<= 1	14302	0.258
>1 and <=2	632	0.178
>2 and <=3	591	0.152
>3 and <=4	561	0.17
>4 and <=5	461	0.136
>5	3920	0.139

Number and rate for different numbers of previous actions

Responses	Number	Rate
0	19458	0.226
1	892	0.242
2	97	0.594
3 or more	20	0.171

Number and rate for different times since most recent prior action

Time since action (years)	Number	Rate
Not applicable	19458	0.226
<= 1	470	0.117
>1 and <=2	196	0.442
>2 and <=3	97	0.337
>3 and <=4	83	0.665
>4 and <=5	58	1.224
>5	105	1.043

the line indicating uptake fell most slowly for quintile 2 (reflecting that PCI was being received more slowly for that group); graphically the lines indicating uptake in other quintiles were very similar. Overall, there was not a substantial difference in uptake between quintiles.

In figure 8.14, I present results from a univariate frailty model modelling times to provision of PCI by deprivation quintile, using the patient practice and treatment hospital as random-effect terms in the model. The multilevel model in this case was a cross-classified model with individuals nested within practices nested within hospitals. I examined 20,467 MIs, following which 5118 PCIs were provided. The ICC for the individual's practice in this case was 0.034. The ICC for the admitting hospital was at 0.351.

An analogous model, this time with age and sex added as covariates, but otherwise performed in the same way, has been presented in figure 8.15. Adjusting for age and sex affected the HRs for the quintile comparison. Quintile 2 now had a hazard ratio 0.90 (95% CI 0.81; 0.99), significantly lower than the reference group quintile 1; quintile 5 had hazard ratio 0.78 (95% CI 0.71; 0.86), suggesting significantly reduced provision in this group as well. As was the case with crude rates, there was evidence of a significant age effect, with decreasing provision with increasing age. For example, the HR was 0.59 (95% CI 0.53; 0.66) in the '65 to 69' age-band; this fell to 0.26 (95% CI 0.23; 0.29) in the '75 to 79' age-band; the HR was 0.04 (95% CI 0.03; 0.05) in the '85+' age-band. There was also a significant effect of sex, where the HR for utilisation in women was 0.83 (95% CI 0.78; 0.89) with men as the reference group. Adjusting for age and sex in this model also reduced the ICC for practice (to 0.012 from 0.034 in the univariate model), and the ICC for hospital (to 0.188, from 0.351 in the univariate model).

In figure 8.16, I again show outputs from a frailty model on similar lines, but this time with a number of additional covariates included. The pattern across quintiles seen in the previous model persisted here. This time the HR for quintile 3 was 0.90 (95% CI 0.82; 0.99), suggesting a lower hazard of receiving PCI than in quintile 1 (the reference group). Individuals in quintiles 2 to 5 were significantly less likely to undergo the procedure, with a HR in quintile 5 of 0.83 (95% CI 0.75; 0.92). The pattern across age groups persisted: HRs in older age groups were significantly less than one (indicating lower hazard of undergoing PCI than in the '50 to 54' age-band that was the reference category). The HR for women was 0.85 (95% CI 0.80; 0.91), indicating, again, that women were receiving PCIs less than men at any given time.

Figure 8.13: Kaplan-Meier plot showing the proportion of individuals who had not received a PCI by time and by deprivation quintile

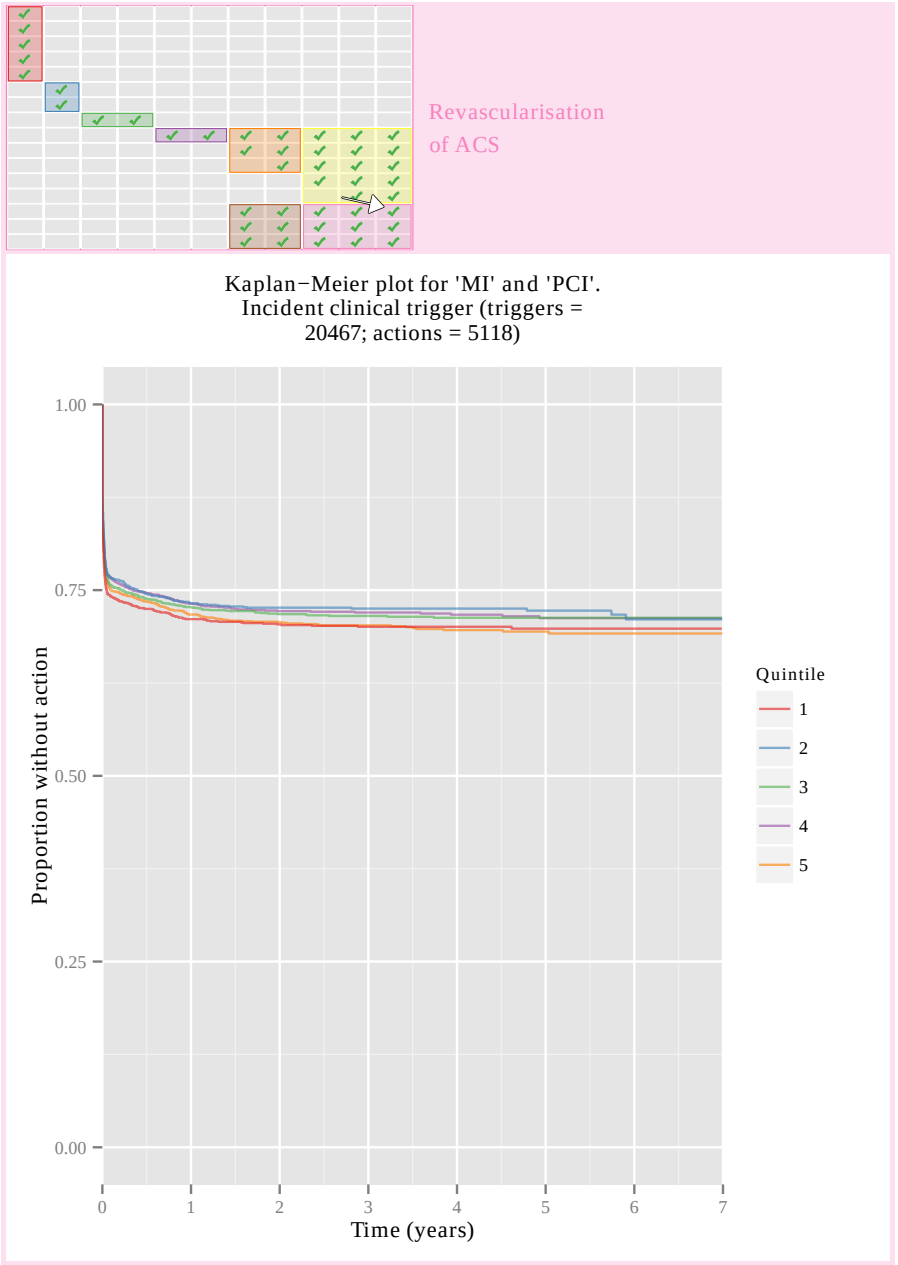
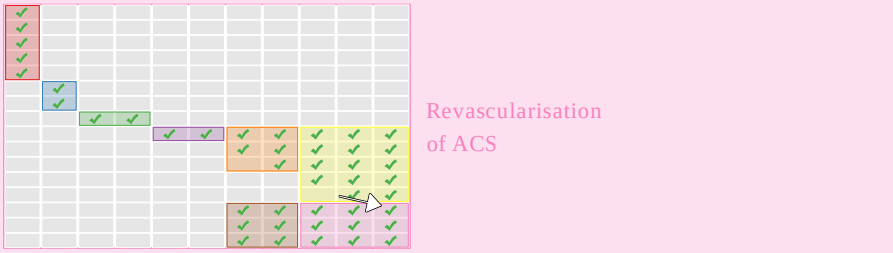


Figure 8.14: Univariate mixed-effect model for the clinical trigger 'MI' and the clinical action 'PCI' by deprivation quintiles and null model

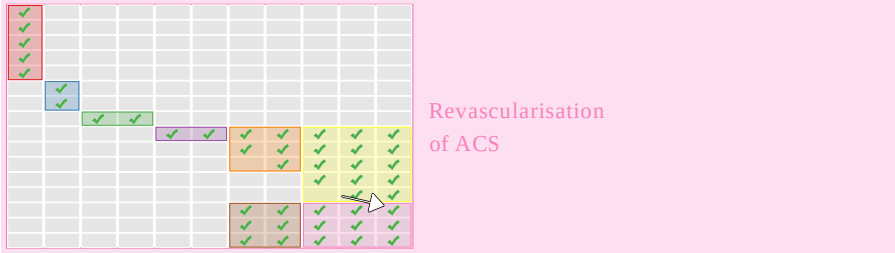


Mixed−effects model for 'MI' and 'PCI'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.96	(0.86; 1.06)
Quintile 3	1.01	(0.91; 1.11)
Quintile 4	0.96	(0.87; 1.06)
Quintile 5	0.95	(0.86; 1.05)

Number of clinical triggers 20467; Number of clinical actions 5118. ICC for practice = 0.034. ICC for hospital = 0.351

Figure 8.15: Multivariate mixed-effect model for the clinical trigger 'MI' and clinical action 'PCI' for deprivation quintiles, adjusted for age and sex



Mixed−effects model for 'MI' and 'PCI'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.90	(0.81; 0.99)
Quintile 3	0.89	(0.81; 0.98)
Quintile 4	0.84	(0.77; 0.93)
Quintile 5	0.78	(0.71; 0.86)
Age 35 to 39	0.86	(0.70; 1.07)
Age 40 to 44	1.04	(0.89; 1.21)
Age 45 to 49	0.93	(0.82; 1.06)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.83	(0.74; 0.93)
Age 60 to 64	0.69	(0.62; 0.76)
Age 65 to 69	0.59	(0.53; 0.66)
Age 70 to 74	0.38	(0.34; 0.43)
Age 75 to 79	0.26	(0.23; 0.29)
Age 80 to 84	0.13	(0.11; 0.15)
Age 85+	0.04	(0.03; 0.05)
Male	1	(Reference)
Female	0.83	(0.78; 0.89)

Number of clinical triggers 20467; Number of clinical actions 5118. ICC for practice = 0.012. ICC for hospital = 0.188

Smokers were significantly more likely to receive PCI, with a HR of 1.14 (95% CI 1.07; 1.21). Overweight individuals were more likely to receive a PCI compared to those of normal or low BMI: HR 1.11 (95% CI 1.04; 1.19). Individuals with undiagnosed hypertension were more likely to receive the intervention, HR 1.15 (95% CI 1.01; 1.31), compared to those with no hypertension. Provision of PCI was made less likely by the presence of covariates – CVA, HR 0.67 (95% CI 0.59; 0.75); diabetes, HR 0.82 (95% CI 0.76; 0.88); and other Charlson comorbidities, HR 0.70 (95% CI 0.65; 0.74). Again, a possible pattern emerged in which factors conferring high cardiovascular risk made interventions more likely while comorbidities made it less likely.

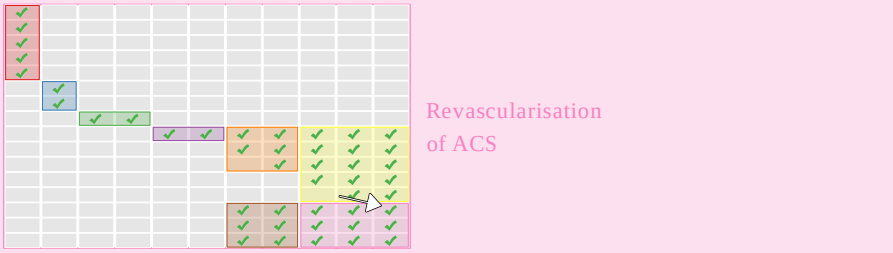
In this model, I also adjusted for admission type, hospital type and specialty. Emergency admission made subsequent PCI more likely (compared to elective admission), with HR 1.66 (95% CI 1.30; 2.13). MIs treated at non-cardiac centres (designated 'Other cen.' in figure 8.16) were less likely lead to a PCI, with HR 0.56 (95% CI 0.33; 0.93). MIs admitted under medical specialties other than cardiology – HR 0.43 (95% CI 0.40; 0.46), and other non-medical specialties – HR 0.07 (95% CI 0.05; 0.09) – were all less likely to go on to PCI than patients admitted under cardiology.

I also adjusted for the derived history variables. Here I found that MIs occurring in individuals for whom previous indications for PCI had been present were significantly less likely to receive that intervention, and that the more previous indications the less likely this was. In those with one previous indication the HR (taking individuals with no previous indications as the reference category) was 0.84 (95% CI 0.77; 0.90); for those with two previous indications (indication number 3), the HR was 0.68 (95% CI 0.60; 0.78); for those with three previous indications, the HR was 0.66 (95% CI 0.54; 0.81). Indication years prior to the current indication was handled as a continuous variable. I also looked at the number of previous responses (PCIs prior to the trigger MI). Where the MI occurred in individuals with one or more previous PCIs, subsequent PCI was less likely, with HR 0.93 (95% CI 0.81; 1.06), compared to those with no previous response as the reference category.

In this model, the ICC for the variation by practice remained the almost the same (0.013 compared with , from 0.012 in the previous model), suggesting that approximately 1.3% of the variation in times from MI to PCI might have been explained by practice-level variation. The ICC for hospital also fell: to 0.128, from 0.188 in the previous

model, suggesting that 12.8% variation related to hospital-level variation.

Figure 8.16: Multivariate mixed-effect model for the clinical trigger 'MI' and clinical action 'PCI' for deprivation quintiles, adjusted for age, sex, and other variables



Mixed−effects model for 'MI' and 'PCI'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.89	(0.80; 0.98)
Quintile 3	0.90	(0.82; 0.99)
Quintile 4	0.87	(0.79; 0.95)
Quintile 5	0.83	(0.75; 0.91)
Age 35 to 39	0.77	(0.62; 0.95)
Age 40 to 44	0.90	(0.77; 1.05)
Age 45 to 49	0.90	(0.79; 1.03)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.90	(0.81; 1.01)
Age 60 to 64	0.80	(0.71; 0.89)
Age 65 to 69	0.78	(0.70; 0.87)
Age 70 to 74	0.56	(0.50; 0.63)
Age 75 to 79	0.43	(0.37; 0.48)
Age 80 to 84	0.24	(0.20; 0.28)
Age 85+	0.08	(0.07; 0.10)
Male	1	(Reference)
Female	0.86	(0.80; 0.91)
Non−smoker	1	(Reference)
Smoker	1.15	(1.08; 1.23)
BMI low / norm.	1	(Reference)
Overweight	1.11	(1.01; 1.22)
Obese	1.08	(0.98; 1.18)
No hyp.	1	(Reference)
Hyp. contr.	0.99	(0.92; 1.06)
Hyp. uncontr.	1.04	(0.95; 1.13)
Untreat. hyp.	1.14	(1.00; 1.30)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.18	(1.09; 1.28)
No CVA	1	(Reference)
CVA	0.67	(0.59; 0.75)
No oth. co.	1	(Reference)
Other co.	0.70	(0.65; 0.74)
No diabetes	1	(Reference)
Diabetes	0.82	(0.75; 0.88)
Elect. adm.	1	(Reference)
Emer. adm.	1.67	(1.30; 2.13)

	HR	95% CI
Other adm.	1.97	(1.53; 2.53)
Cardiac cen.	1	(Reference)
Other cen.	0.56	(0.34; 0.92)
Cardiology	1	(Reference)
Med. spec.	0.43	(0.40; 0.46)
Other spec.	0.07	(0.05; 0.09)
Indication 1	1	(Reference)
Indication 2	0.84	(0.77; 0.91)
Indication 3	0.68	(0.60; 0.78)
Indication 4	0.67	(0.55; 0.82)
Indication 5+	0.65	(0.50; 0.84)
Indic. years	1.00	(0.99; 1.01)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.93	(0.81; 1.06)

Number of clinical triggers 20467; Number of clinical actions 5118. ICC for practice = 0.013. ICC for hospital = 0.127. Missing values imputed using MICE.

Again, for this 'fully adjusted model', I determined a slope index of inequality across quintiles, with an estimated regression coefficient of -0.0395, with a p value of 0.036, suggesting a statistically significant gradient across quintiles of decreasing hazard of receiving PCI with increasing deprivation, and nearly 4% fall in the chances of having a PCI by quintile. I checked the plausibility of the assumption of linearity by examining the log hazard ratios (quintile 2: -0.117; quintile 3: -0.105; quintile 4: -0.139; quintile 5: -0.186).

Below, I present a summary of the main findings relating to the clinical trigger-action 'MI' and 'PCI':

- Of the 20467 MIs that I identified in our data, 5118 went on to have a PCI following that event, representing 25.0%
- Women were significantly less likely to receive a PCI when adjustments were made for other covariates
- Older age groups were significantly less likely to have a PCI, again in the adjusted model
- There was evidence that adverse risk factors were more likely to be present in those receiving PCI (smoking, BMI, hypertension, and cholesterol:HDL), whereas comorbidities (diabetes, CVA, and the composite variable relating to other Charlson comorbidities) were less likely to be present, notwithstanding the fact that some of these comorbidities also increased risk
- Emergency admission to cardiac centres under cardiologists was associated with a subsequent increased chance of a PCI, compared to admissions that did not have these characteristics
- If the trigger MI was the first indication that the individual and had for PCI, subsequent intervention was more likely. Intervention was more likely with increasing time from any previous PCI that might have occurred. PCI was less likely in those who had a previoius PCI prior to the trigger MI
- In the fully adjusted model, variation at practice level accounted for 1.3% of the variation in times to PCI; variation in treating hospital accounted for 12.8%
- In univariate comparison, there was no significant difference between deprivation quintiles; when age and sex were adjusted

for, significantly reduced HRs occurred in more deprived quintiles compared to quintile 1; this pattern persisted in the fully adjusted model

8.3 SUMMARY

In this chapter, I have reviewed detailed results from only two points in the pathway of care for CHD. When looking at provision of statins to those in whom a cardiovascular risk assessment suggested the individual was high risk, I found no significant difference between deprivation quintiles. This was despite adjusting for available covariates, and taking account of variation at practice level.

I have also reported in detail results relating to the provision of PCI in patients following MI. Here, though univariate modelling suggested no difference between deprivation quintiles, I found evidence, when adjusting for other variables, that individuals in more deprived groups were less likely to undergo subsequent PCI.

By presenting detailed results for two pathway points I aimed to give the reader an insight into the nature of the analysis performed at each point in the pathway of care. It would have been completely impractical to present detailed results in the same way for all the analyses performed. Important results relating to other points in the pathway are included, without accompanying discussion, in appendix D. For those interested, all of the main results equivalent to those presented in this chapter can be accessed there.

Because of the focus on comprehensiveness, I needed to develop an approach to presenting the results based on the pathway as a whole. I present these results in the next chapter.

9 RESULTS OVERVIEW

This chapter is concerned with summarising the large number of results produced from my analysis. While I have described specific sections of the pathway of care for CHD in the preceding chapter, with a view to elucidating the approaches used at each specific point on the pathway, the overall aim in this thesis was to address healthcare inequity in the pathway of care for CHD as a whole.

Using the approach to presentation described on page 183, I present summaries of the pathway results using different modelling approaches, and using different underlying assumptions. In overview, I present summary results for the following:

1. The main analysis of clinical trigger-actions for the pathway, components of which were presented in the previous chapter. This looks at incident clinical triggers using the Framingham non-laboratory risk assessment tool.

2. The main analysis of clinical trigger-actions for drug cessation for the part of the pathway where drug treatments were indicated.

3. The main analysis repeated with important underlying assumptions changed

There are three main levels of modelling presented, as discussed in detail in the previous chapter when considering specific components of the pathway of care for CHD: univariate modelling (looking only at deprivation quintile, with practice, and, where relevant, hospital, as random effects); age-sex adjusted multivariate modelling, again with random-effect terms; multivariate models which adjust for all available, potentially-relevant covariates, as well as having the above random-effect terms – referred to throughout as 'fully-adjusted models'.

9.1 MAIN ANALYSIS

The first set of models looked at, univariate models comparing HRs across deprivation quintiles with adjustment for hospital and practice as random effects, are summarised in the first of the pathway diagrams, figure 9.1. To aid discussion, I have divided the pathway into eight

different regions, corresponding to broad categories of clinical trigger-action.

In the first of these, 'Risk and risk factors attainment', two of the five clinical trigger-actions significantly favoured the most deprived quintile (looking at smoking status and BMI). The HR was 1.20 for smoking status, for example, suggesting that the most deprived group was 20% more likely to have a smoking status recorded over time. Measurement of cholesterol and of BP was not significantly different between the most and least deprived quintiles; time to the availability of information in GP records sufficient to perform a full cardiovascular risk assessment was significantly less in the least deprived quintile, with a HR of 0.97. Thus, when looking at 'Risk and risk factors attainment', I found a slightly paradoxical picture in which the most deprived quintile was more likely to have individual components of the risk assessment tool measured, but was less likely to have a complete set of these measurements available to allow calculation of a risk.

In the second region of the pathway, 'Smoking management', it was found that smokers identified in more deprived quintiles were significantly more likely to receive smoking-cessation advice and to be referred to smoking-cessation services.

For the region 'BP management', low-risk individuals with a raised BP and high-risk individuals with a raised BP were both significantly more likely to receive an antihypertensive in the most deprived quintile compared to the least. In the next region, 'High-risk statin management', there was no significant difference between quintiles.

Next, I looked at provision of drugs. In chronic CHD, defined as stable angina and stable angina with diabetes, shown in region 'Drug management of chronic CHD', individuals with stable angina in the most deprived quintiles were significantly less likely to receive a statin than those in the least deprived quintile, with a HR of 0.86. This was not the case in the group who had stable angina and diabetes, nor were there any significant differences in aspirin or ACE inhibitor treatment. In acute disease, shown in the region 'Drug management of ACS', I found no difference in statin, aspirin, or beta-blocker prescription. In those with an old ACS, the most deprived quintile were less likely to receive an ACE inhibitor, with a HR 0.80.

I looked at revascularisation, shown in the two regions 'Revascularisation of chronic CHD' and 'Revascularisation of ACS'. Those in the most deprived quintile with stable angina were less likely to receive

PCI (HR 0.74) or CABG (HR 0.78), as well as to receive revascularisation overall – a composite outcome comprised of PCI and CABG combined – with a HR of 0.76. For those with stable angina and diabetes there was no significant difference in provision of PCI but for CABG the HR was 0.67 for the most deprived quintile.

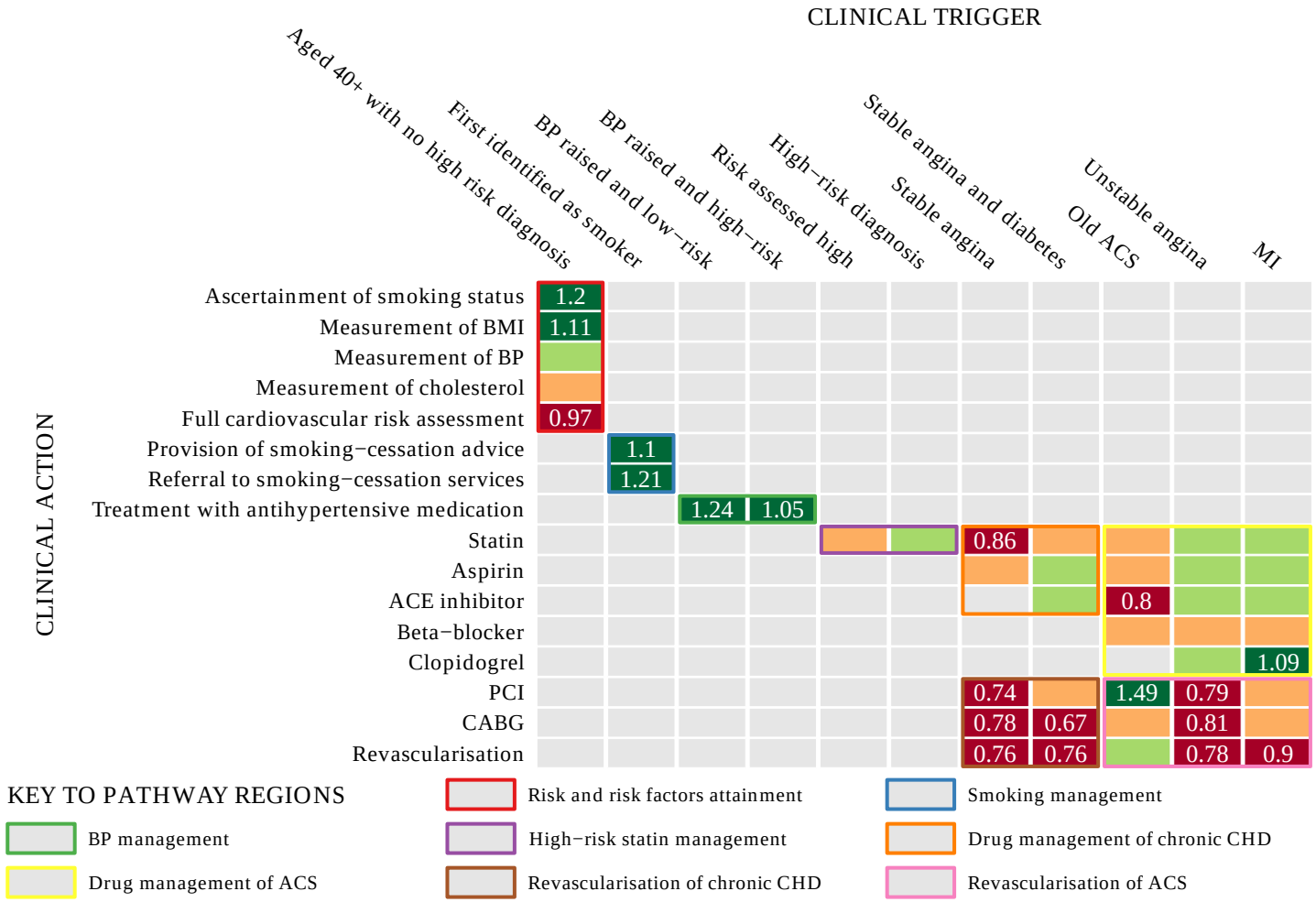
Those in the most deprived quintile were significantly less likely to undergo a PCI or CABG following an episode of unstable angina, with HR of 0.79 and 0.81 respectively.

For the purpose of summarising these findings, I considered the first four regions in the pathway ('Risk and risk factors attainment', 'Smoking management', 'BP management', and 'High-risk statin management') as primary prevention of CHD. Here one could say that, aside from being less likely to have all data available for a full cardiovascular risk assessment, achievement of clinical actions in response to clinical triggers broadly favoured the most deprived quintile. Six of the points in the pathway here significantly favoured that group; two other points leant towards it without achieving significance.

In contrast, for clinical triggers related to established CHD, in the remaining four regions of the pathway considered, where significant differences arose, they generally favoured the least deprived quintile. I made 19 comparisons when looking at drug provision: two of these significantly favoured the least deprived group and one (clopidogrel in MI) favoured the most deprived. I made 15 comparisons when looking at revascularisation, though these are not independent because the revascularisation composite outcome is dependent on the outcomes PCI and CABG. Here I found nine clinical trigger-actions that significantly favoured the least deprived quintile, and one favouring the most deprived.

Notwithstanding the issues of multiple comparison, discussed later, a plausible pattern that emerges from this initial modelling suggests absence overall of healthcare inequity in primary prevention, with, in contrast, a suggestion that in established disease provision of care might not be equitable, particularly with respect to revascularisation procedures. In order to examine this further, I present below results from multivariate modelling.

Figure 9.1: Pathway overview of univariate frailty models



In figure 9.2, I summarise results from frailty models which include age and sex as covariates, in addition to deprivation quintile. When I looked at the pathway region 'Risk and risk factors attainment', I found that, as before, there was a significant difference in ascertainment of smoking status, and measurement of BMI and BP, favouring the most deprived quintile. Moreover, HRs had increased slightly, when compared to the univariate models: 1.20 for smoking status; 1.13 for measurement of BMI; 1.05 for measurement of BP. The significant difference for 'Full cardiovascular risk assessment' in those 'Aged 40 and over with no high risk diagnosis' disappeared in this multivariate model.

When I looked at 'Smoking management', I found a more or less unchanged pattern: both provision of smoking-cessation advice and referral for smoking advice were significantly more likely in the most deprived quintile. 'BP management' favoured the most deprived quintile in those who were low risk – HR slightly reduced to 1.23; there was no longer a significant difference favouring the most deprived quintile in those who were high risk.

For the region 'High-risk statin management', there was, again, no significant difference between quintiles in provision, either to those who were high risk based on risk assessment or those who were high risk based on diagnoses.

When looking at 'Drug management of chronic CHD', I found an unchanged pattern: individuals with stable angina in the most deprived quintile were less likely to receive a statin, this time with a slightly lower HR of 0.84 (compared to 0.86); difference in provision of aspirin was not statistically significant for these individuals. For those with stable angina and diabetes, there was no significant difference in provision of statins, aspirin, or ACE inhibitors. For 'Drug management of ACS', those in more deprived quintiles with an old ACS were again less likely to receive a statin, aspirin or ACE inhibitor. Those with unstable angina were more likely to receive aspirin.

With revascularisation, for 'Revascularisation of chronic CHD', those in the most deprived quintile with stable angina was again less likely to receive PCI (HR 0.68, down from 0.79) and revascularisation overall (HR 0.75, down from 0.78). The HR for CABG was no longer significant. For those with stable angina and diabetes, the most deprived quintile was again less likely to receive revascularisation overall, with a HR of 0.74, down from 0.76. When looking at the region of the pathway 'Revascularisation of ACS', there was no significant difference,

as previously, in the provision of revascularisation for those with an old ACS. As before, those in the most deprived quintile with unstable angina were less likely to receive PCI, with a HR of 0.72, down from 0.79; and to receive revascularisation overall, with a HR of 0.74, down from 0.78. In addition, they were less likely to receive a CABG, where the difference was unchanged with a HR of 0.81. In the univariate model, there had been little difference in provision for those with MI. This changed in the age-sex adjusted model; the most deprived quintile were significantly less likely to receive a PCI, HR 0.78; and significantly less likely to receive revascularisation overall, HR 0.77.

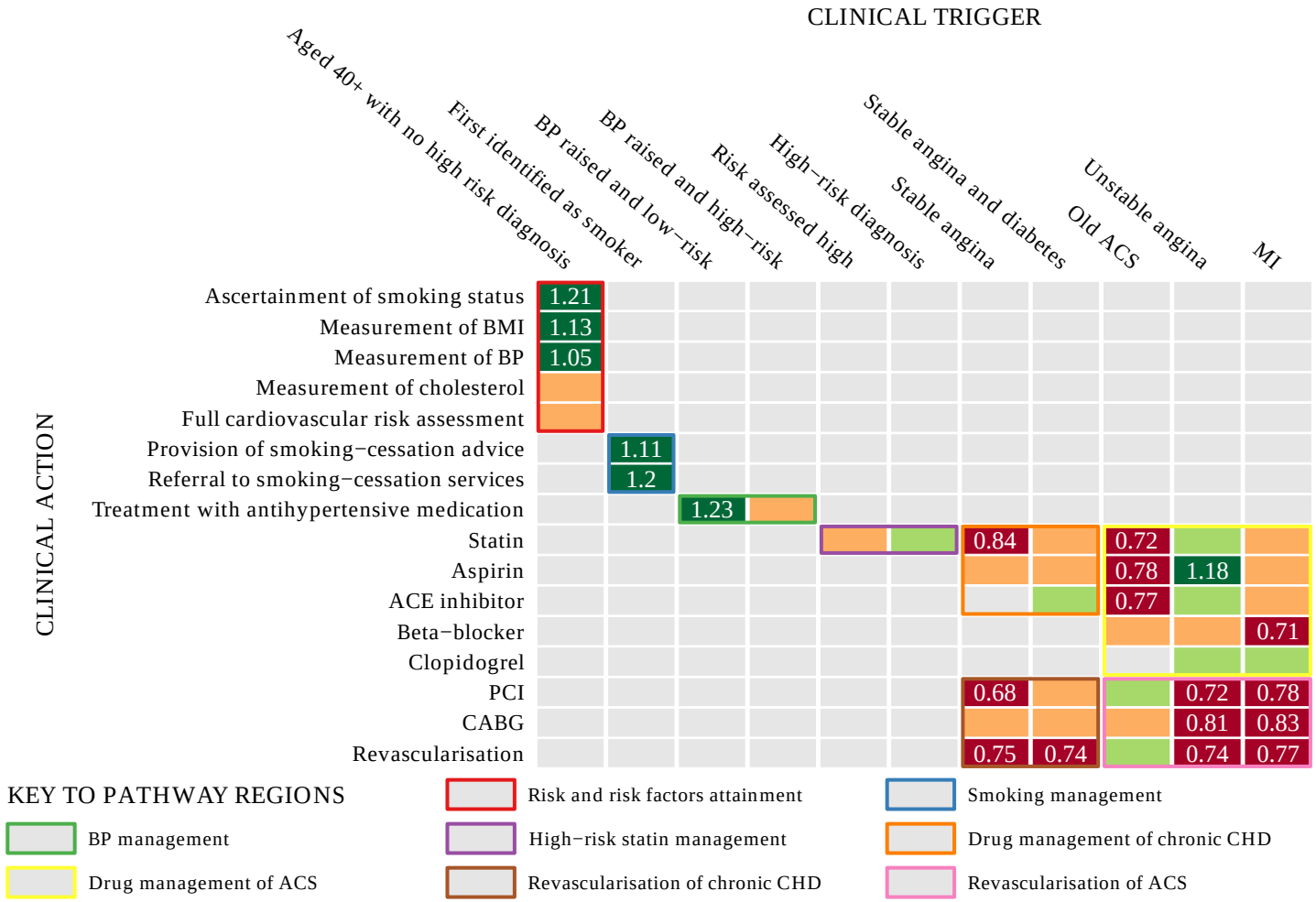
Summarising again, when employing multivariate models that took account of the age and sex of the individual in the primary prevention (the first four regions of the pathway), I found that the previously observed difference in the chance of an individual having all necessary variables recorded to allow performance of a full cardiovascular risk assessment was no longer significant. Overall, for this part of the pathway, six clinical trigger-actions favoured the most deprived group; in five there was no significant difference (one tended towards favouring the most deprived group, without achieving significance; four tended towards favouring the least deprived group, again without achieving significance). In this picture, there was no evidence of inequity of provision for primary prevention.

The picture that emerged for the management of established disease (the last four regions of the pathway) contrasted with this. Of the 34 comparisons made, 14 suggested that the most deprived quintile was less likely to receive the clinical action in question. This was less pronounced in the 'Drug management of chronic CHD' where one of the five comparisons suggested inequity (statin provision in those with stable angina), and in 'Drug management of ACS' where four out of fourteen comparisons suggested inequity. Again, bearing in mind and that the 'Revascularisation' outcome is not independent of the PCI and CABG outcomes, I found that nine out of fifteen clinical trigger-actions relating to revascularisation suggested reduced provision in the most deprived quintile. Moreover, adjusting for age and sex in these models tended to reduce the HRs, as well as making more of these results significantly different.

When considering the age and sex adjusted models in overview, I found a similar pattern to that observed in the univariate models, but this time more pronounced: there was no evidence of inequity in the primary prevention part of the pathway of care; there was a

suggestion of inequity in drug management of established disease; there was a much more pronounced suggestion of inequity in provision of revascularisation. To further investigate this relationship, I now consider an overview of the models that I refer to as 'fully-adjusted'.

Figure 9.2: Pathway overview of age and sex adjusted multivariate frailty models



In figure 9.3, I show the results from models which used all appropriate and available covariates. For the region 'Risk and risk factors attainment', the picture remains largely unchanged from the previous set of models. 'Ascertainment of smoking status', 'Measurement of BMI', and 'Measurement of BP' clinical actions were all significantly more likely in the most deprived quintile (the HR for 'Measurement of BP' fell slightly, from 1.05 to 1.03). As before, there was no significant difference for 'Measurement of cholesterol' and for 'Full cardiovascular risk assessment' the HR was 0.97.

The picture for the region 'Smoking management', was also little changed: in smokers, 'Provision of smoking-cessation advice' was again more likely in the most deprived quintile, HR 1.10. 'Referral to smoking-cessation services' showed no significant difference between the most deprived and least deprived quintiles.

For the region 'BP management', a significant difference, favouring the most deprived quintile, remained for the provision of antihypertensive medication to those with raised BP who were otherwise at low risk for CVD; HR 1.22, down slightly from 1.23. There was no significant difference for individuals who were high risk and had a raised BP.

There was no significant difference in the provision of statins to individuals who were at high risk of CVD, whether this high-risk status arose as a result of risk assessment or whether from the presence of a high-risk diagnosis. This finding was unchanged from that observed using the earlier modelling approaches.

When I looked at the region 'Drug management of chronic CHD', I found no substantial difference from the previous pattern of findings: individuals with stable angina in the most deprived quintile were less likely to be treated with a statin with HR 0.87, up from 0.84. Otherwise there was no evidence of significant differences between the most and least deprived quintiles in this region of the pathway.

When looking at 'Drug management of ACS' I found that the previously identified reduced provision of beta-blockers to those with MI in the most deprived quintiles was no longer significant. The only remaining significant difference between the most and least deprived quintiles was for ACE inhibitors in those with an old ACS, with HR 0.80, up from 0.77.

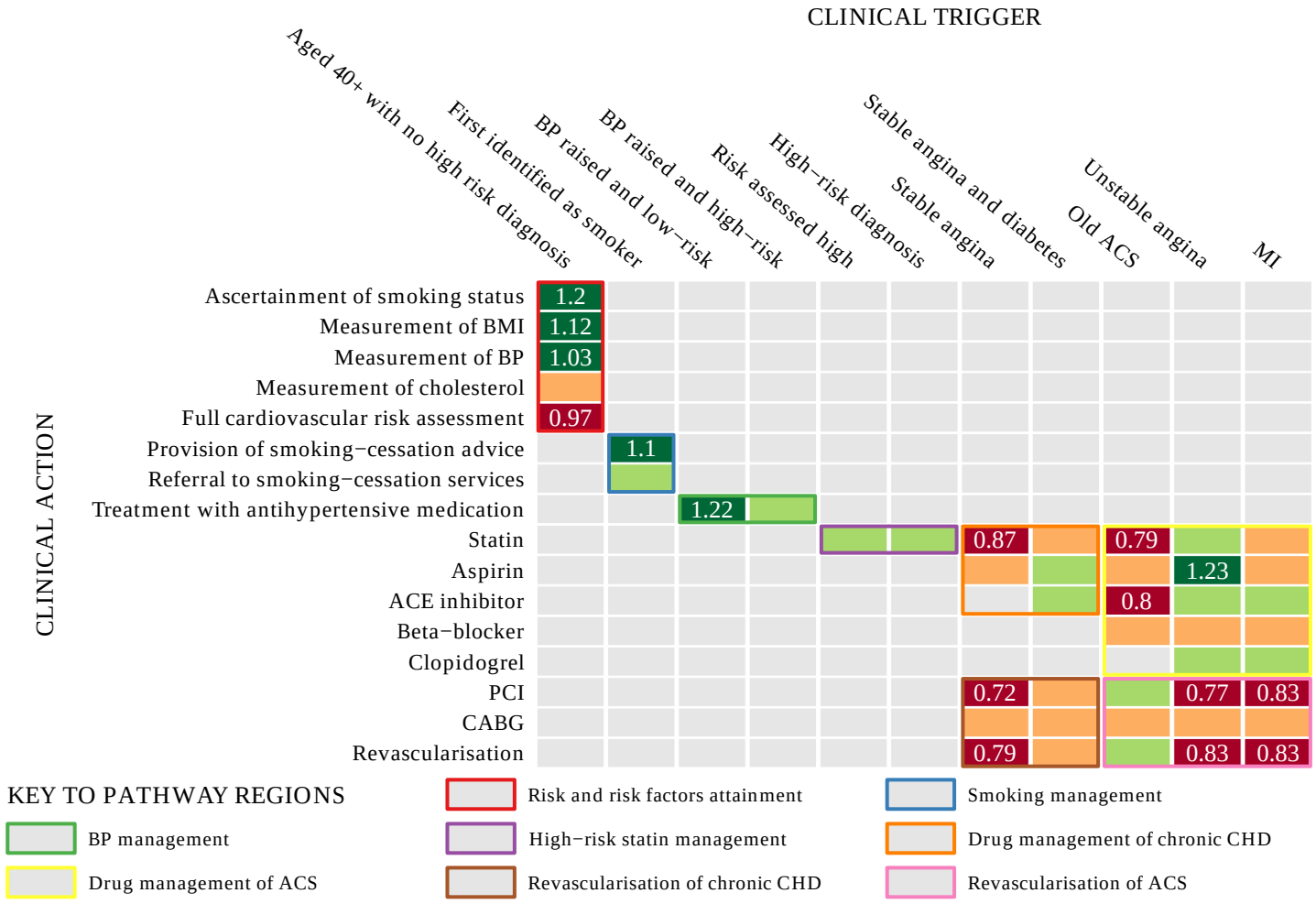
For 'Revascularisation of chronic CHD', I found that the difference in provision of PCI for those with the clinical trigger 'Stable angina and diabetes' was no longer significant (nor in turn for CABG and

for revascularisation overall). Differences remained for the 'Stable angina' clinical trigger, both for PCI and for revascularisation overall. Here, each of the HRs was higher than in the previous model (age-sex adjusted models): it rose to 0.72 for PCI from 0.68; and to 0.79 from 0.75 for revascularisation overall.

When I looked at 'Revascularisation of ACS', I found, as before, no significant differences for the 'Old ACS' clinical trigger. There was no longer a significant difference for the provision of CABG between quintiles in those with unstable angina. The difference for PCI remained significant, with the HR rising to 0.76, having been 0.72 previously. The difference for revascularisation overall in those with unstable angina was also significant as before, with HR of 0.83, up from 0.74. The difference between quintiles for individuals with an MI remained significant for PCI and for revascularisation overall. Here the HR for PCI rose to 0.83, from 0.78; for revascularisation overall it rose to 0.83, from 0.77.

When I examined the fully-adjusted models, which were summarised in figure 9.3, I found a broadly unchanged overall picture. In the first four regions of the pathway, which deal with primary prevention, there was no evidence that provision of treatment was inequitable, five significant differences that were uncovered favouring the most deprived quintile, and one favouring the least deprived. When looking at drug management, I found a significant difference that favoured the least deprived quintile for two of the clinical trigger-actions: 'Stable angina' to 'Statin' and 'Old ACS' to 'ACE inhibitor'. Thus, of the 19 comparisons made here, two show some evidence of inequity. One ('Aspirin' in 'Unstable angina') favoured the most deprived quintile. Evidence of inequity in provision of revascularisation, particularly PCI, persisted in the fully-adjusted models. This was the case for the provision of both PCI and revascularisation overall in those with stable angina, unstable angina or MI.

Figure 9.3: Pathway overview of fully-adjusted multivariate frailty models



9.2 DRUG CESSATION ANALYSIS

In this section of my analysis, I looked at the times from an individual initiating treatment with the drug for a particular indication to the time they stopped taking the drug. Clearly, this was only relevant at stages in the pathway of care where a drug was being prescribed. I did not look at drug cessation for the region 'BP management', because there I had looked at prescription of any major antihypertensive medication – having not specified the medication, examining cessation became much more difficult. Thus, I addressed three regions of the pathway when looking at drug cessation: 'High-risk statin management', 'Drug management of chronic CHD', and 'Drug management of ACS'. In this section, I have considered the findings from these models in overview.

When looking at the findings from these models it was important to be clear that a situation representing inequity in provision would be one in which more deprived individuals were stopping taking their drugs more quickly; in other words were inequity occurring, the times to the outcome (cessation of the drug) would be shorter; thus, evidence of inequity would arise where the HR for the comparison of quintile 5 (most deprived) to quintile 1 (least deprived) was greater than one, and statistically significant. Clearly, this is the opposite way around from the situation when I considered the main analysis. In this section, I have coloured the graphics to take account of this difference: for example, dark green still indicates a situation in which the most deprived quintile appears to be receiving healthcare in a favourable way compared to the least deprived (though the HRs in this instance would now be less than one, rather than, as before, greater than one).

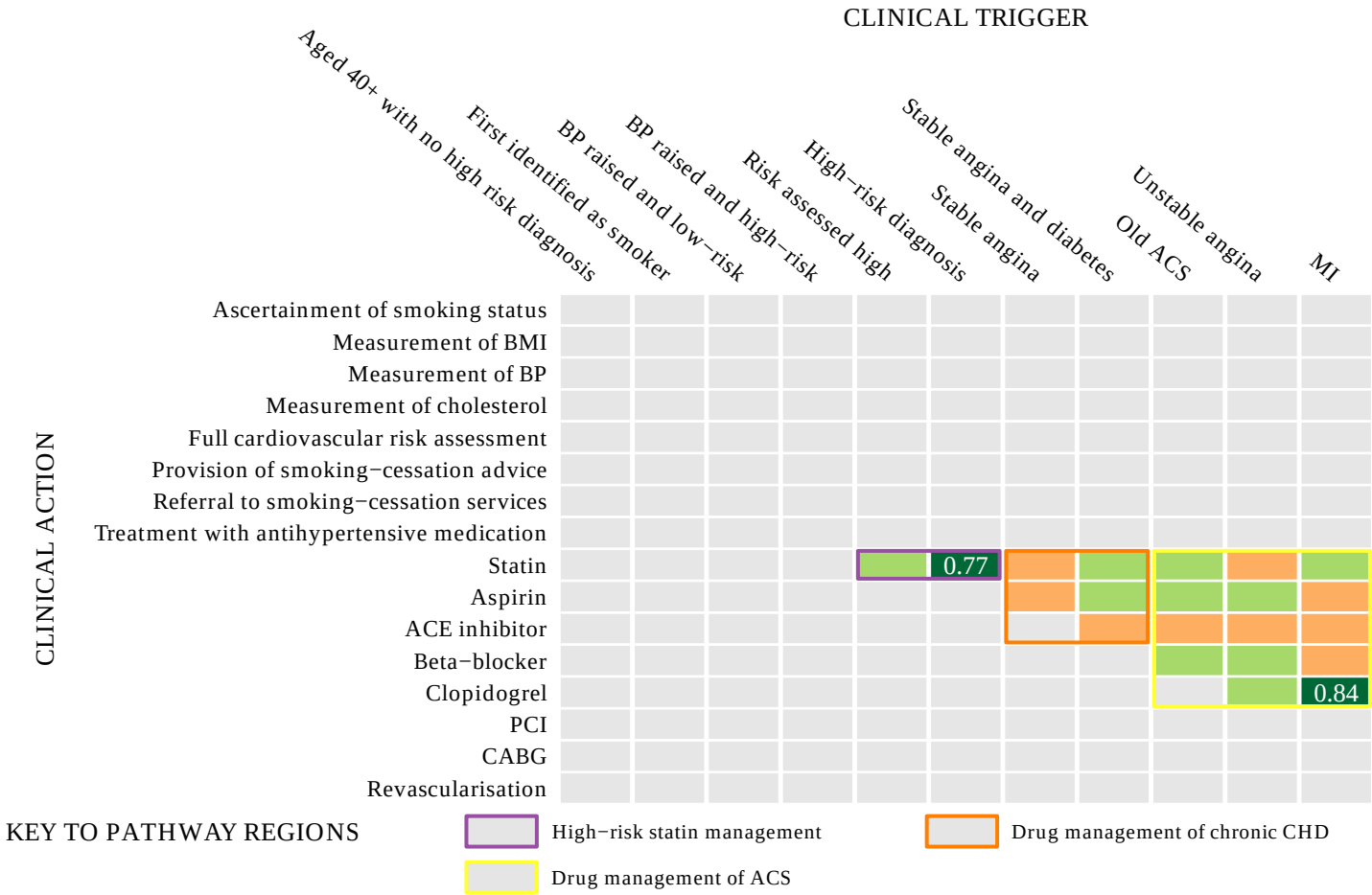
In figure 9.4, I have summarised the univariate models (taking account only of deprivation quintile, with practice, and where relevant hospital, as random effect terms). In the region of the pathway 'High-risk statin management', I considered the persistence of prescription of statins in individuals who had started taking them either because they were risk assessed as being at high risk of CVD, or because they had a high-risk diagnosis. Individuals with a high-risk diagnosis in the most deprived quintile were significantly less likely to stop taking a statin (HR 0.77).

In the region of the pathway 'Drug management of chronic CHD', no significant differences emerged.

For 'Drug management of ACS', I made 14 comparisons, only one showing a significant difference: those with MI in the most deprived quintile were less likely to stop taking clopidogrel (HR 0.84).

In overview, when I performed univariate modelling to look at the overall pattern of drug cessation I found only two significant differences in the 21 comparisons, both favouring the most deprived quintile.

Figure 9.4: Pathway overview of univariate frailty model of drug cessation



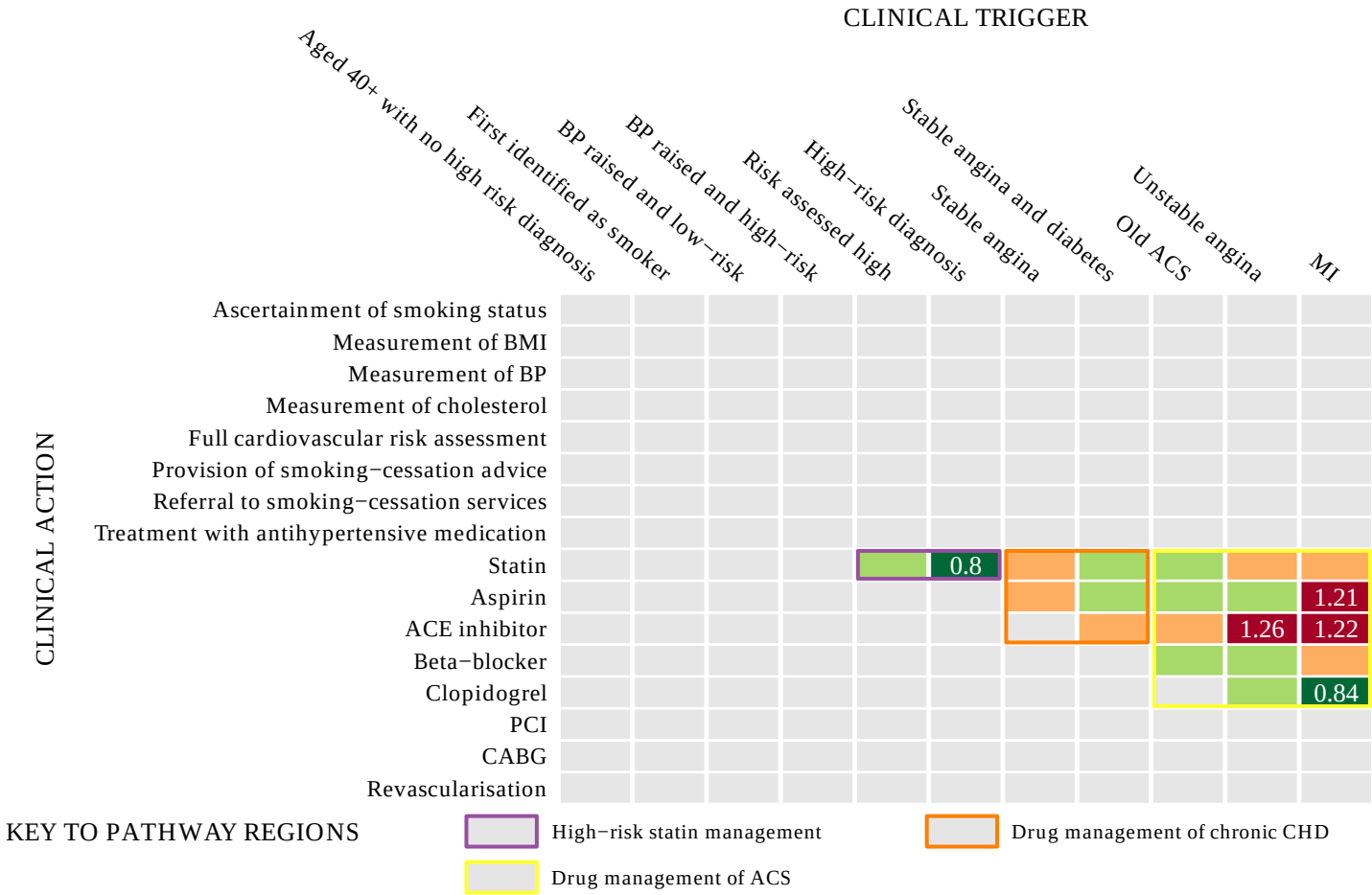
In the next set of models, I looked again at drug cessation, this time adding age and sex as covariates in the models. I summarise these findings in figure 9.5. For the region of the pathway 'High-risk statin management', individuals in the most deprived quintile who were high risk on the basis of a high-risk diagnosis, were again less likely to stop taking a statin, the HR rising slightly to 0.80, from 0.77.

In the 'Drug management of chronic CHD' region of the pathway there were again no significant differences.

For the 'Drug management of ACS' region, I found that those in the least deprived quintile with unstable angina or MI, were less likely to stop taking an ACE inhibitor (HR 1.26 and 1.22 respectively) and those with MI were less likely to stop taking aspirin (HR 1.21).Individuals in the most deprived quintile with MI remained less likely to stop taking clopidogrel, HR 0.84 (unchanged).

When considering drug cessation, adjustment for age and sex revealed the three significant differences described above relating to those with unstable angina or MI, but overall the picture remained one in which there was little evidence of inequity.

Figure 9.5: Pathway overview of multivariate frailty model of drug cessation adjusting for age and sex



In figure 9.6, I show an overview of the findings from the fully-adjusted frailty models with which I examined cessation of drug prescription. These models are therefore analogous to those presented in the previous figure (figure 9.5), but include additional covariates.

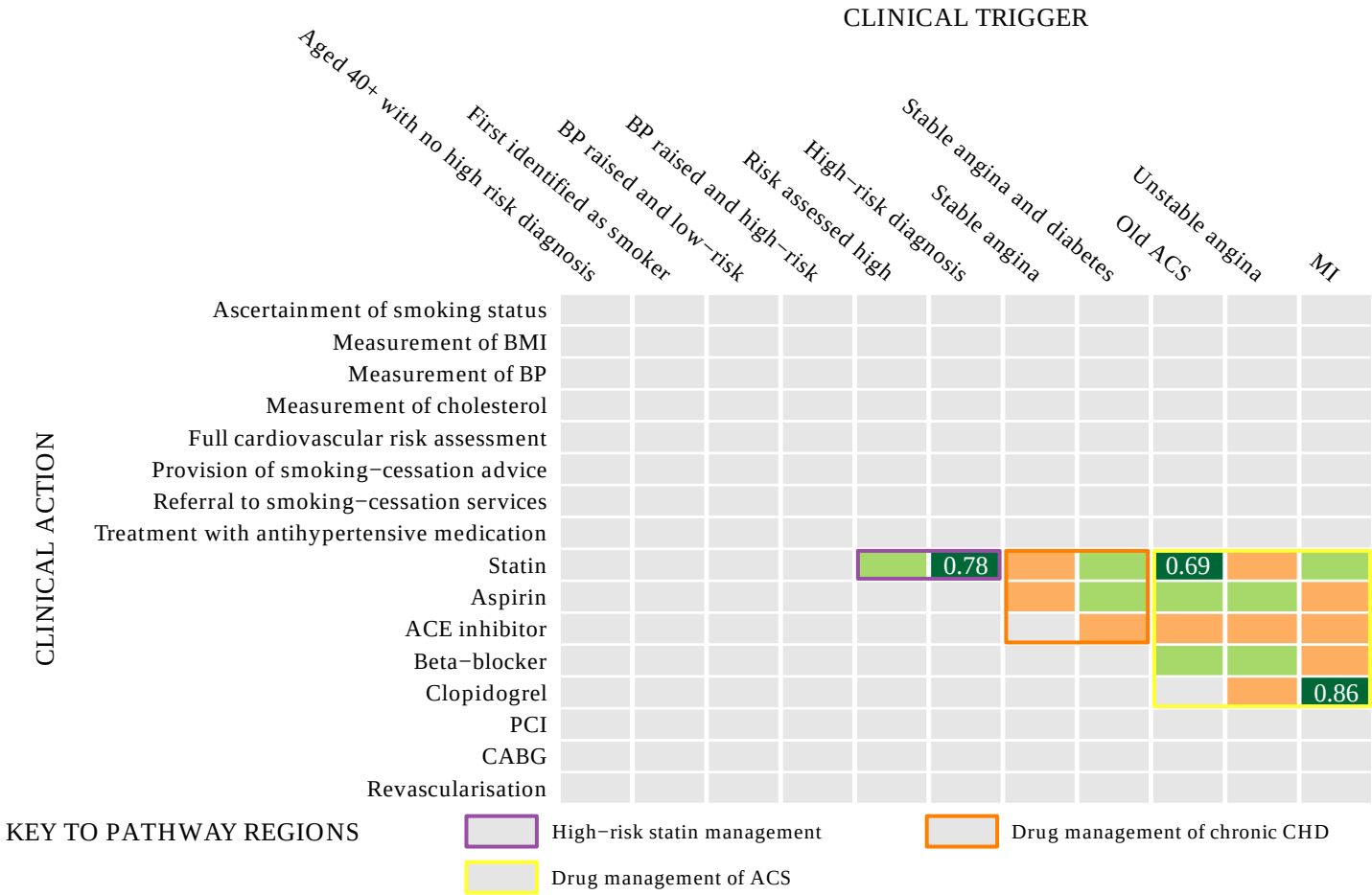
Again, I found, when looking at the region 'High-risk statin management', a pattern suggesting that individuals who were high-risk through high-risk diagnoses in the most deprived quintile were significantly less likely to stop taking statins: the HR was 0.79, down from 0.80.

When looking at 'Drug management of chronic CHD' I found no significant differences.

For the region 'Drug management of ACS', three significant findings favouring the least deprived no longer appeared in the fully-adjusted model : these related to cessation of aspirin and ACE inhibitors in ACS. However the finding favouring the most deprived (clopidogrel cessation in those with MI) persisted.

When looking in overview at drug cessation as a model using fully-adjusted frailty models, I found no suggestion that individuals from the most deprived quintile were more likely to stop taking any of the indicated drugs than those in the least deprived quintile. Of the 21 comparisons made, three showed showed that individuals in the most deprived quintile were significantly less likely to stop taking the drugs in question, and none showed that they were more likely to do so. In summary, there was no suggestion of inequity in the persistence of prescription of drugs at those points in the pathway of care where drugs were indicated.

Figure 9.6: Pathway overview of fully-adjusted multivariate frailty models of drug cessation



9.3 SENSITIVITY ANALYSIS

As alluded to in chapter 6, I was aware that my work was founded on a number of assumptions, that these assumptions might substantially affect the findings, and that a thorough analysis would check whether such assumptions might undermine the conclusions. I present the results of such checks in this section. I examined the following assumptions, each time looking only at the summary of results from fully-adjusted models.

1. Using the Framingham 1991 risk assessment tool, as opposed to the non-laboratory risk assessment tool
2. Making comparisons across 2001 Townsend deprivation quintiles, as opposed to using WIMD 2005
3. Using 20 as opposed to 5 imputations when using multiple imputation using chained equations (MICE)
4. Prevalent as opposed to incident clinical triggers for the main analysis

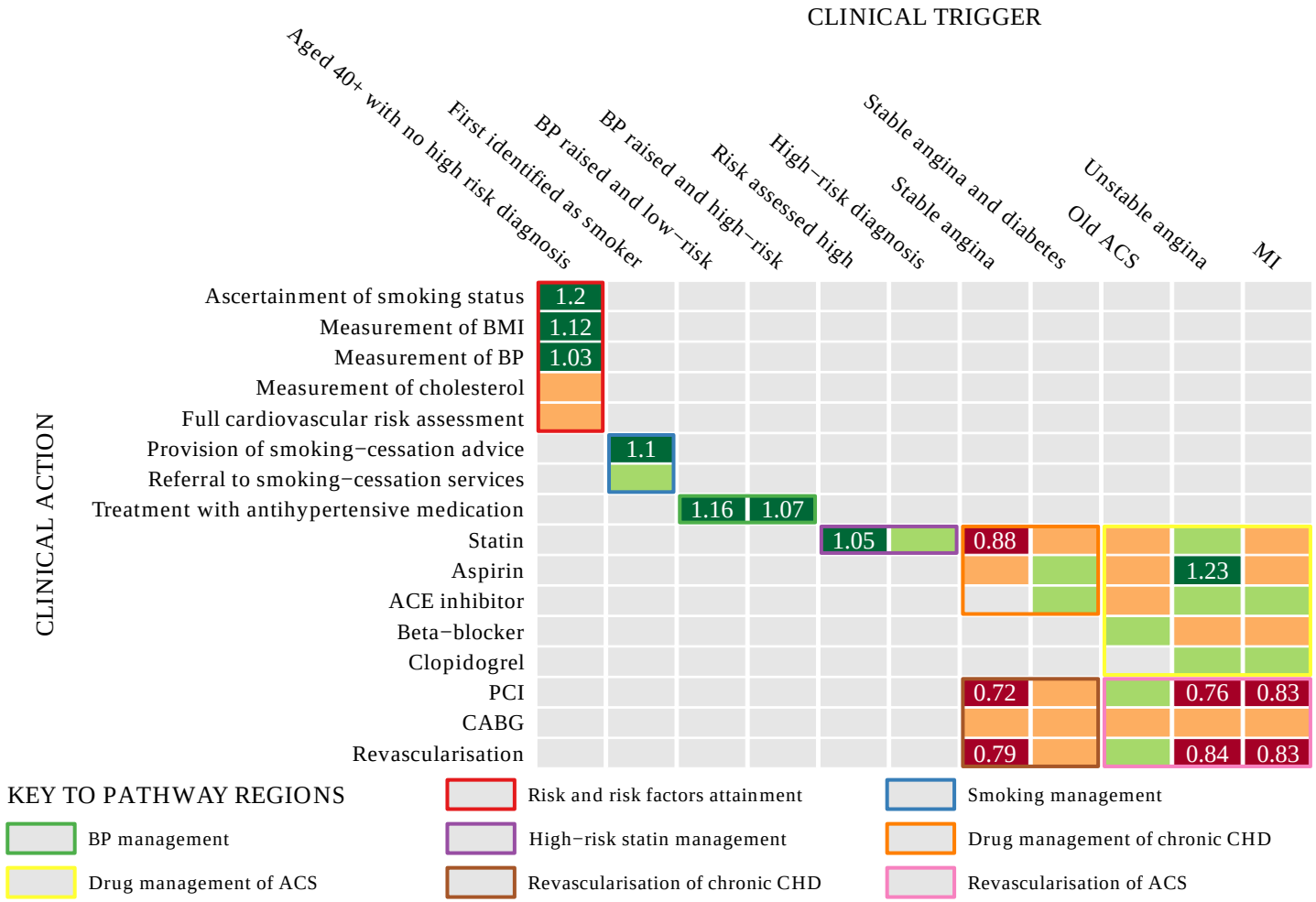
9.3.1 *1991 Framingham risk-assessment tool*

Findings when using the Framingham 1991 risk-assessment tool (results summarised in figure 9.7, compared to 9.3) are similar to my main analysis. The HR for 'Full cardiovascular risk assessment' is no longer significant. The HR for 'BP raised and low-risk' and 'Treatment with antihypertensive medication' decreases slightly to 1.16 (from 1.22); that for 'BP raised and high-risk' is now significant, with HR 1.07 (favouring the most deprived quintile). Likewise, 'Risk assessed high' and 'Statin' is now significant, with HR 1.05.

In the area of the pathway looking at drug management of established CHD, results are broadly unchanged, though the result for 'Statin' in 'Old ACS' and 'ACE inhibitor' in 'Old ACS' are no longer significant.

The pattern of results for revascularisation is essentially unchanged other than some small adjustments to some HRs. Overall, changing the underlying risk-assessment tool used in the analysis has no pronounced effect on the broad pattern seen.

Figure 9.7: Pathway overview of fully-adjusted frailty models using the 1991 Framingham risk assessment tool



9.3.2 *Townsend deprivation quintiles*

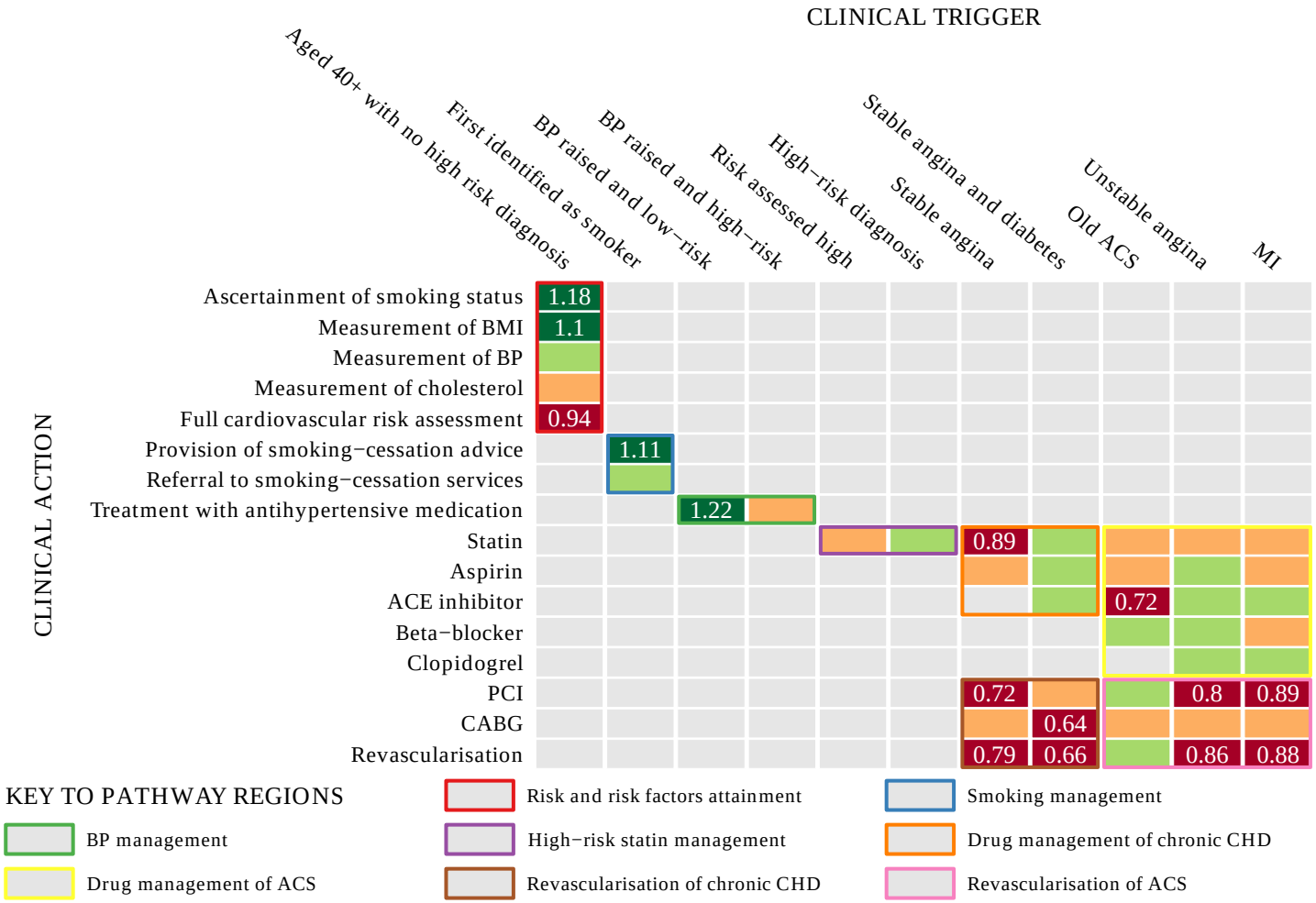
Analysis using the Townsend 2001 deprivation quintiles, rather than those for WIMD 2005, are shown in figure 9.8 (compared to 9.3). Findings for the 'Aged 40 and over and no high risk diagnosis' trigger are no longer significant for 'Measurement of BP', and HRs are slightly reduced for 'Ascertainment of smoking status' (1.18 from 1.2), 'Measurement of BMI' (1.1 from 1.12), and 'Full cardiovascular risk assessment' (0.94 from 0.97).

Other findings for clinical triggers in those without established CHD are essentially unchanged; there is a small increase in HR for 'Provision of smoking-cessation advice' in 'First identified as smoker' to 1.11 from 1.1.

The part of the pathway dealing with drug management of established disease is also largely unchanged. There are small changes in HRs and the results for 'Statin' in 'Old ACS' and 'Aspirin' in 'Unstable angina' are no longer significant.

Similarly, in the revascularisation part of the pathway, there are some small changes in HR (for example, 'PCI' in 'Unstable angina' up to 0.8 from 0.77; 'PCI' in 'MI' down to 0.83, from 0.89). The HR for 'CABG' in 'Stable angina and diabetes' is now significant, at 0.64, as is that for 'Revascularisation' at 0.66.

Figure 9.8: Pathway overview of fully-adjusted frailty models using Townsend deprivation quintiles



9.3.3 *Imputation number*

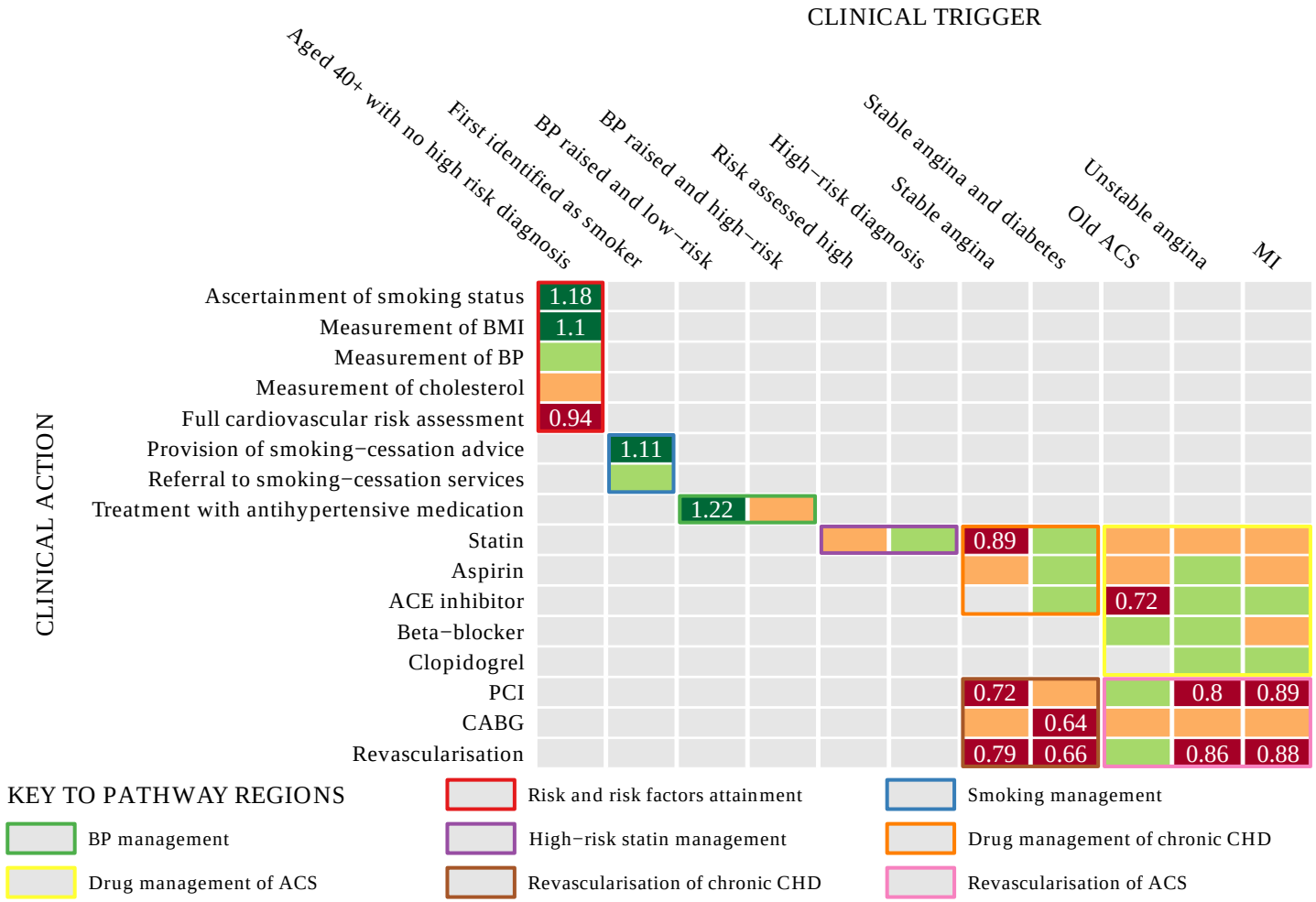
My original analysis, summarised in figure 9.3 employed five imputed datasets to manage missing data. I also checked the impact on the broad conclusions of using a larger number of invitations. The results of this additional analysis are summarised in figure 9.9.

Firstly, it is clear that in this revised analysis a number of HRs are slightly different: for 'Ascertainment of smoking status' the HR falls to 1.18 from 1.2; that for 'Full cardiovascular risk assessment' drops to 0.94; 'Statin' for 'Stable angina' rises from the 0.87 to 0.89; beta-blocker for 'Old ACS' falls to 0.72. For 'Unstable angina' and 'PCI' the HR rises to 0.83 (from 0.77); for 'Unstable angina' and 'Revascularisation' to 0.86 (from 0.83). 'MI' and 'PCI' has an increase in HR from 0.83 to 0.89; 'MI' and 'Revascularisation' again rises to 0.88 (from 0.83).

Secondly, the statistical significance of some of the results changes. 'Measurement of BP', 'Statin' and 'Old ACS', and 'Aspirin' for 'Unstable angina' are no longer significant. 'CABG' for 'Stable angina and diabetes' becomes significant, with HR 0.64, as does 'Revascularisation' in 'Stable angina and diabetes' with HR 0.66.

Thirdly, these changes do not substantially alter the overall interpretation of these findings. It remains the case that the primary prevention component of the pathway showed no evidence of healthcare inequity (with the exception of 'Full cardiovascular risk assessment'), that there is some evidence of inequity in the management of established CHD with drugs, but that, particularly in view of the number of comparisons made, this is far from systematic. For revascularisation, the results suggest evidence of inequity of utilisation, most obviously with PCI, but also with revascularisation overall.

Figure 9.9: Pathway overview of fully-adjusted frailty models using 20 imputations instead of 5



9.3.4 *Prevalent clinical triggers*

Making an assumption of the importance of clinical triggers that were already in place at the start of the observation period has a very noticeable impact on results (compare figure 9.10 to figure 9.3).

The first important point to bear in mind is that the 'Aged 40 and over with low high risk diagnosis' clinical trigger now includes all individuals aged 40 and over at the time that they entered the dataset (that is to say at the start of the cohort period for each individual). Here, the situation contrasts with incident clinical triggers in that for 'Measurement of BP', 'Measurement of cholesterol', and for 'Full cardiovascular risk assessment', there is evidence of some inequity. HRs for 'Measurement of BP' and for 'Measurement of cholesterol' are 0.98, suggesting a small effect; the significance here needs to be seen in the light of the larger number of triggers analysed (491,886) for these clinical actions.

Another impact on the broad picture from the use of prevalent triggers arises when considering statin use in individuals at high risk of CHD, but without established disease. Here significant HRs for the 'Risk assessed high' and 'High-risk diagnosis' triggers suggest inequity in provision of statins in those who were already at high risk of CHD at the time they entered the study (HRs both 0.94).

Broadly speaking, the results for drug management of individuals with established CHD are unchanged in the sense that this area of the pathway does not favour any deprivation group in a systematic way. The specifics do change: clinical-trigger actions in this part of the pathway that did show statistically significant evidence of a difference no longer do so. Two points now suggest a significant difference, with 'Aspirin' in 'Stable angina' favouring the more deprived quintile (HR 1.14) and 'Aspirin' in 'Old ACS' favouring the least, with HR 0.78.

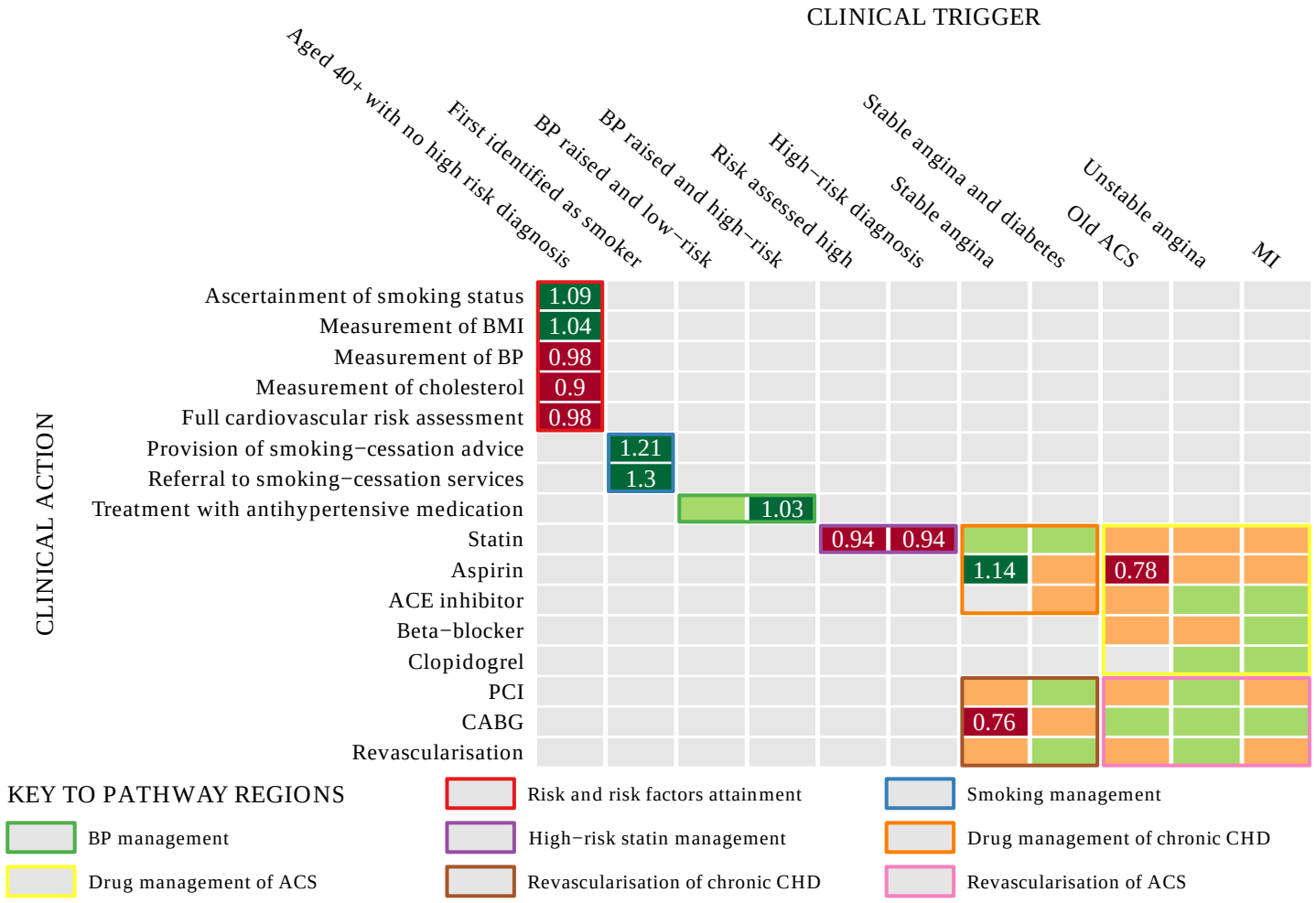
With prevalent triggers, the situation in the revascularisation area of the pathway changes. Previously significant results are no longer so; there is now evidence of inequity for 'CABG' and 'Stable angina' with HR of 0.76.

In the region 'revascularisation of chronic CHD', no differences were significant other than that CABG in stable angina now favoured the least deprived (HR 0.76).

In overview, the use of prevalent triggers, which essentially entails looking at individuals who already had these triggers at the start of the study, shows no systematic picture of inequity, particularly when

one considers that the 'Aged 40 and over with no high risk diagnosis' trigger, probably due to large numbers, generates HRs which are significant, but not generally far from 1.

Figure 9.10: Pathway overview of fully-adjusted frailty models using prevalent clinical triggers



9.3.5 *Comparison of gradients rather than quintile 5:1*

In this thesis, I employed the simplified method of examining the HRs for quintile 5 and quintile 1 as a means of identifying inequity. While there were clearly several advantages to this simplification, I wanted to check that the conclusions of the study would not be substantially altered by the use of an alternative: the slope index of inequality approach, as outlined in chapter 6.

Table 9.1 shows each of the clinical trigger-actions for which the fully-adjusted model suggested that a social gradient existed (on the basis of inspection). For each of these, I show the results: firstly, using the 5:1 HR approach (showing an estimate of the HR, whether the result is statistically significant, and noting which social group was favoured on the basis of the result), secondly using the slope index of inequality (for which I show comparable information in the table).

As might be expected, the direction of effect does not change for any of the clinical trigger-actions with use of the different method. In six of the 20 cases, the statistical significance of the results does change.

Most commonly, results which significantly favoured the least deprived quintile in the 5:1 comparison lost significance when the slope index of inequality was used. This applied to three of the six results which changed: old ACS and ACE inhibitor; unstable angina and PCI; unstable angina and revascularisation. One result which previously faavoured the most deprived quintile in the 5:1 analysis also lost significance: unstable angina and aspirin.

There were two results which had previously not been significant in the 5:1 comparison that became significant when using the slope index of inequality: MI and CABG (favouring the least deprived); first identified as a smoker and referral to smoking cessation services (favouring the most deprived).

In summary, use of the slope index of inequality approach does lead to a small number of changes in significance of some results. Broadly, using this approach produce a picture slightly less suggestive of inequity in health care across the whole pathway of care for CHD. The overall pattern seen is not markedly affected, and the influence of these changes on the conclusions that can be drawn about inequity across the pathway of care is minimal.

Table 9.1: Comparison of findings for clinical trigger-actions with an apparent social gradient using 5:1 hazard ratio compared to slope index of inequality

		5:1 Hazard Ratio			Slope index of inequality		
Trigger	Action	HR	Significant	Favours	Estimate	Significant	Favours
aged 40+ with no high-risk diagnosis	ascertainment of smoking status	1.2	Yes	Most deprived	0.047	Yes	Most deprived
aged 40+ with no high-risk diagnosis	measurement BMI	1.12	Yes	Most deprived	0.026	Yes	Most deprived
first identified as smoker	smoking–cessation advice	1.1	Yes	Most deprived	0.025	Yes	Most deprived
first identified as smoker	referral to smoking-cessation services	1.17	No	Most deprived	0.039	Yes	Most deprived
BP raised and low-risk	treatment with antihypertensive medication	1.22	Yes	Most deprived	0.043	Yes	Most deprived
unstable angina	aspirin	1.24	Yes	Most deprived	0.049	No	Most deprived
old ACS	ACE inhibitor	0.8	Yes	Least deprived	-0.047	No	Least deprived
stable angina	PCI	0.72	Yes	Least deprived	-0.088	Yes	Least deprived
stable angina	CABG	0.87	No	Least deprived	-0.045	No	Least deprived

Continued on next page

Table 9.1 – *Continued from previous page*

		5:1 Hazard Ratio			Slope index of inequality		
Trigger	Action	HR	Significant	Favours	Estimate	Significant	Favours
stable angina and diabetes	CABG	0.77	No	Least deprived	-0.043	No	Least deprived
stable angina	revascularisation	0.79	Yes	Least deprived	-0.068	Yes	Least deprived
stable angina and diabetes	revascularisation	0.79	No	Least deprived	-0.039	No	Least deprived
unstable angina	PCI	0.76	Yes	Least deprived	-0.05	No	Least deprived
MI	PCI	0.83	Yes	Least deprived	-0.04	Yes	Least deprived
old ACS	CABG	0.78	No	Least deprived	-0.091	No	Least deprived
MI	CABG	0.89	No	Least deprived	-0.026	Yes	Least deprived
unstable angina	revascularisation	0.83	Yes	Least deprived	-0.035	No	Least deprived
MI	revascularisation	0.83	Yes	Least deprived	-0.04	Yes	Least deprived
high-risk diagnosis	statin cessation	0.78	Yes	Most deprived	-0.054	Yes	Most deprived

Continued on next page

Table 9.1 – *Continued from previous page*

		5:1 Hazard Ratio			Slope index of inequality		
Trigger	Action	HR	Significant	Favours	Estimate	Significant	Favours
old ACS	statin cessation	0.7	Yes	Most deprived	-0.083	Yes	Most deprived

9.4 CHAPTER DISCUSSION

Particularly with the next chapter in mind, in which I discuss my findings, I now summarise the results from this chapter.

9.4.1 *Quintile comparisons*

I characterise the findings according to four broad areas of the pathway:

1. Risk and risk factors attainment
2. Other primary care management of individuals without established CHD
3. Drug management of patients with established CHD
4. Revascularisation

Risk and risk factors attainment The main findings from the principal investigation are shown in figure 9.3, on page 283. Here, with respect to risk factors and assessment of full cardiovascular risk, a paradoxical picture emerges. Individuals from the most deprived quintile are more likely to have their smoking status ascertained, their BMI measured, and their BP taken; at the same time, they are not significantly less likely to have their cholesterol:HDL ratio measured. The paradox arises from the fact that they are significantly less likely to have full information available to ascertain cardiovascular risk using the Framingham non-laboratory risk-assessment tool, despite the fact that smoking status, BMI, and systolic BP are all components of that score.

Clearly, the paradoxical appearance of this result reflects an underlying situation in which more deprived individuals are more likely to have any one of these three risk factors recorded, but less likely to have recordings for all three: in other words, ascertainment of one risk factor in the least deprived quintile is more likely to be accompanied by corresponding progression to ascertainment of the other two risk factors.

This difference is not large, as reflected in the HR of 0.97 for progression to a full cardiovascular risk assessment. The pattern is broadly resistant to changes in the underlying assumptions: when the 1991 Framingham risk assessment tool is used instead (see figure 9.7 on page 292), the HR for full cardiovascular risk assessment is no longer significant; when Townsend quintiles are used (see figure 9.8 on page 294), the difference in measurement of BP is no longer significant, while the HR for full cardiovascular risk assessment is significant, with a HR that has fallen to 0.94. In part, the significance of these findings relates to the large sample size: the effect sizes here are small in many cases.

Particularly in this area, it was important to look also at prevalent clinical triggers, which also will include individuals who had already turned 40 at the time of their entry into the study (see figure 9.10 on page 299) – that is to say to look also at older individuals. Doing so changes the picture only slightly, with measurement of BP and cholesterol:HDL now slightly less likely in the most deprived quintile; full cardiovascular risk assessment remains less likely in the most deprived quintile, with HR of 0.98.

Thus, at this stage of the pathway, the situation in which risk factor ascertainment broadly favours the most deprived quintile, with a picture slightly depending on underlying assumptions, but where ascertainment of full cardiovascular risk appears less likely in the most deprived quintiles; the effect does not appear to be large.

Other primary care management of individuals without coronary heart disease There is no evidence here that more deprived individuals utilise less care in this part of the pathway. The only slight proviso is that when prevalent triggers are examined (that is to say examination of retrospective clinical triggers that occurred prior to the start of the study is taken account of), individuals in the most deprived group who could in theory have been assessed as being high risk and individuals with a high-risk diagnosis were both significantly less likely to receive statins. Not-

withstanding this finding, the overall picture, even when changes in the underlying assumptions are considered, suggests that more deprived individuals do not receive less care in these clinical situations, and appears to point to a higher utilisation of care by the most deprived group in this part of the pathway.

Drug management of patients with established CHD The evidence from the two areas of the pathway concerned with drug management of CHD is equivocal (see figure 9.3 on page 283). Most results suggest no significant difference between the groups; two in the problematic 'Old ACS' category suggest a reduced likelihood of utilisation in the most deprived quintile. Use of this clinical trigger may be best thought of as a means of excluding individuals who might be classified inappropriately with other clinical triggers. In view of the number of comparisons made in these two areas, one would expect one or two significant results on the basis of random variation alone. Thus, I have been cautious about not lending undue weight to the implications of the significant results for 'Statin' for the clinical trigger 'Stable angina', and for 'Aspirin' for the clinical trigger 'Unstable angina'. Overall, I suggest that it would be over-interpreting the findings to conclude that there is a substantial difference either way in the utilisation of drug management for established CHD, in view of the difficulty in interpreting the 'Old ACS' category and while remaining cognisant of the implications of multiple comparison.

Revascularisation I found a consistent picture with revascularisation. Firstly, PCIs were significantly less likely in quintile 5 in those with the 'Stable angina', 'Unstable angina', and 'MI' clinical triggers. This relationship drove a corresponding effect for revascularisation as a whole. Further, there was a tendency towards inequitable provision of CABG at each stage, though this did not achieve statistical significance. This plausibly might reflect a lack of power to identify a genuine relationship, particularly in view of

> the relatively small numbers of CABGs performed: 1645, compared to 5118 PCIs in the 20,467 individuals with an incident-MI trigger. At the very least, one can be sure that the apparent inequity in PCI is not compensated for by increased utilisation of CABG.
>
> Overall, I consider that the evidence around revascularisation suggests that there is inequity in utilisation, particularly with PCI, but potentially also with CABG as well. Further, the HRs suggest that this effect is not negligible, with for example HRs 0.72 for 'Stable angina' and 'PCI'; 0.77 for 'Unstable angina' and 'PCI'; and 0.83 for 'MI' and 'PCI'. While such effects are not present in a systematic way when looking at provision of revascularisation retrospectively (prevalent triggers), the findings are, in broad terms, unchanged by the adjustment of my other main assumptions.

I also looked at comparison of drug cessation (see figure 9.6 on page 290),

> *Drug cessation* I found no evidence that deprived groups stopped receiving prescriptions for indicated medications more quickly; indeed, there was some suggestion of the opposite, though given the issue of multiple comparison, it would be hard to assert this with great certainty (I made 25 comparisons looking at drug cessation in all). This picture remains essentially unmodified when the results are repeated with the 1991 Framinghham risk-assessment tool and when using the Townsend deprivation quintiles. In short, there is no evidence that differential outcomes relate to differences in the time for which prescriptions are issued to individuals from different quintiles – though clearly this is not the same as actual adherence to treatment protocols.

I have, for practical reasons, deliberately kept presentation of results here to discussion of those directly relevant to my research questions. In fact, many other results were produced by my analysis, which it is beyond the scope of this thesis to consider in detail. I discuss some of these in section 10.4.

In this chapter, I have presented the results of my overview approach to examining healthcare inequity across the pathway of care for CHD.

A number of broad findings emerged, which I have summarised as follows:

- There is no evidence of inequity of care in the regions of the pathway relating to primary prevention of CHD
- There is some evidence, which must be regarded as equivocal in the light of the number of comparisons made, of inequity in the provision of drug treatments for those with established CHD
- There is persistent evidence of inequity in provision of revascularisation, particularly related to PCI

In the next chapter, I discuss the implications of these findings further, and set them in the context of previous work.

Part IV

DISCUSSION

10 DISCUSSION

In this chapter I will discuss:

- my key findings, offering explanations for them and placing them in the context of existing literature
- strengths and limitations of the study
- challenges and lessons
- implications for further work
- conclusions and the policy recommendations that can be based on them

10.1 KEY FINDINGS

As indicated in the previous chapter, the overall pattern of my findings suggests that in the early part of the pathway (primary prevention) results tend slightly to favour the more deprived, and in the later part of the pathway (management of established CHD and revascularisation) results tend to favour the less deprived. However, it is notable that of all the comparisons made a majority indicate no significant difference between quintile 1 and quintile 5. A broad picture of my results can be seen clearly in figures 9.1, 9.2 and 9.3.

10.1.1 *Revascularisation*

The clearest difference found in this study was that PCI, and revascularisation overall, were consistently less utilised in quintile 5 than in quintile 1. Figure 9.3 summarizes the data of the fully adjusted model. Significant differences (quintile 1 versus quintile 5) were seen in the following trigger-action combinations:

- stable angina and PCI
- stable angina and revascularisation (composite)
- unstable angina and PCI
- unstable angina and revascularisation (composite)

- MI and PCI
- MI and revascularisation (composite)

Revascularisation did not appear inequitable in a category of limited usefulness ('Old MI'), or in relation to CABG in the fully adjusted model but it is possible that my analysis of CABG data was underpowered. Indeed, analysis using a slope index of inequality approach suggested that the gradient across quintiles for this clinical trigger-action was significant. Thus, it appears that inequity in revascularisation in my population during the study period is a valid observation. This is therefore consistent with evidence in published literature[150–156], although a number of the studies reviewed in chapter 3 showed no evidence of inequity in revascularisation.[141,158–160] It is of concern that in addition to the deprivation-related differences found there were also gender differences. For example in the mixed effects model for stable angina and PCI the HR for females receiving the intervention was 0.6. For stable angina it was 0.32. Throughout the models relating to revascularisation and the different triggers there were strikingly fewer interventions in females. This finding is consistent with other reports from the published literature.[200–204]

We did not design this study specifically to identify the causes of any inequity detected, but my pathway approach enables us to infer that this revascularisation inequity is not a knock-on effect and is not related to any general, systematic failure to prevent, recognise and treat CHD equitably. An explanation of the inequity might be related to features of the health service, with respect to its structure and operation, that affect provision of revascularisation. While I have made an effort to adjust for some such factors in my work, this adjustment is inevitably incomplete. Revascularisation services rely on quite different parts of the health service to the earlier parts of the pathway (secondary and tertiary rather than primary care) and it is quite plausible that supply-side effects could operate specifically in relation to revascularisation.

It is notable that immediately before and during my study period there were very marked increases in numbers of revascularisation procedures carried out in the UK, even more so in Wales than elsewhere. Between 2000 and 2012 rates of PCI (all types) increased as follows: in England from 590 to 1423 per million population; in Wales from 550 to 1363 per million population. During the period 2004 to 2008 the increase in Wales was from approximately 900 to approximately 1150 PCI procedures per million population. In the UK the proportions of

PCIs by indication also changed. From 2006 to 2012 the proportion indicated by STEMI rose from 11% to 24.7 %, and the proportion indicated by stable angina fell from 50% to 34%. There was very marked increase in provision of primary PCI for STEMI in Wales, rising from 111 per million population in 2009 to 303 per million population in 2012. Comparable figures from England were 230 per million population and 390 per million population.[205] Such an increase partly reflects national policy guidelines such as the NICE guidelines that offer clear protocols for the use of revascularisation in stable angina and in ACS.[206–208] Clearly therefore, during my study period there was a background of very rapid change in provision of revascularisation. I will suggest in the final section of this chapter that this emphasizes the importance of sensitive monitoring of such changes, and that a distinctive ability of the methodology in my study is that it allows the detection of 'knock-on effects' in relation to revascularisation.

Further explanation of the revascularisation inequity might also relate to the individuals in the study population. Several papers reporting inequity in revascularization postulate that attitudes, expectations, illness behaviour and consultation thresholds (differing according to socioeconomic status) may be explanatory.[150,152,209,210] This suggestion has been explored more effectively in qualitative studies, particularly that of Gardner, who reports that a number of deprivation-linked attitudes, including fear of hospitals and low expectations, may have formed a barrier to referral for angiography and subsequent revascularisation.[211] Similarly, Tod, in a study based in a relatively deprived area in Yorkshire, found that comparable social and cultural factors were likely to deter uptake of CHD care.[212] These studies used a qualitative approach to examining demand, and, as I have emphasized, the absence of information about demand in data sources such as ours greatly limits direct interpretation.

Another possible explanation is that the more deprived individuals do not have the same capacity to benefit from revascularisation interventions (or perhaps are not perceived to do so by the health service), because of characteristics of their clinical state. While I have adjusted for comorbidity in my study, there is little doubt that such adjustment is incomplete. Further, when I did so, the evidence for inequity in revascularisation appeared to weaken (contrast figure 9.2 on page 280 and figure 9.3 on page 283). The reduced provision of revascularisation that so clearly occurs with increasing age also points to the possible importance of a comorbidity effect. In view of the pattern seen, while

the evidence is insufficient from this study, I suggest that differing levels of comorbidity may act as a significant part of the explanation for apparent inequity in revascularisation, as evinced by the following considerations:

- Deprived groups generally have worse risk-factor profiles, including with respect to poorly characterised risk factors
- Adjustment for comorbidity appears to improve the picture (reduce the observed level of inequity in revascularisation)
- Intuitively, complex revascularisation procedures may be more 'sensitive' to concerns about comorbidity and patient suitability than is the case for drug management or, in particular, evaluation of risk factors and risk

10.1.2 *Ascertainment of risk factors*

The identification of significant inequity in achievement of full cardiovascular risk assessment (shown in figures 9.1 and 9.3) may represent a genuine finding, although the effect size is small (HR 0.97). Nonetheless, a possible explanation is suggested by the fact that observational studies have frequently noted reduced attendance by more deprived social groups at screening arranged by formal invitation.[213] Contrastingly, the ascertainment of individual risk factors favoured the more deprived. For example in the fully adjusted model the HR was 1.2 for ascertainment of smoking status. The process of assessing smoking, BMI, and BP in individuals where these risk factors are already recognized or obviously problematic may differ from the more formal approach required to perform full risk assessment. Measuring and recording risk factors such as smoking status or BMI is often done opportunistically in primary care in a piecemeal way during consultations that may be unrelated to CHD. Therefore the paradox in my findings conceivably relates to subtle differences in the way primary care consultations are conducted with individuals from different socioeconomic groups, or to their differing consultation rates. While such a pattern is speculative, it may mean that, if equity grounds are considered important, an ad hoc case-finding approach to cardiovascular risk screening may be more appropriate than a programme of formal invitation.

10.1.3 *Management of risk factors and medication in primary prevention*

The findings of the fully adjusted model showed significant differences favouring quintile 5 in relation to smoking cessation advice and in relation to treatment of raised BP in the low-risk group. In addition, the univariate and the age-sex adjusted models showed differences favouring quintile 5 in relation to referral to a smoking-cessation service. In my literature review, I found one study suggesting that smoking-cessation advice was better provided to the less deprived[104], and three studies showing no difference.[105–107] To this extent, my finding on smoking cessation advice is surprising. A possible explanation could relate to the surge in activity in measuring and recording risk factors during the early years of QOF, and the higher consulting rates seen in more deprived areas could conceivably contribute an effect. I reviewed in detail in section 3.5.2.1 studies reporting on BP treatment in CHD prevention, and my finding that treatment of raised BP in the low-risk group favoured quintile 5 contrasts with evidence from three studies.[104,117,119] Most of the studies reviewed showed either no difference or a mixed picture. Therefore my finding can be regarded as surprising.

10.1.4 *Secondary prevention*

My findings in this area gave patchy and slight evidence of inequity. In relation to medication in established CHD the only significant differences found in the fully adjusted model favouring quintile 1 were statin use in stable angina and in 'old ACS', and ACE inhibitor use in 'old ACS'. In chapter 3, I reviewed studies reporting on lipid lowering medication in CHD prevention (section 3.5.2.2). Five studies found some evidence of a social gradient (favouring the less deprived) in either prescription of lipid lowering drugs or reaching cholesterol targets. A majority of studies found no significant differences by deprivation or other socio-economic measures. These studies are summarised in table C.2.

In the fully adjusted models, I found a difference favouring quintile 5 in aspirin use in unstable angina. In addition, in the age-sex adjusted model, aspirin use in 'old ACS' and beta-blocker use in MI, favoured quintile 1, whereas aspirin use in unstable angina favoured quintile 5. Studies reporting on aspirin use in CHD were discussed in section 3.5.2.3, two papers[104,110] showing evidence favouring the less

deprived, most studies showing no significant differences, and four studies[111,130,134,214] showing evidence favouring the more deprived. Overall, in relation to secondary prevention, twenty comparisons were made for medication in established CHD and therefore the majority (17 out of 20 in the fully adjusted model) did not show significant differences favouring quintile 1. This is consistent with the result of a large 2012 study[103] that found no evidence of inequity in provision of major drug treatments for secondary prevention.

10.1.5 *Drug cessation analysis*

Twenty three comparisons were made using the fully adjusted models. There were significant differences favouring quintile 5 in three comparisons of persistence of prescription: statins in the 'high risk' groups, statins in 'old ACS' and clopidogrel in MI. No significant differences favouring quitile 1 were found for these models. On the basis of this overall finding, I conclude that patterns of drug-cessation cannot be driving differences in CHD outcomes (given that outcomes are poorer in more deprived groups). Indeed, to the extent that prescription-persistence is better in more deprived groups it may be acting to reduce inequality in outcome – though I have no strong evidence that prescription-persistence is a valid indicator of true adherence to treatment regimes.

10.1.6 *Suboptimal care*

Determining the extent to which health care delivered is truly optimal is not straightforward. Sub optimal, as distinct from inequitable care appears to have been received by some of those in my study population. The criteria for optimal care are generally reflected in NICE guidelines, but it may be difficult exactly to measure performance against them – as when there is latitude in a prescribing recommendation. For example in NICE guidelines it is clearly recognised that factors such as a patient's preference or intolerance to drug would affect prescribing decisions. Therefore to know whether such care was optimal in a population one might need complex information about patient demand, non-compliance, drug intolerance, and so one. In some cases, this information is available from GP data, but we elected not to use it in our study, as outlined above, because of our emphasis on examining the effects of healthcare inequity at a whole population

level. A more practical way of identifying sub optimal care may lie in comparison – nationally, regionally, or practice by practice. However, the problem arises of determining which area is providing optimal care to benchmark other areas against.

Despite these caveats, a number of findings from the analysis presented here give a strong suggestion either that sub optimal care was taking place or that the interventions in question are of limited benefit when used at population scale. It is important here to remember that I am talking not about comparisons across quintiles, but about *volume* of healthcare, which in itself has implications for healthcare equity (as discussed in chapter 2).

While in many cases it is difficult to be certain that issues such as refusal, intolerance, contraindication and so on are not in part responsible for observed population-level uptake of interventions, there is a section of the pathway of care where this is much less likely to be an important factor – namely the part of the pathway dealing with ascertainment of risk factors and provision of smoking advice. Thus, I see that for those turning 40 'ascertainment of smoking status', 'measurement of BMI', 'measurement of BP', and 'measurement of cholesterol' all show declines in the Kaplan-Meier plots which in an ideal healthcare response should be much steeper. Thus, three years after turning 40 approximately 30% of individuals do not have a smoking status recorded, approximately 60% do not have a BMI recorded, and approximately 40% do not have a BP measured. Only about 25% have a cholesterol measured.

Similarly, while approximately 60% of those first identified as smokers receive smoking cessation advice immediately, approximately 40% do not, and by three years approximately 15% of individuals still have no record of such advice being given. Given the importance of smoking as a driver of CHD, it is clear that this is suboptimal (either the provision of the advice or the recording of such provision).

In other parts of the pathway, sub optimal management is harder to identify with certainty, because of the issues outlined at the start of this section. Again, notwithstanding these limitations, a number of important findings emerge. Because I used only the requirement that at least one BP medication be used for the clinical action 'BP raised and low risk' and 'BP raised and high risk', individuals intolerant of one BP medication could be treated with another and the clinical action would still be achieved. Further, intolerance to a medication is identified by a trial of a drug: according to my methodology that

trial would count as the drugs starting. Thus, for the BP medication, intolerance of medication is unlikely to be an explanation for the absence of treatment.

In low-risk individuals with a high BP three years after such a BP was identifiable from GP records, approximately 25% of individuals had not started on a BP treatment. For those with high cardiovascular risk, approximately 30% had not begun treatment at three years. While the caveats from above obviously apply to statin therapy, it is striking that for those with high CVD risk but no diagnosis, three years after this was first identifiable, approximately 75% of individuals had not started on a statin. The picture with those with a diagnosis was quite different – at three years approximately 30% had not received a statin.

When looking at secondary prevention of CHD, I identified numerous examples of situations suggestive of suboptimal care, particularly with beta-blockers, where I found disappointing levels of initiation of treatment: more than 90% of individuals were not started on treatment at three years in those with unstable angina or MI.

With revascularisation, identification of suboptimal care is much more problematic, because of the absence in my data of many bits of information relevant to whether an individual has a genuine need for a revascularisation procedure.

Overall, though not the focus of my study, I found several instances indicative of the existence of suboptimal care for the study population in the study period. As a comparison, using a different methodology in a different population, Hawkins et al found, when looking at secondary prevention of CHD and management of MI, better proportions of individuals with these indications treated then I identified in my study. For example at one year follow-up, I identified less than 75% of those with myocardial infarction being treated with aspirin, compared to more than 90% in the Hawkins study. This discrepancy may be explained by the fact that the Hawkins study used the Myocardial Ischaemia National Audit Project (MINAP) dataset to identify MIs. This will provide a more valid denominator of MIs and a numerator (individuals treated with aspirin) that included information on in-hospital management.

With ACE-inhibitor management, I found approximately 70% treated by one year in those with MI, comparable to the Hawkins figures. With clopidogrel, Hawkins found substantial differences between 2003 and 2007, with a rise from 42 to 91%. This is broadly consistent with my finding of approximately 50% treatment at one year, again taking into

account the fact that inpatient prescribing was not captured in my data. The very poor rates of prescribing of beta-blockers in our study were not reflected in the Hawkins paper, and this constitutes a surprising finding, worthy of further investigation to examine whether this is a real effect.

10.1.7 *Relating these findings to national policy and guidelines*

The measurement of health inequalities, which would include measurement of healthcare inequity, has been repeatedly recommended in the policy documents and reports in the UK.[8,215,216] My study has importance for these recommendations in a number of ways. Firstly it fulfils these ambitions in a systematic way with respect to healthcare inequity for CHD in Wales. It provides proof of concept that such an approach can be used to systematically address the existence of healthcare inequity across a wide range of components of the pathway of care for a particular condition using an automated population level approach, in such a way that could be repeated with a view to monitoring changes in provision. Thus, this work provides a concrete example of a methodology that could be employed to meet the recommendations laid out in policy documents and guidelines in a systematic and repeatable way. Further, I have demonstrated the detail of an implementation approach and have written programmatic algorithms that could underpin such work both in relation to CHD and for other conditions. In addition, the work presented in this thesis reassures stakeholders that widespread inequity in healthcare is not occurring with respect to CHD in Wales.

NICE and the NSFs are explicit that major determinants of risk (smoking, diet, other lifestyle factors, and so on) must be addressed proportionately. That is to say that undue focus on for example revascularisation is not an appropriate population-level approach to managing CHD. These recommendations concur with the findings of my study, which, as I discuss further below, imply that in order to affect differences in rates of CHD between deprivation groups, the main focus ought to be on affecting social gradients in the important determinants of cardiovascular disease.

10.2 APPRAISAL OF STUDY

10.2.1 *Strengths*

My analysis was based on data from a large number of individuals (over one million). Using such a large electronic cohort as a basis for my study meant that I was able to identify large numbers of clinical triggers for which I ascertained times to clinical action. While the absolute numbers of specified clinical triggers varied markedly according to type, employment of a large underlying cohort population increased my chances of identifying sufficient clinical triggers to provide a good level of precision in my final estimates. Likewise, the large size of the cohort meant sufficient data were available to adjust for relevant covariates. Furthermore, one of my key aims in this work was a comprehensive examination of healthcare delivery across a pathway of care at a truly population level; the availability of a dataset based on such a large number of people allowed me to do that. In undertaking a pathway-level analysis, I hoped to be able to identify systematic effects with respect to healthcare inequity, rather than simply identify its effects at isolated points in the pathway. I consider that, despite the limitations discussed later in this chapter, my study achieved this through its key strengths: the the comprehensive view of the pathway and the development of innovative ways of measuring utilisation, timeliness and continuation of indicated interventions.

With the exception of the definition of deprivation quintile for an individual (which is based on inferring an individual's deprivation from the small-area geography in which they live), my data were at individual level. This meant that I was largely able to circumvent issues arising from ecological biases in our data. Moreover, access to data of this nature allowed me to employ the chosen methodology using a survival analysis approach, with adjustments for important covariates, and a hierarchical model structure (individual–practice–hospital) taking account of supply-side factors as random variables.

Using a survival approach eliminated the need to decide on a particular time-period that should be considered important in analysing outcome. It is widely used and accepted in health research; it allows appropriate adjustment and, with the use of frailty models, allowed me to extend my analysis to take account of effects at practice and hospital level, modelled in a hierarchy. While a 'glass-half-empty' perspective might see the use of random effects within models as only necessary

where insufficient information is available to determine what characteristics of hospitals or practices are affecting outcome, a more positive perspective would judge that use of these techniques maximised the insight that one could gain into the observable relationships with the available data.

I believe the real strength of this study was in the development of a simple but novel methodology to address population-level analysis of healthcare implementation, using the clinical trigger-action approach. I used a carefully-developed theoretical framework to underpin a rigorously-defined set of algorithms to identify, classify, and collect relevant information on these clinical trigger-actions from a large and unrefined underlying data source. This allowed me to use the statistical techniques of survival analysis using frailty models to model my data. Further, I developed the idea of drug cessation, looking at progress from drug initiation to drug cessation as an additional level of my analysis, but employing the same survival analysis techniques – thereby ensuring that the complete analysis could be subsumed within a consistent theoretical framework.

The real strength of this approach becomes clear when one considers that it allowed one to look globally at a comprehensive pathway in such a way as to address potential knock-on effects in individuals' progress through it. For example, I was concerned at the outset of this work that examining the management of only those individuals with an assessed high cardiovascular risk could fail to identify inequity if assessment of risk itself were inequitable. My approach relieves such concerns. In other words, in attempting to capture any differences in management that might exist as individuals flow through the system, my approach allows me to be sure that progression of individuals through disease states of increasing severity (no disease; angina and chronic CHD; ACS) is not facilitated by differential disease management at an upstream stage. Without such attention to the nature of the pathway, differential management lurking in unexamined parts of the pathway of care could exert inequitable knock-on effects, even if downstream management were completely equitable.

A further advantage of this approach is in examining the effects of derived history variables within models. By using available information on the length of time for which a particular clinical action had been indicated for an individual and by looking at the number of different previous indications that had occurred, I was able, by taking account of the pathway perspective, to adjust for these elements of an

individual's history as potential confounders in my models. Similarly, I was able to take account of whether an individual had previously received a clinical action prior to the clinical trigger in question. My approach focused on taking account of progression of individuals through an overall system in a way not previously attempted when examining healthcare inequity.

I made strenuous efforts to validate the data, both by examining its volume in comparison with expectation and by making prevalence comparisons against external sources. Without such an approach it would have been very difficult to identify subtle but critical failings in the original data extract with which I was supplied. Prevalences of major conditions and risk factors in my dataset corresponded to those in the most similar available dataset (Welsh QOF). Available evidence suggests therefore that the content of our dataset was in line with expectations from other sources (notwithstanding the difficulties of defining hypertension).

In my analysis, in addition to looking in a comprehensive way across the pathway of care for CHD, I looked at the potential effects on my findings of altering some of the important underlying assumptions of my analysis, thus allowing one to clarify that such assumptions are not critical in driving the pattern of relationships encountered. This allows one to be more certain that the findings are robust, rather than being highly sensitive to the underlying assumptions in question.

10.2.2 *Limitations*

10.2.2.1 *Limitations related to data sources*

Individuals were included in the study on the basis of the GP practice with which they were registered; about 40% of the Welsh population were registered with a SAIL-submitting practice. Any systematic difference between individuals or the management of individuals between practices included in and excluded from SAIL might bias the results. The cohort of individuals included was, for example, not geographically representative of the Welsh population: SAIL-submitting practices were disproportionately based in West Wales (as was displayed in figure 7.7). Furthermore, the individuals within our dataset on whom readings and results were available did not represent a random sample of our study population. For example, it seems extremely likely that very overweight individuals will be more likely to have their BMI recorded than individuals of normal weight; similar effects

are likely to occur at numerous points in our data. While I have taken all reasonable steps to use multiple imputation techniques to address issues of missing data, there is nevertheless an inevitable issue of representativeness in this study and studies of its kind.

In addition to issues with representativeness of the Welsh population, there are also issues that arise when wishing to generalise to the UK-population. Health service arrangements are distinctive in Wales, and any generalisation from our population to the population of the UK needs to take account of this.

Routine data quality is dependent on the way in which data is entered into the raw datasets. Misclassification and absent data are problems that inevitably occur in a proportion of records of this type. As an example of misclassification, it is widely appreciated that a proportion of deaths are given an incorrect cause; likewise, I suspect that referrals to smoking cessation services from primary care are not always accompanied by the entry of the relevant Read code into clinical systems – resulting in absent data. The classification of ACSs within the PEDW data was unsatisfactory, given the presence of codes for old MI and the difficulty of differentiating different types of ACS. Furthermore, the difficulty of which coding positions to regard as being relevant within PEDW arises – here I have used codes in any coding position to define diagnoses. This increased sensitivity at the expense of specificity. Clearly, in some situations this was not a problem – for example in relation to risk factor ascertainment. However, the designation of clinical triggers based on a simplified three-way classification of ACS, involved use of the MI code at any coding position and I recognize this as a potential limitation.

There were a number of specific examples within our data that were poorly coded. Admissions to the Liverpool specialist cardiac centre (Liverpool Heart and Chest Hospital) were indifferently coded, such that I had to classify all admissions to the trust as being cardiac centre admissions; the variable admission type in PEDW data is poorly coded; the Read codes for referral to smoking cessation services from primary care are not widely used; the Welsh Demographic Service administrative information overestimated populations in younger age groups (a known problem with this data). I would have liked to have used data on an individual's ethnicity in the analysis. Though Read codes are available to code this information, in practice, they are very rarely used, so I was unable to include this information in our analysis.

Besides absent data arising because it does not find its way into datasets appropriately, there are also complete absences within PEDW at a systematic level: most importantly, it would have been extremely valuable for this work to have examined the drugs given to patients from different patient groups as inpatients within hospital following an ACS; this was not possible, because in-patient drugs are not available from PEDW records. Not only did this preclude investigation of an important area of treatment, it also meant that I was unable to begin my analysis of the period during which an individual received a medication until after they had returned to being under the care of their GP. Allowing time for drugs taken home from hospital by the patient, this meant that I was usually unable to identify initiation of treatment until 28 days plus the length of the admission had elapsed; this also meant that admission length might potentially confound the relationship between deprivation and drug provision. Other data that were not available to me included data on cardiac rehabilitation, data on admissions and procedures in the private health sector, and over-the-counter prescriptions of aspirin and statins. Data relating to the type of admission (emergency, elective or other) for MI suggests that the coding gave inadequate detail. For example, in relation to the trigger-action MI and PCI I have presented figures for admission type: elective 3%, emergency 80.7% and 'other' 16.1%. This seems implausible; my understanding is that this difficulty may relate to the decision to use codes to define MI in any diagnostic position, with the result that some admissions are misclassified as MI-related. Ideally, I would have had access to a source of data relating to general practices and hospitals, detailing specific characteristics of each of these such that I could have investigated in detail the real drivers behind hospital-level and practice-level effects – thus obviating the need for the random effects approach used.

A limitation in the use of the LSOA, by which one infers an individual's level of deprivation through small-area geography, is that health-selection effects (individuals with health problems tending to 'gravitate' to poorer areas) and exposure-lag effects (accumulating effects related to the area on an individual's health over time) could not be allowed for.

10.2.2.2 *Limitations related to analytical approach*

A number of criticisms might legitimately be directed at my analytical approach. It might be argued that the approach of basing the find-

ings primarily on the comparison between deprivation quintile 5 and deprivation quintile 1 constitutes a limitation, though I have tried to allow for any potential sensitivity of the analysis to this simplification by re-examining the areas of the pathway for which social gradients were apparent using a slope in the of inequality approach (section 9.3.5 on page 300).

In modern epidemiology, confidence intervals are preferred to p-values because of the additional information they provide; in the overview approach I have focused, for presentational reasons, on using p-values and HRs. Similarly, the use of HRs might be subject to criticism in the sense that the statistic is not additively symmetrical – for example, a HR of 0.8 does not represent an effect size equivalent (though opposite) to a HR of 1.2. It might be argued that this muddies the presentation of pathway overviews as presented here, but, after consideration, I decided that more confusion would be inherent in use of log HRs as an alternative, especially as most HRs presented were close to 1.

The covariates were defined at the time-point of the clinical trigger. I did not analyse subsequent changes in covariates during the clinical trigger-response period – that is I did not include time-dependent covariates in the models. While I did consider pursuing this approach, it proved impractical within the context of the other analytical demands faced. When using age as a covariates in models, I used age as a categorical rather than continuous variable, because age is often most appropriate modelled as a non-linear term, something which would have been difficult using my automation approach.

In my discussion of pathway simplifications in chapter 5, I indicated that, for reasons of practicability in this study, I regarded an individual assessed as 'high risk' as being unable to return to 'low risk', irrespective of any subsequent risk assessment. I recognised this as a potential limitation but saw it as unavoidable.

A weakness in the analysis using the pathway approach is an inherent problem with multiple comparison. In very simple terms, using a significance level of 5% implies that in making 20 comparisons, on average, one might expect one to be significant purely on the basis of random variation. In the pathway overview analysis, I have made substantially more than 20 comparisons. Thus, some significant findings in overview would be expected on the basis of chance alone in my analysis. While statistical techniques exist to take account of multiple comparison (the Bonferroni correction or similar techniques), I did not

apply them in the context of this study. Instead, I have sought, when interpreting my results, to keep very clearly in mind the problem of multiple comparison.

I used multiple imputation, in instances where certain data were unavailable, as a means of minimising the effect of missing data on findings. On page 176 in chapter 6, I discuss some of the limitations associated with this approach, for example, the introduction of additional assumptions, complexity and practical difficulty into the analysis.

While the study gained much from the ethos of automation of analysis brought to the work, there were inevitable negative implications. In a situation in which only one model was being developed, a large element of human input and judgement would have been used. When selecting models, though my approach allowed me to specify the model differently at each point in the pathway, I did this in a pragmatic way, without pursuing an extensive process of trial and error as one might have if automation had been unnecessary. Ideally, I would have liked to have introduced interaction terms into the models, but the process of automation made it impractical to do so – a further limitation of this approach. Likewise, I was unable to test some of the assumptions of my approach in detail, particularly the assumption of proportional hazards when using frailty models, the assumption that five imputations were sufficient (though I did test this assumption in broad terms in the sensitivity analysis), and the assumption of linearity when using indication years as a continuous term in models.

When looking at survival times in relation to clinical trigger-actions I was concerned that my approach might be biased by a competing risks effect from an individual dying. Put simply, I knew that individuals from more deprived groups had higher age-sex-standardised death rates; the potential issue was that individuals might die before contributing time to the models, thus meaning that individuals who died more quickly were more likely to contribute time to the denominator but less likely to receive the clinical action (and thus enter the numerator). After detailed discussions with experts in the field, I believe the survival approach inherent in using frailty models takes account of this effect and that no bias is in fact occurring.[217]

When developing the methods, I made a number of simplifications that helped make the analysis possible in the face of the problems presented by a daunting array of clinical codes from which I needed to define clinical states, an extremely large analytical work load that

made automation necessary, the comprehensive nature of the pathway under investigation, and the complexity of the underlying data sources. Such simplifications might be considered limitations.

I removed individuals from our dataset when they had a discontinuous period of registration within SAIL GP; I analysed our cohort using annualised time-points of registration, rather than looking at every time-point of registration change. When considering transfers between hospitals, I created separate trigger periods for each admission (hospital transferred from and transferred to). Because of the structure of my algorithms, the effect of this was to generate some very short clinical trigger-action periods in which no action occurred, which were quickly superseded. When examining the management of hypertension, I considerably simplified the nature of the clinical action I looked at. In reality, clinical algorithms for managing hypertension are quite complicated, and producing computer algorithms to address the extent to which clinical recommendations were followed in detail would have been extremely difficult. When examining management of hypertension, I looked only at the most routinely used drugs, excluding others such as spironolactone and alpha blockers. When examining risk assessment, I assumed that risk-factor measurements stayed relevant for an indefinite period. Finally, for simplicity, I did not look at temporal effects within our study period. In other words, I assumed that any differences in times-to-event would be consistent over the time-period of this study. This assumption may have been inappropriate in relation to revascularisation: in the literature review I found some evidence of a temporal trend in its provision, and during the study period there were significant increases in the resources to provide revascularisation in the population studied. When using the Charlson Index as a covariate to adjust for comorbidity in the analysis, I collapsed the full index to a binary variable, thereby potentially weakening the adjustment as compared to an approach using the validated index itself. My analysis did not consider issues of informed dissent and contraindications to treatment when looking at achievement of clinical actions, something which might have been possible on the basis of available Read codes, but which I did not carry out. As a further simplification, I used the Framingham non-laboratory risk assessment tool (though I did test the effect of doing so in sensitivity analysis). There are limitations with the non-laboratory risk assessment approach, as outlined on page

A number of other limitations have implications for further work and are therefore discussed under that heading later in this chapter. These relate to:

- The possible incorporation of CIs round HRs into graphical summaries to give clearer overviews
- Refining the selection of simplified models
- Extending the statistical analysis so that models included time-dependent covariates
- The need to check in detail assumptions of proportional hazards
- The need to check for linearity using indication years as linear term
- Calculating the numbers of imputations needed to account for variation produced by missing data
- Adjusting formally for effects of multiple comparisons
- Awareness of possible limitations relating to simplifying assumptions

10.2.2.3 *Limitations and study validity*

Clearly, all studies are subject to limitations, and such limitations predispose study to a greater or lesser extent to issues of bias, confounding, chance findings, and reverse causation. Appraising the extent to which such issues arise for my study is therefore important.

In performing this analysis, I was, in simple terms, looking for an association between socio-economic deprivation and the time to achievement of certain clinical actions following clinical triggers at different points in the pathway of care. A number of methodological characteristics of the study may have caused biases towards the null, that is to say made it more difficult to identify a true association against a background of random variation. For example, the approach of using a 5:1 HR approach has the potential to bias the results towards the null, because information on the middle three quintiles in the analysis is not taken into account (though I did examine the implications of this in our sensitivity analysis). Likewise, the use of area-based deprivation, age as a categorical variable, the Charlson index as a collapsed binary variable, and the limitations of routine coding introducing misclassification, could all act to introduce 'noise'

into models and reduce the strength of the 'signal' which the study sought to identify.

Issues of representativeness of the population in the study could also potentially introduce bias. Were it the case that the population included in the cohort was systematically different from that excluded, bias might be introduced. The lack of geographical representativeness of the population with respect to the population of Wales (and the UK more generally) makes the existence of such bias more likely.

While I adjusted for potential confounding variables in our models, it is quite likely that under adjustment for relevant confounders occurred, because some potentially useful variables were not available (for example ethnicity). Residual confounding within models might have the effect either of suggesting associations between deprivation and healthcare utilisation that are not in fact valid or of concealing true associations.

As discussed above, given the number of comparisons made, the potential role of chance in underlying identified associations needs to be carefully borne in mind. While I have tried to take this carefully into account, I acknowledge the potential effect of chance in producing spuriously positive results with the methodology employed.

10.3 CHALLENGES AND LESSONS

It is tempting when reporting academic activity in a document such as this – aimed as it is primarily at an academic audience – to gloss over or put spin on particular difficulties or oversights, and to attempt to give the impression that the courses of action that were eventually followed had been intended right from the start: I resist that temptation here, because other researchers may wish to undertake similar projects; an honest appraisal of these issues might, I hope, be of use to them. Moreover, I intended to progress to cover some areas that time-constraints have relegated to the further work (section 10.4). This necessity is in part attributable to the difficulties described in this section. While many of these are, no doubt, common to all projects of this nature, some are not; in my view, honesty about and description of such challenges, is important in giving a clear picture of the work involved in producing a thesis of this nature.

By far the biggest frustration with this work arose from the difficulty of obtaining an extract from the main SAIL databank that conformed to my specification. Problems, which stemmed from a range of causes,

resulted in delays in the project and required that code be significantly rewritten in places. SAIL is a relatively new framework: it is quite likely that many of the problems confronted would not occur in projects started now.

Particular difficulties arose at two stages. Firstly, the process of IGRP approval for the project took a long time. An initial application that I submitted was rejected on the basis that the specification of the GP data was not meaningful in the context of the SAIL GP table. I was obliged to rewrite and resubmit an application, having spent time being schooled in the structure of the SAIL GP table by one of the SAIL analysts. Including the delay for this rewrite, the approval process took seven months from initiation to granting of formal approval.

Secondly, following approval, the extraction of data itself was extremely time-consuming and fraught with difficulty. The extraction required that a complex set of linkages be performed accurately on several different tables, and in relation to the PEDW data this was a particularly demanding exercise. It was necessary to undergo numerous cycles of an iterative process, in which I examined the extract provided by SAIL so as to identify errors, which I then pointed out for correction. These ranged from quite simple and easy to spot problems (for example, an entire year missing deaths data; incorrect linkage in the PEDW) to subtle and difficult to identify problems.

Each error or set of errors that I identified meant that that I had to point out and characterise the error and wait for it to be identified in the SQL code relating to the extraction, for the extraction to be performed, and for a further set of processes to be performed by the technical team to re-encrypt the data. As a result, any such iteration introduced a delay of between one and two weeks (sometimes more) in access to a definitive data extract – which, in turn, I would then need to run through my own algorithms. The identification and characterisation of problems in this way was extremely time-consuming and delayed the project on numerous occasions.

The software that I developed to perform my analysis pulled data out of the DB2 databank and processed it in an external file structure. I did this in an effort to 'play safe', because at the outset of the project I did not have a clear indication of the extent to which I would be able to manipulate data within DB2. Were I doing this project again, rather than relying on C# and SQLite for implementation of my algorithms, I would consider making much more use of DB2 to store data and to perform routines on them. It is quite likely that this would result in a

performance improvement, and might solve some of the difficulties of running time encountered.

10.4 FURTHER WORK

In considering further work that might be undertaken, I have looked at four areas:

1. Using an expanded dataset, with the same approach, addressing the same question
2. Using other methodological approaches
3. Using other definitional starting points, but addressing the same broad question
4. Generalisation of approach

10.4.1 *Using the same approach on an expanded dataset to address the research question*

Further work might be undertaken to look at a different dataset, either by expanding the current dataset or by looking at an entirely different data source, but with a focus on the same research question.

Expanding the current dataset might be achieved in a number of ways. Most simply, data could be re-extracted from SAIL with the date criteria for the extract extended forward. At the time of writing, data are available to the end of 2012 (an extension of two years in the study period). Moreover, the proportion of GP practices in Wales submitting data to SAIL has increased since the original extract was performed, meaning that geographical coverage within Wales might also have increased. Because the SAIL databank is increasingly linked into other similar sites in the UK, as part of the Farr Institute, it might potentially be possible in future to obtain an expanded dataset that included data from those sites. The data extract used in this thesis was based on demographic information on individuals linked to GP, PEDW, and mortality data. The dataset might potentially be expanded by linking into other data sources. For example the MINAP dataset contains information on individuals in Wales with MIs, separate data exists for PCI data, and potentially radiology and other datasets might be linked in as well. Such additional linkage might make available other useful variables on individuals, potentially allowing additional

analysis to be refined and making it possible to validate previous results.

Were it impossible to arrange additional linkage to data from other parts of the UK, another approach might be to repeat the analysis on datasets from other areas. Scottish linked hospital discharge and death data has been used for many years for epidemiological analysis of CHD and a similar study using this data could clarify the generalisability of the findings presented here.[218] During the time in which this thesis was prepared, the Cardiovascular Disease Research Using Linked Bespoke Studies And Electronic Records (CALIBER) dataset has been established, which contains data similar to that addressed in this thesis. CALIBER (for example) might be a data source on which the analysis could be repeated; it has previously been used for work with a similar emphasis.[219] Comparison of the work presented here with findings from studies employing different data from different UK populations would be useful in establishing whether the patterns I have observed are area- and time-specific. Such triangulation would allow the findings presented here to be set in the context of other results. Furthermore, while in my analysis I validated prevalences of important CVD diagnoses and risk factors in our population against other available data sources, an extension of this process, whereby a more in-depth validation of our data against other sources in Wales and in other parts of UK would be an important area for further work.

10.4.2 *Using other methodological approaches*

The approach in this work is best characterised as an observational epidemiological study. Other broad classes of study could contribute greatly to increasing understanding in this area, both with respect to detailed understanding of the causes of the observed patterns and their likely impacts.

Qualitative studies in this area, which seek to elucidate the mechanisms by which healthcare inequity might be arising, particularly with respect to revascularisation procedures, could make an important contribution to understanding what is happening at the population level. While in the current work I have developed an approach that allows me to examine the pathway in overview, based as it is on routine data, it cannot provide information about why healthcare inequity specific to revascularisation might have occurred. Qualitative studies looking at in-depth analysis of interviews with individuals from different

deprivation groups and with clinicians could provide this information, which could potentially prove invaluable in understanding the mechanisms by which healthcare inequity arises. Some studies of this type have previously been performed.[209,220,221]

10.4.3 *Other definitional starting point, but addressing the same question*

At the inception of this work, I decided, for reasons discussed in chapter 2, to base my analysis on identifying healthcare inequity on the presence of differential utilisation-for-need. As previously pointed out, this is by no means the only way to approach the subject. Depending slightly on ideological viewpoint, further work might be directed at examining differences in expenditure, resource input, access, health outcome, or healthcare quality between deprivation groups as markers of healthcare inequity. Further work, at a philosophical level, to clarify which perspective on healthcare inequity really matters could contribute to clarity and understanding in the field.

For example, in a seminal 1979 commentary, Julian Tudor Hart postulated the existence of an 'inverse care law'.[222] He cited examples of inequity that included number-of-doctors-per-population (resource), differences in infrastructure (quality), differences in care given (utilisation), and differences in outcome. Thus, in this influential articulation of the problem of healthcare inequity, no primary definition of healthcare inequity was identified, and, further, the definitions implicitedly cited are not necessarily mutually compatible. These issues have been discussed in academic literature[30–36], but it is not clear that consensus has been achieved.

10.4.4 *Generalisation*

When designing this work, I mentally designated this project as one specific implementation based on a particular ethos that could be extended in a general way: this work, therefore, represents, as much as an end in itself, proof-of-concept for a class of investigations that might readily be carried out in several other areas. By carrying out this work, I believe that I have demonstrated that projects of this kind are feasible. The ethos that underpins it is based on a very simple principle: maximise the quality of information available about implementation of things that work, and do so in a systematic, population-level way; in other words, work out if we are doing as well as possible the things

that we already know how to do. The approach uses large linked routine datasets; relies on a programmatically automated analysis; and is built upon a rigorous and generalisable set of concepts, built around the idea of a clinical trigger-action. In performing this work, I believe that I have demonstrated how such an approach might be pursued, proving that the implementation of the complex algorithms necessary to perform it is possible in a reasonable timeframe, demonstrating the feasibility of prioritising comprehensiveness and a population-level perspective, and providing pathway figures, such as figure 9.3, that mean that very complex information can be presented in an assimilable way.

Insofar as this project has succeeded as a proof-of-concept, I believe that it points towards a generalised approach that can provide a useful future contribution in both a research and health service context.

It is of not only academic interest to understand the patterns of implementation of healthcare interventions of proven benefit. Investigation might focus on equity, as in this work, but might extend to looking at the population effectiveness of interventions, and the factors affecting the level of their utilisation. Benchmarking an achievable, population-level performance, based on real-world activity and controlling for case-mix might be extremely useful to those planning and directing health services. Further, observational studies could be augmented by modelling approaches that could usefully inform strategic and policy-level approaches.

In an operational service context, it is clear that detailed information on service utilisation of the sort envisaged here is likely to be extremely useful to health service planners and managers, as well as to political decision-makers. The concepts implemented here could, in some cases, act as an extension of *ad hoc*, small-scale, clinical-audit. I envision the possibility of providing a framework that would provide automated, population-level audits of implementation along pathways of care. For example, the code written for this project could quite readily be used to provide regularly updated feedback on clinical implementation related to CHD. The approach itself could be generalised much more widely to other populations and areas of clinical care, particularly those relating to chronic diseases with complex pathways of care.

10.4.5 *Illustrative example of population effects*

It would clearly be valuable to estimate the population benefits if the findings in this study of inequity and of suboptimal care were effectively addressed. The existing literature provides indications of how this might be approached. For example, Capewell et al[223], used the IMPACT model to integrate data on numbers of CHD patients, treatment uptake, treatment effectiveness, population risk factor trends, and median survival among US adults. They concluded that modest reductions in the prevalence of several major cardiovascular disease risk factors accounted for more than twice as many life-years gained as did treatments, although these gains were partially offset by substantial increases in obesity and diabetes.

Fidal et al used the IMPACT CHD model to calculate the number of life-years gained from specific cardiological interventions from 2000 to 2010 in the UK.[224] They found that aspirin and beta-blockers for secondary prevention following MI or revascularisation, for angina and heart failure were highly cost-effective. Other secondary prevention therapies, including cardiac rehabilitation, ACE inhibitors and statins, were reasonably cost-effective, as were CABG surgery and angioplasty. Primary angioplasty for myocardial infarction was intermediate, and statins in primary prevention were much less cost-effective. The cost-effectiveness ratios for standard CHD treatments varied by over 100-fold. They concluded that large amounts of NHS funding are being spent on relatively less cost-effective interventions, such as statins for primary prevention, angioplasty and CABG surgery.

Barton et al, in a modelling study[225], estimated that a programme across the entire population of England and Wales that reduced cardiovascular events by just 1% would result in savings to the health service worth at least £30m a year compared with no additional intervention. For example, reducing mean cholesterol concentrations or blood pressure levels in the population by 5% (as already achieved by similar interventions in some other countries) would result in annual savings worth at least £80m to £100m. They also estimated reduction in cardiovascular events and in costs if salt intake and trans-fat intake were reduced.

To provide an illustrative example, I employ here the sort of approach use in the IMPACT model to give an idea of the population impact of some of our findings. Taking the specific example of the provision of PCI to individuals with an MI, one of the main areas of

the pathway at which we identified evidence of inequity, I can work through a simple example of the likely population impact were this inequity to be addressed.

As a simplification, in this illustrative example I have not considered the many covariates identified as important in our 'fully-adjusted' model, but have used the HRs from that model to indicate the likely magnitude of effect. The method used to do this is shown in appendix F. Clearly, there are a number of limitations with this approach, but it does provide an estimate of the magnitude of the impact of my findings.

Table 10.1: Numbers of procedures that might have been carried out and numbers of procedures that might have been prevented or postponed had quintile 1 rates of utilisation occurred in other quintiles throughout the study period

Quintile	Difference in procedures	Potential deaths saved
1	0	0
2	105	27
3	130	34
4	153	40
5	223	57

Broadly, the approach I have employed here is to apply the quintile 1 rate of utilisation of PCI in those with an MI to the other quintiles. I did this for rates across the study period for the year following the MI. Using this approach, it is possible to calculate the number of PCIs that might have been done in the study period in quintiles 2–5 and the number of deaths that might have been prevented or postponed.

I show my estimates based on these calculations in table 10.1. Over the seven years of the study period, 105 additional procedures might have been utilised by individuals in quintile 2, rising to 223 for those in quintile 5. The estimates for the number of deaths saved also suggest that applying these rates to quintiles 2–5 could hypothetically have reduced deaths in these groups. As an indication of overall impact, the 57 deaths that might have been prevented or postponed in quintile 5 represent 7.4% of the total difference in the number of deaths between quintile 5 and quintile 1 over the study period (769). These estimates are based on the assumption that it would have been clinically feasible for some of the individuals in quintile 5 who did not have the procedure to have it, takes no account of age and comorbidity, and assumes a relative risk reduction from PCI in the year following

MI in line with that from primary angioplasty, using the effect size used in the 2009 study by Capewell et al.[226] Each of these assumptions will tend towards over estimating the number of deaths that might be prevented or postponed.

It appears that on the basis of these illustrative calculations that healthcare overall is likely to be responsible for no more than 7.4% of the difference in the numbers of deaths between quintile 1 and other quintiles that occurred during the study period. In practice, the percentage is very likely to be less than this, because of the simplifying assumptions in the model, the fact that this calculation takes no account of areas of the pathway where healthcare utilisation appears to favour more deprived groups (especially drug persistence), and because in other quintiles where there is a large difference in deaths from quintile 1 (3 and 4) less of the observed difference in deaths relates to PCI.

Detailed modelling of the likely implications of my findings in relation to healthcare inequity is beyond the scope of the work in this thesis, but would likely be a fruitful avenue for further work.

10.5 CONCLUSIONS

10.5.1 *Research question*

There are a number of important conclusions from this work:

1. With respect to utilisation adjusted for need, healthcare in the NHS in Wales is equitable at most points of the pathway of care for CHD, with the important exception of revascularisation
2. There is evidence of healthcare inequity for revascularisation with PCI
3. This is likely to contribute only a modest impact on the observed differences between deprivation groups in CHD outcomes

Points one and two above allow me to address the main research question – is there a systematic difference in the utilisation of healthcare for CHD between different deprivation groups across the pathway of care for the disease? The answer is a qualified 'yes', in that while inequity in revascularisation occurred in my study in what appeared to be a systematic way, this was a finding essentially confined to one area of the pathway of care. Inequity was not therefore found to occur in a generally systematic way or to do so with a law-like tendency.

The answer to the second research question (To what extent is any difference in utilisation of healthcare for CHD between different deprivation groups across the pathway of care contributing to differences in CHD mortality between those groups?), again subject to proviso, is that, while differences (in revascularisation) are likely to have an effect on differences in CHD mortality, it is likely that this is modest. Using the results of the illustrative example that I have presented above is the best estimate available, I suggest that no more than 7.5% of the difference in the number of deaths observed should be attributed to differences in PCI provision. Clearly this estimate itself is subject to uncertainty, and its clarification should be a subject of further investigation.

While not intuitively surprising, these conclusions imply that the NHS is not systematically inequitable, but that inequity can arise in specific areas; it would be of great importance to understand further why this may be occurring. Notwithstanding this, the implication is that inequitable utilisation in the NHS is by no means inevitable, and that in areas where it is identified it may be amenable to remediation.

10.5.2 *Proof of concept*

Beyond the above specific conclusions related to this work, I can, in addition, conclude on the basis of the project presented here that ambitious efforts to understand patterns in healthcare delivery across pathways of care in a systematic and automated way are feasible based on routine, linked datasets. Further, such projects are increasingly favoured by current health service conditions and improved data resources, and thus it is likely there will be future opportunities for real, population-level feedback on health service performance across whole pathways of care to contribute important findings in future. A frequently heard complaint when considering health service evaluation is that what is not measured is not improved. If this maxim holds true, I have an opportunity with projects of this kind to improve and innovate in the ways health service activity can be observed and the ways in which feedback can be provided. Potentially such processes might be invaluable to driving ongoing improvements in the delivery of care so that outcomes can be influenced by health services at a truly population level.

10.5.3 *Recommendations*

On the basis of my study, I can make a number of recommendations:

1. The clearest recommendation that emerges from the work is that, though evidence of healthcare inequity in the pathway of care for CHD exist, it is not a key driver of the outcome difference in mortality seen, and therefore organisations and policymakers should focus instead on the clear social gradients in cardiovascular risk factors – particularly smoking – that are likely to be key drivers of mortality differences between deprivation groups. Reductions in smoking in such a way as to reduce in both relative and absolute terms the social gradients in smoking will be needed if substantial progress is to be made on reducing differences in outcomes for CHD.

   Where agentic approaches are employed, careful efforts need to be made to monitor effects on inequality using approaches similar to those employed in this work. My findings suggest that agentic approaches are not inevitably inequality promoting, but that they can be and this possibility should be addressed.

   It is doubtful that agentic approaches alone can exert sufficient effect. Thus, the continued and expanded emphasis on structural interventions (social and fiscal policy and legislation to address risk factors) is important, if policymakers and stakeholders are serious about reducing inequalities in outcome from CHD.

2. I recommend that steps are taken to remedy the apparent inequity in revascularisation which would include taking steps to continue monitoring, using appropriate methodology along the lines of that employed here, the social gradients in PCI and CABG provision. Rapid change has occurred and is occurring in the provision of the services in Wales, and an ongoing understanding of social patterning is important to allow inequities to be addressed. If gradients persist, investigation of the underlying reasons should be prioritised.

3. I recommend ongoing monitoring of components of care identified in this study as suboptimal. This might be accomplished using the algorithms developed for this thesis, with a view to providing continuing population-scale clinical feedback. Where problems are apparent, local clinical audit could be used to confirm findings and address shortcomings.

4. In view of my finding relating to risk ascertainment (section 10.1.2) and evidence from the existing literature, I tentatively recommend that more deprived groups might best be screened for cardiovascular risk with an *ad hoc* case-finding approach, rather than with a formal screening approach.

5.The term 'Inverse Care Law' is sometimes used in public health and related disciplines. Evidence from this thesis and from other available literature suggests that, when looking at utilisation-by-need for CHD, healthcare inequity is not appearing in a law-like way. I recommend that the term may be best avoided when discussing healthcare inequity, which, rather than appearing as a law or law-like tendency, is apparent at specific points and times in the pathways of care for CHD.

6. With respect to the SAIL databank, the experience of using the facility for the large project undertaken for this thesis, means that I can make a number of recommendations for improvements to an already excellent system. I would have recommended that the timescales for the Information Governance approval be shortened and run to a formal timescale, but this change has already been made. I recommend that to facilitate research within SAIL, serious consideration should be given to the construction of continuously updated research-ready datasets to exist as an intermediate additional layer within the databank. This could be carried out in a number of areas, cardiovascular disease being an obvious one. I also recommend that,

where possible, extraction procedures be standardised with a view to preventing the necessity to rewrite difficult bits of code. This could be achieved with the use of templates and guides and by making available information on frequently encountered problems and solutions to them.

7. As mentioned above, to an extent this work was a proof of concept. Large amounts of data exist within the SAIL databank and within similar systems. The technical capability exists for linking these datasets together, and in this project I have developed what I believe is a robust way of looking at issues relating to delivery of health care. I recommend that consideration be given to the carrying out of an ongoing electronic audit of healthcare delivery in Wales. This could start with a focus on CHD, employing the methods and algorithms developed in this thesis. Potentially, additional data sources might be added (as discussed above in the further work section). Further, similar techniques and approaches could be applied to other major diseases, for example cancers in Wales. A generalisation of the methodology employed here to achieve a population level understanding of patterns of delivery of healthcare in an automated, continuously updated way might prove an invaluable resource in guiding the delivery of healthcare in Wales, and I recommend that consideration be given to pursuing such an approach.

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Part V

APPENDICES

A

THE WELSH INDEX OF MULTIPLE DEPRIVATION

In this section, I provide additional material relating to WIMD 2005, which was the principal deprivation measure used in this work.

A.1 INDICATORS USED FOR THE INCOME DOMAIN

1. Adults and children in income support households
2. Adults and Children in Income-Based Job Seekers Allowance households
3. Adults and Children in Working Families Tax Credit Households below a low income threshold
4. Adults and Children in Disability Tax Credit households below a low income threshold

A.2 INDICATORS USED FOR THE EMPLOYMENT DOMAIN

1. Claimants of Unemployment-related benefits
2. Claimants of Incapacity Benefit
3. Claimants of Severe Disablement Allowance (for women under 60 and men under 65)
4. Participants on New Deal for Young People and Intensive Activity Period (for New Deal 25+) not included in unemployment-related benefit counts

A.2.1 *Indicators used for education domain*

1. Key Stage 2, average point scores
2. Key Stage 3, average point scores
3. Key Stage 4, average point scores
4. Secondary school absence rates

5. Proportion of 16 to 18 year olds not entering further or higher education
6. Proportion of adults with low or no qualifications

A.2.2 *Indicators used for health deprivation domain*

1. Limiting long-term illness
2. Standardised all-cause death rate
3. Standardised cancer incidence rate

A.2.3 *Indicators used for access to services domain*

1. Food shop within 10 minutes
2. GP surgery within 15 minutes
3. Primary school within 15 minutes
4. Post office within 15 minutes
5. Public library within 15 minutes
6. Leisure centre within 20 minutes
7. NHS dentist within 20 minutes
8. Secondary school within 30 minutes

A.2.4 *Indicators used for housing deprivation domain*

1. Lack of central heating
2. Overcrowding (excluding all student households)

A.2.5 *Indicators used for physical environment domain*

1. Population averaged estimated air quality for each LSOA in relation to Air Quality Strategy objectives
2. Population averaged estimated emissions to air per LSOA
3. Proportion of residential population living within 1km from current and recent waste disposal sites (landfills and incinerators)

4. Proportion of residential population living within 1km from a significant industrial source (those identified in Part A(1) of The Pollution Prevention and Control Regulations 2000)

5. Proportion of residential population living in an area with a significant risk of flooding

Additional information on the technical underpinnings of the WIMD 2005 are available from the Welsh Assembly Government.[227]

B

ADDITIONAL BACKGROUND MATERIAL

B.1 ADDITIONAL BACKGROUND MATERIAL RELATING TO INEQUITY, SOCIO-ECONOMIC DEPRIVATION AND HEALTHCARE NEEDS ASSESSMENT

B.1.1 *Geographical divisions*

This thesis required information on the geographical area of residence for an individual to assign deprivation-decile to that individual based on the deprivation-level of the area in which they live. To accomplish this I utilised a statistical unit of geography called the LSOAs; these are census-based geographical units developed by the ONS.[228] They were introduced with the aim of reducing the kinds of problems caused by the inconsistent and unstable electoral ward geography.[229] Super output areas themselves are based on output areas (OAs), which are census-derived small areas of geography, which were developed with the aim of grouping together postcodes so that OAs had similar population sizes, had approximately regular shapes and were socially homogeneous.[228] LSOAs based on the 2001 census were first released in 2004. Their creation was based on the amalgamation of output areas (typically four to six)[229]. There are 1896 LSOAs in Wales for the 2001 census data, with approximately 1500 individuals in each.[228]

B.2 ADDITIONAL BACKGROUND MATERIAL RELATING TO CHD

B.2.1 *Pathophysiology*

CHD* shares its underlying pathological mechanism, namely atherosclerosis, with other major CVDs – see section B.2.5.1. What distinguishes the clinical picture of CHD from these others is the anatomical location of atherosclerotic pathology (in the coronary rather than other arteries).[230]

*Coronary heart disease, ischaemic heart disease, and coronary artery disease are, I believe, interchangeable terms; in this thesis I have used the term coronary heart disease throughout

Contemporary models of the pathophysiology of atherosclerosis emphasise the *response-to-injury hypothesis*. Here the initiator of pathology is thought to be endothelial injury and subsequent dysfunction. Ongoing atheroma development is seen as an attempt at healing in response to insult with a key role played by the immune system.[231] In contrast to the historical picture of a passive accumulation of lipids and fibrotic material in the vessel wall[232], the newer model emphasises chronic inflammation as a key driver of atheroma progression.[231,233–236]

Initial endothelial injury arises from two paramount insults: hypercholesterolaemia[231] and haemodynamic disturbance.[237] Lesser, though still important, contributors to endothelial injury include hypertension, toxins from tobacco smoke, homocysteine[91], immune complexes and inflammatory cytokines.[230] There is also some tantalising evidence of a role for infectious agents in the development of atheroma.[238] Genetic evidence suggests that atherosclerosis-related genes are predominantly involved in mechanisms of inflammation and stem cell biology[239], suggesting that though initial endothelial injury is necessary for atherosclerosis development, it is not sufficient, emphasising the critical role of the inflammatory response to injury.

This chronic inflammatory process incorporates a number of concurrent and interrelated processes; the most important of these are summarised schematically in figure B.1. Initial accumulation of low-density lipoprotein (LDL) in the intima is followed by the oxidation of component lipids.[231] These modified molecules can activate the endothelium, resulting in the recruitment of circulating monocytes and their adhesion to the endothelial surface, from where they emigrate to the arterial intima and transform to macrophages; they are joined, in smaller numbers, by other immune cells, including T lymphocytes and dendritic cells;[231] subsequently these cells help to sustain an immune response at the site[230] with the release of a variety of proinflammatory mediators. Smooth muscle cells and smooth muscle precursors are recruited to the intima from both the media and the circulation.[230] Macrophages and smooth muscle cells take up oxidised LDL, causing them to develop into foam cells. Cytokines and growth factors induce smooth muscle cells to lay down an extracellular matrix composed of collagen, proteoglycans, and other molecular components.[230] Smooth muscle cells themselves proliferate.

Platelets play a critical role in thrombus formation and ongoing atheroma progression;[240] they bind subendothelium (particularly collagen and von Willebrand factor) in areas where it is exposed due

to endothelial rupture.[241] They subsequently release adenosine diphosphate, thromboxane A_2, and thombin[241], which contributes to their role in the further activation and recruitment of platelets[241], with subsequent thrombus formation.

Beyond an established role for innate immunity in atherosclerosis, there is some evidence of an adaptive response with possible antigens including autoantigens(oxidised-LDL, heat-shock protein 60) or microbial molecules (possibly *chlamydia pneumoniae*, cytomegalovirus, or others);[231] components of the adaptive immune response are present in lesions throughout the course of atherosclerosis.[231]

A further role in atheroma progression is played by the renin-angiotensin system, which contributes to atherosclerosis development by promoting a number of coordinated cellular and molecular events that occur in the lesion, with angiotensin II known to have a number of pro-inflammatory actions on the vessel wall that lead to atheroma progression.[242] Patients with chronic kidney disease (CKD) undergo accelerated atheroma progression, in part related to the activation of the renin-angiotension system which CKD causes.[243]

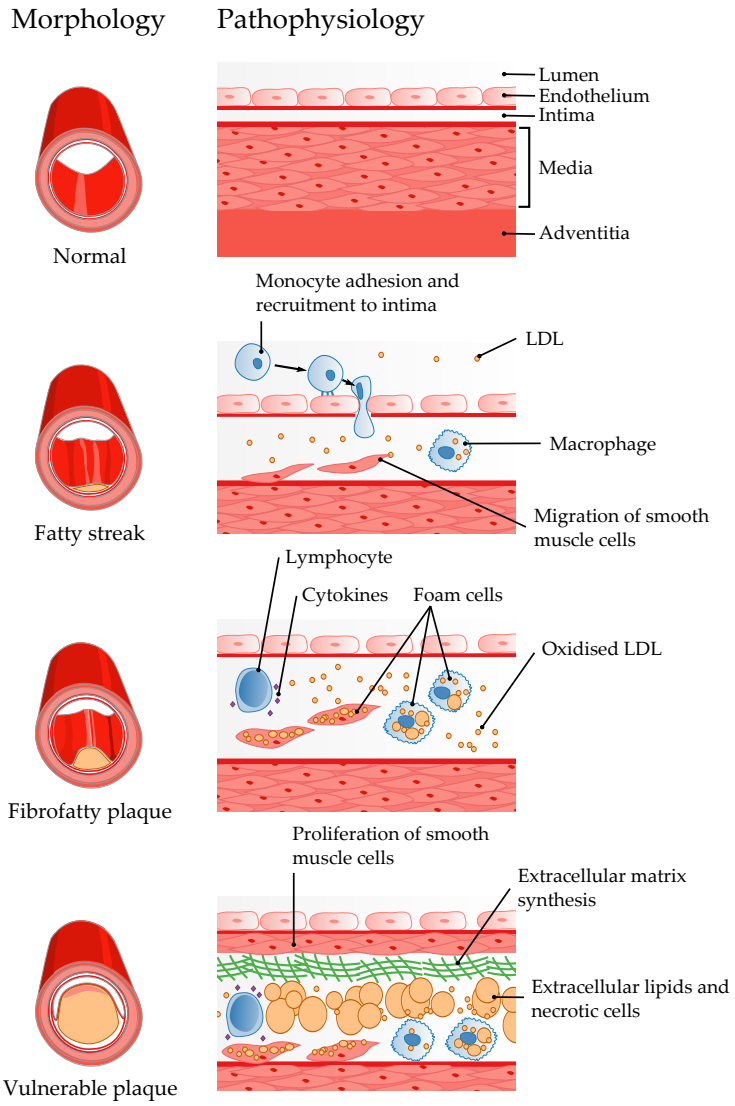
The complex evolution of atheroma, while impossible to characterise in precise detail, can be seen to give rise to

- Accumulation of extracellular lipids, necrotic cells, and extracellular matrix
- Cellular recruitment and proliferation
- Release of pro-inflammatory cytokines and growth factors
- Predisposition to thrombus formation with further plaque growth
- A possible role for an adaptive immune reponse mediated by B cells and mast cells

This complex cascade of events gives rise to morphological change from normal arterial wall structure, through the development of fatty streaks beneath the endothelial wall, to the emergence of fibrofatty plaques – characterised by a fibrous cap overlying a lipid core.[230] With continuing progression, such plaques become vulnerable to rupture or erosion, with such events inducing platelet adhesion around the site of rupture, thrombosis, and subsequent growth and remodelling of the plaque.[230]

The clinical consequences of atherosclerosis emerge by three principal means.[230] Either progressive plaque growth leads to a critical

Figure B.1: Morphological and pathophysiological changes of atherosclerosis



Adapted from figures in *Robbins and Cotran pathologic basis of disease*; Kumar V et al[230]

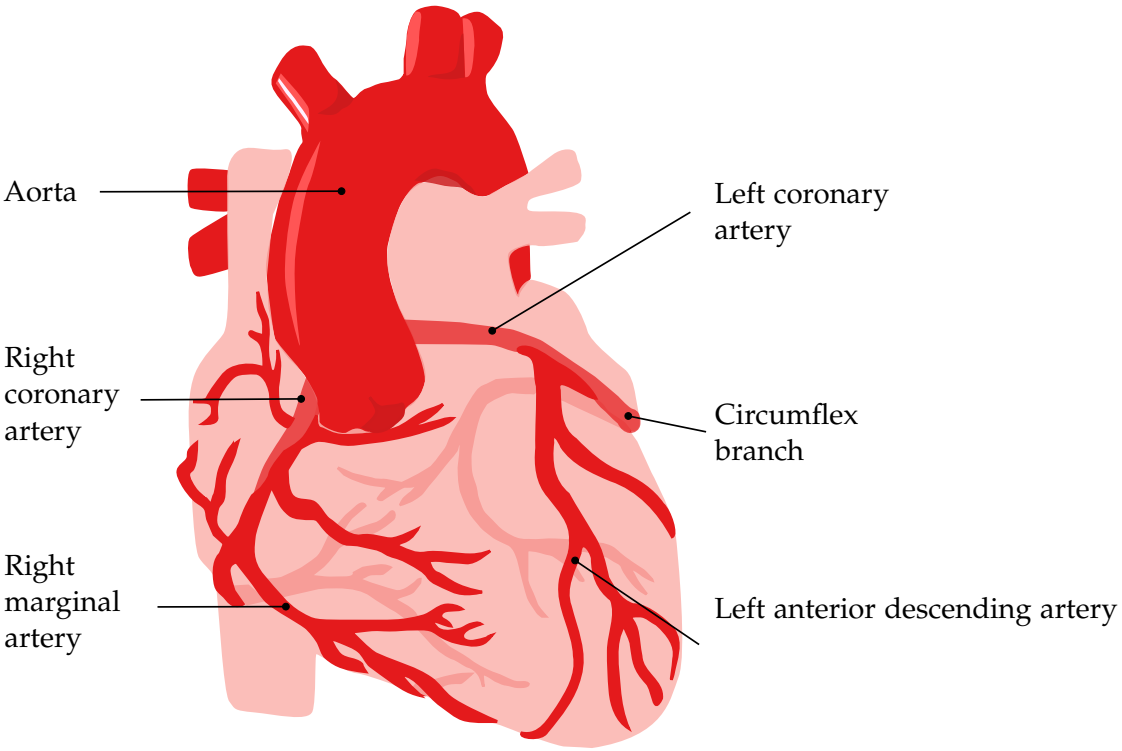
stenosis of the artery, resulting in sufficiently impaired blood flow to provoke symptoms.[230] With plaques in the coronary arteries the resulting clinical picture is angina pectoris.[230] Alternatively, acute changes[244] in the plaque, such as rupture or erosion, with accompanying thrombosis, might result in complete occlusion of the arterial lumen.[230] If occurring at a coronary site, such an event gives rise to the clinical picture of myocardial infarction, in which complete cessation of coronary blood flow results in downstream tissue necrosis due to lack of oxygen, with further injury subsequently arising from reperfusion injury if blood supply is restored.[230] Furthermore, embolisation of thrombus or material from the atheroma can result in occlusion at sites distant from the plaque itself.[230] Finally, weakening of the arterial wall as a consequence of atheroma progression can result in sudden rupture and aneurysm of the artery.[230]

B.2.2 *Clinical classification*

The permutations of anatomical distribution of atherosclerosis and progression to critical stenosis, occlusion or aneurysm account for the range of clinical pictures to which CHD, and more generally CVD, give rise. In the case of critical stenosis of the artery, in the absence of acute rupture and thrombosis, a fairly stable clinical condition may result, in which the inadequacy of coronary blood flow produces symptoms when the myocardium is exerted – typically patients experience symptoms during exercise or when under emotional stress; the relationship of these symptoms to exertion is fairly constant over time; such a clinical picture is termed stable angina. Symptoms typically involve anterior chest pain, which may radiate into the neck, shoulders, arms, or jaw.[207] In some patients the resultant symptoms are less typical, and can include gastrointestinal discomfort, breathlessness, or nausea[207]. People with stable angina have an increased risk of progression to acute coronary events[207]. In some individuals, continuing anginal symptoms are present yet on angiographic investigation the coronary arteries appear normal. Such a clinical picture is termed cardiac syndrome X[245].

Acute changes in an atherosclerotic plaque can lead to fast-evolving and life-threatening clinical pictures, resulting from rapidly narrowing or occluding coronary arteries. Such events are termed ACSs[246]. They range from unstable angina, resulting from sudden worsening of anginal symptoms (either in frequency or intensity), through NSTEMI

Figure B.2: Schematic representation of the principal coronary arteries; anterior view



Adapted from figures in *Essential Clinical Anatomy*; Moore et al[247]

that involves myocardial ischaemia together with biochemical evidence of myocardial necrosis, to STEMIs with ST-elevation on ECG – implying infarction of the full-thickness of the myocardium; the latter can be further subdivided on the basis of the anatomical region of myocardium that has infarcted, for example anterior, inferior, posterior, lateral and septal MIs. The anatomy of the principal coronary arteries is illustrated in figure B.2; exact coronary artery anatomy varies by individual. The anatomical region of infarction correlates to the artery in which occlusion has occurred; for example anterior MI is associated with occlusion of the left coronary artery; inferior with the right coronary artery; and posterior with the left circumflex coronary artery or sometimes right coronary artery[230] – see figure B.2. The development of an ACS can result in arrhythmias, catastrophic compromise of the myocardial architecture, acute left ventricular failure and sudden cardiac death. Less acutely, survivors of ACS may rarely develop pericarditis (Dressler's syndrome) and are predisposed to the development of chronic heart failure due to myocardial loss.

B.2.3 *Treatments and management*

The management of CHD encompasses a number of quite distinct circumstances in which the aims of management and the precise means of achieving these aims are different. In these contrasting situations, a variety of interventions are employed. Fully articulating the precise details of management in this chapter would involve presenting material from several clinical guidelines. To circumvent the impracticality of discussing all such information, I limit myself here to highlighting the important principles of management under the major circumstances that arise in relation to CHD[183,206,207,245,246,248–266] namely

- Management of stable cardiac pain and secondary prevention of disease
- Management of acute coronary syndromes and secondary prevention of disease
- Primary prevention

B.2.4 *Management of stable cardiac pain*

The optimal management of stable angina requires its correct identification, by clinical means or with the aid of diagnostic tests. NICE recommend that in individuals with intermittent, stable chest pain that appears cardiac in nature, if clinical assessment suggests angina and the likelihood of this is greater than 90% (estimated from the age, sex and other CVD risk factors), no diagnostic testing is necessary and an individual can be treated as having stable angina. In other cases, depending on risk, individuals can be investigated with coronary angiography (risk of angina 61–90%), functional imaging (risk of angina 30–60%), or computed tomography (CT) calcium scoring (risk of angina 10–29%)[245].

Coronary angiography requires that radio-contrast agent be released into the coronary arteries to allow x-ray visualisation of blood flow within the lumen; to achieve this it is necessary to pass a catheter from a peripheral access site (the radial or femoral artery) through the arterial circulation to the opening of the coronary arteries. Functional imaging includes a number of procedures: myocardial perfusion scintigraphy; stress echocardiography; first-pass contrast-enhanced

magnetic resonance perfusion; and magnetic resonance imaging for stress-induced wall motion abnormalities[245].

Once diagnosis is satisfactorily confirmed, the aims of treatment are to relieve and reduce symptoms – thereby improving quality of life – and to optimise secondary prevention (in an effort to reduce the impact of CHD that is already present)[207]; Lifestyle advice, drug treatment and revascularisation are the mainstays of treatment[207].

To provide immediate symptomatic relief from anginal symptoms, individuals with stable angina should be offered a short-acting nitrate. Further, a regular dose of one or more antianginal drugs should be initiated with a view to reducing symptoms, administered in line with the following principles[207].

- Use beta-blocker or calcium-channel blocker (CCB) as first line treatment
- Consider using a beta blocker and CCB if one drug does not control symptoms
- Where beta-blockers or CCBs or both are not tolerated consider using one of the following instead: a long-acting nitrate, ivabradine, nicorandil, ranolazine
- Do not offer a third drug to those with uncontrolled symptoms unless they are awaiting revascularisation or unless revascularisation is not appropriate

For those in whom it proves impossible to control anginal symptoms with medical management, revascularisation should be considered with the choice of treatment between PCI and CABG guided by angiographic findings (additional non-invasive or invasive functional testing may also be required)[207]. The decision about whether to recommend PCI or CABG should be based on the following considerations.[207]

- The anatomical distribution of disease
- The suitability of the patient to undergo PCI or CABG
- Whether the patient has multivessel disease and has characteristics that mean that CABG will lead to better survival, namely diabetes, age over 65 years, or anatomically complex three-vessel disease

PCI, often simply known as angioplasty, involves widening of the artery from within by expanding a balloon to open up the lumen. Frequently, this is accompanied by the use of a stent – a thin wire-mesh tube – which is loaded over the angioplasty balloon. As the balloon inflates, the stent expands and is left in place to hold the artery open[256,264]. The stent itself may be bare metal or drug-eluting (bare metal stents coated with a drug, such as an immunosuppressant, which is gradually released at the site of stent insertion). Evidence suggests that drug-eluting stents may reduce the need for repeat procedures[256,264].

CABG is a surgical procedure in which arteries or veins from elsewhere in the patient's body are harvested and grafted to the coronary arteries to bypass areas affected by atheroma. Surgery is either carried out by stopping the patient's heart and maintaining circulation to the tissues using cardiopulmonary bypass (such 'on-pump'surgery is the traditional method), or is performed while the heart is still beating – so-called 'off-pump' CABG[262]. Regardless of the approach used, vessels commonly used for grafting include the left internal mammary artery, great saphenous vein, and radial artery.

In those whose angina symptoms are well controlled, there is a sub-group of patients for whom CABG confers a prognostic advantage: those with left main-stem or proximal three-vessel disease. In these patients, where appropriate, functional or non-invasive imaging techniques can be used to identify individuals who may gain a survival benefit from undergoing surgery (despite their anginal symptoms being well controlled)[207]. If such investigations suggest that an individual is in this subgroup, they may progress to angiographic investigation and then, if appropriate, to surgery.

Finally, a number of preventive treatments can reduce the risk of progression to ACSs and other CVD events. Secondary prevention in individuals with stable angina involves lifestyle advice, aspirin 75mg daily (where appropriate), statin treatment, management of hypertension and ACE inhibitors (in those with diabetes only)[207]. In the case of individuals with established CHD leading to anginal symptoms, no risk assessment is necessary prior to initiating secondary prevention, as these individuals are by definition in a high-risk group for the development of further CVD.

B.2.5 *Management of acute coronary syndromes*

As outlined in section B.2.2, acute changes in atherosclerotic plaques can result in ACS – which includes unstable angina, NSTEMI and MI. Clinically, patients with each of these conditions present with acute cardiac chest pain. Where a patient presents with acute chest pain that is thought to be cardiac (on the basis of clinical history, CVD risk factors, history of CHD, and previous investigations), management involves investigation to determine the exact diagnosis and administration of treatments to relieve symptoms and improve outcomes. In clinical reality these processes run in parallel; here I consider them in turn.

Three main sources of information underpin the decision-making process that differentiates between different types of ACS and alternative diagnoses: clinical history, biochemical markers of myocardial injury, and ECG findings. The clinical history is consistent with ACS where a cardiac-type pain persists for greater than 15 minutes, and where it is accompanied by nausea, vomiting, sweating, shortness of breath, palpitations and haemodynamic instability[245,267]. Abrupt deterioration in stable angina (with increased frequency of pain, increased duration of pain, or pain on minimal exertion) is also suggestive[245]. Substantial variation in presentation exists, and even with a full-thickness infarct some individuals – particularly women, diabetic or elderly patients – may experience little or no pain[267].

A widely-used contemporary definition of MI gives prominence to the presence of a rise (above the 99th percentile) and subsequent fall in biochemical markers; troponin I or T is usually used. An MI is diagnosed where this biochemical picture is accompanied by symptoms of cardiac ischaemia and ECG changes consistent with ischaemia (also where imaging evidence exists of myocardial damage)[268]. Biochemical markers like troponins provide evidence of myocardial damage; they are therefore important in distinguishing between unstable angina, in which acute ischaemic chest pain is not accompanied by evidence of myocardial injury, and MI (either STEMI or NSTEMI). There is a time-lag in the response of troponin levels to myocardial injury, with levels peaking approximately 12 hours after damage; clinicians need to take a delayed troponin sample to account for this (in addition to an initial measurement)[245].

ECG changes indicating a STEMI are ST-segment elevation and new onset left bundle branch block; subsequently pathological Q-waves

may develop if blood flow to the affected region is not promptly restored.[245] Patients with NSTEMI and unstable angina may have a number of changes on their ECG that evince myocardial ischaemia (but not full thickness infarction); these include ST-segment regional depression and deep T-wave inversion.[245] By definition, ECG findings allow STEMI and NSTEMI to be distinguished, and in the acute setting are important in guiding management[245].

The diagnostic pathway for the assessment of ACS recommends that individuals with ST-elevation on ECG are managed as a STEMI until the diagnosis is confirmed by troponin measurements[245]. Alternatively, where the ECG shows regional ST-segment depression or deep T-wave inversion, patients should be managed as unstable angina or NSTEMI while differentiation between unstable angina and NSTEMI on the basis of troponin levels is awaited[245]. Patients with other changes on the ECG such as Q-wave and T-wave changes, can be managed as unstable angina or NSTEMI if these conditions appear likely on the basis of clinical assessment[245]. Where diagnosis is difficult, it may be necessary to record and review multiple resting ECGs[245]. A normal ECG does not rule out ACS, and where there is clinical suspicion patients still need monitoring[245]. The possibility that symptoms may relate to conditions other than ACS – pulmonary embolism, aortic dissection, pneumonia, and others – may mean that other investigations are indicated[245].

Initial management of ACS involves pain management with glyceryl trinitrate (GTN), which may be buccal or sublingual, and, where necessary, intravenous opioids. All individuals with ACS should be given aspirin 300 mg, provided they are not allergic to it. Oxygen should not be routinely administered, but oxygen saturations should be monitored and, in those without chronic obstructive pulmonary disease, kept above 94%[245] .

In cases of STEMI, restoring the patency of the affected artery or arteries is vital in minimising the extent of myocardial damage and in optimising prognosis; this should be done as soon as possible[267]. The principal options for achieving this include primary PCI and fibrinolysis (thrombolysis). In the former, the obstruction is removed mechanically; in the latter, pharmacological agents are used to break down thrombus and restore blood flow. Evidence suggests that primary PCI provides better outcomes for this patient group[269–274] provided that it can be delivered quickly, though logistic considerations mean that primary PCI is not always available within an appro-

priate time-frame (120 minutes from the first contact of the patient with medical services)[267]. Whichever method of re-perfusion is employed, the shorter the time to the commencement of therapy the better, as minimising delay has been shown to improve outcomes[267]. Where available, primary PCI is the preferred treatment option.

A number of pharmacological agents are available that influence clotting – anti-thrombotic medications – and these may be used to reduce the progression and severity of ACS; they include anti-platelet drugs (aspirin, clopidogrel, and glycoprotein IIb/IIIa inhibitors such as tirofiban, eptifibatide and abciximab), heparins (unfractionated heparin, low molecular weight heparin, and synthetic pentasaccharides such as fondaparinux), and direct thrombin inhibitors (for example bivalirudin). These bring with them an inherent increased risk of bleeding. They play a role at different stages in the management of STEMI and other ACSs.

Beyond intitial management with aspirin, patients with STEMI should be offered clopidogrel 300 mg, continued at the standard dose[267]. Patients undergoing primary PCI should receive adjunct bivalirudin in addition to aspirin and clopidogrel[257]. Patient undergoing fibrinolysis in situations where primary PCI cannot be performed within 120 minutes of first medical contact, normally receive antithrombin therapy, the choice of which depends on the fibrinolysis agent employed, as an adjunct[267]. It is recommended the fibrinolysis itself be with fibrin-specific agents (tenecteplase, alteplase, reteplase), rather than with streptokinase[267].

In the absence of ST-elevation on ECG, while waiting for biochemical evidence of myocardial damage from troponin levels, NSTEMI and unstable angina are managed according to a common pathway that differs from that employed in STEMI[206]. The principle of management in cases of NSTEMI and unstable angina is to balance the risk of serious cardiac events against the risk of life-threatening bleeding associated with anti-thrombotic medications, and to provide drugs to reduce thrombus formation on the basis of this assessment.

All patients with NSTEMI and unstable angina should remain on regular aspirin once they have received their 300 mg initial dose[206]. If they are not at high risk of bleeding and no angiography is planned in the next 24 hours they should receive antithrombin therapy with fondparinux; otherwise, unfractionated heparin should be used, with dose adjusted to clotting function as appropriate[206].

A risk assessment tool (based on clinical assessment, ECG and blood tests – for example the GRACE score) can be used to estimate 6-month mortality for patients with NSTEMI or unstable angina[206]. Likewise bleeding risk can be estimated (based on age, known bleeding complications, renal function, and body-weight). These estimates guide management[206]. Those at low risk (with predicted 6-month mortality less than 1.5%) receive less aggressive treatment; where this estimate is 1.5% or more clinicians should offer clopidogrel 300mg and should continue clopidogrel for 12 months)[206]. In those with predicted 6-month mortality greater than 3%, adding a glycoprotein IIb/IIIa inhibitor may add additional benefit, depending on the balance of mortality and bleeding risks[206].

Beyond the provision of such drugs, angiography with the possibility of follow-on PCI should be offered to patients with a predicted 6-month mortality greater than 6% and also to patients at lower risk with positive ischaemic testing[206], within 96 hours of first admission. Abciximab may be used as an adjunct to PCI in patients not already on a glycoprotein IIb/IIIa inhibitor[206]; patients on fondaparinux undergoing PCI should be offered unfractionated heparin[206]; bivalirudin should be offered to those with a predicted mortality greater than 3% who are not already on fondaparunix or a glycoprotein IIb/IIIa inhibitor[206].

Following the acute phase, having taken into consideration angiographic findings, a multidisiplinary team with expert input should consider patients for revascularisation, either with PCI or CABG[206]. Further considerations arise with regard to the following[206,254].

- Assessment of left ventricular function
- Cardiac rehabilitation
- Lifestyle changes
- Management of CVD risk factors for secondary prevention

Cardiac rehabilation offered in the wake of ACS involves the provision of advice, psychological and social support, and health education to patients in the period following the acute event[254]; this should include an exercise component to support patients in achieving an appropriate physical activity level[254]. Lifestyle changes that patients should be encouraged to make, and which evidence suggests can reduce risk of subsequent events and improve outcomes (secondary prevention), for the most part overlap with those recommended

for primary prevention. Measures include smoking cessation, weight management, physical activity, controlling alcohol consumption, and dietary changes[254].

NICE guidance[275] suggests that properly trained individuals should provide tailored advice, counselling and support to those who smoke (particularly targeted at those from minority ethnic groups and from deprived communities). Moreover, the guidance suggests that such groups should be treated at least in proportion to their number of smokers compared to the general population. Smoking cessation treatments and advice provided on the NHS should employ methods that have been rigourously evaluated[275] and shown to be effective. Such interventions include so-called brief interventions[276] (opportunistic discussions, negotiation, encouragement and potentially referral to more intensive NHS Stop Smoking services, possibly in combination with pharmacotherapy), individual behaviour counselling, group behaviour counselling, self-help materials, and pharmacotherapy.[275] Principles and techniques of smoking cessation are common to primary and secondary prevention.

Beyond efforts to modify lifestyle, a number of drug treatments are recommended for secondary prevention:

1. ACE inhibitor
2. aspirin (with clopidogrel continued if it was started in the acute phase)
3. beta-blocker
4. statin

For some individuals with contraindications or in those unable to tolerate the above medications, alternative regimes may be employed[254]. In addition, hypertension should be managed to below target levels where blood pressure is raised[254].

Notwithstanding the availability of advanced pharmacological and technical options to improve outcomes in those with established CHD, many emphasise the continued need to implement preventive strategies for the disease – an area which I now address.

B.2.5.1 *Primary prevention*

In the context of CHD, primary prevention means preventing disease arising in the first place. Individuals for whom primary prevention is

relevant may have subclinical vascular pathology, in which a process or atheroma development is occuring in the coronary (or other) arteries, but they do not, by definition, have overt clinical disease; rather, the aim of primary prevention is to avoid or delay the onset of any such symptomatic pathology. This can be achieved by modification of an individual's risk factors for disease development, which in terms of the pathophysiology of CHD, outlined in section B.2.1, corresponds to reducing atheroma progression, averting plaque rupture and avoiding thrombus formation. In terms of practical risk reduction, this entails mitigating the CHD-risk associated with a number of lifestyle factors – smoking, poor diet, lack of exercise, binge drinking – as well as with a number of physiological states to which lifestyle factors, to a greater or lesser extent, predispose an individual, namely high blood pressure (hypertension), adverse lipid profiles, diabetes, chronic renal disease and obesity.

CHD shares many of these lifestyle and physiological risk factors with a number of other CVDs, and thus primary prevention of CHD can have a more generalised effect in preventing all forms of CVD. The major CVDs are cerebrovascular disease (ischaemic stoke and transient ischaemic attack), peripheral artery disease (PAD), renovascular disease and aortic atherosclerosis. CHD is also linked to heart failure, because hypertension and CHD itself predispose to its development.

In seeking to prevent CVD, two broad categories of interventions are available: structural (or population-level) interventions and agentic (or individual-level) interventions[101]. The former seek to modify risk in whole populations, principally by addressing behavioural risk factors. Examples include efforts to improve the population diet (reducing salt, saturated fat and trans fats), to increase population physical activity and to reduce smoking rates[248]; approaches to achieving this would typically include some combination of legislation, regulation, fiscal policy, and taxation. The individual-level approach seeks to reduce risk in defined individuals (usually those at higher risk of disease development); examples include weight-loss, smoking-cessation, and dietary interventions which can be offered to individuals, as well as interventions to manage an individual's physiological risk factors, such as hypertension, adverse lipid profiles, and blood glucose.

The availability of these two categories of intervention presents options about the strategic approach to take to implementation. Either a whole-population or a high-risk approach to primary prevention might be emphasised[213]. Structural interventions are by their nature

more or less limited to whole-population approaches to disease prevention. Agentic interventions are typically targeted at a subset of the population; it is feasible that they might be used for the whole population, but this is normally undesirable due to the balance of risks for some people in the population (for example potential adverse effects from medications in low-risk individuals) or impractical due to resource constraints (for example in delivering health improvement programmes to everyone).

Detailed consideration was first given to these issues by Geoffrey Rose in a seminal 1981 paper[277] and in subsequent work[278]. Importantly, Rose noted that the number of cases of disease resulting from a risk factor depends on the product of the excess risk that an individual with the risk factor has and the prevalence of that risk factor in the population[277]. From this it follows that achieving substantial risk reductions in high-risk groups may prevent fewer cases of disease overall than achieving small reductions in risk in the population as a whole. The former situation involves a large risk reduction multiplied by a small population, contrasted with the latter situation where a small risk reduction is multiplied by a large population. Moreover, these considerations give rise to what Rose termed the 'prevention paradox' whereby 'a measure that brings large benefits to the community offers little to each participating individual'[277], because many individuals at moderate or low risk might undergo a preventive intervention when in fact they were not going to develop the disease anyway. Furthermore, this highlights the extreme importance of the long-term safety of any interventions that are used for population-level prevention, as only a small proportion of the group of individuals to which such interventions are given would subsequently have become cases[277]. Some commentators have posited that in the time since Rose wrote on this subject a number of factors, including better risk prediction and using baseline risk rather than individual risk factors, has changed the situation in favour of high-risk strategies[279,280], though this view is not universally held[281].

In practice, prevention involves the combination of a population strategy, using population-level interventions, and a high-risk strategy, which uses individual-level preventive interventions. As Rose commented

> "...the conclusion will be that preventive medicine must embrace both [population and high-risk approaches], but, of the two, power resides with the population strategy"[278, p 49].

Structural interventions such as banning of tobacco advertising, bans on smoking in public place, escalation of tobacco taxation and changes to food labeling have been employed by UK and devolved governments of the UK in recent decades, though government commitment to systematic implementation of such interventions is variable, with many recommendations in the NICE guideline on prevention of CVD in populations unaddressed[248]. Individual-level interventions have become increasingly sophisticated with, for example, the emergence of new classes of drugs to treat hypertension and raised cholesterol, new antiplatelet agents, and the systemisation of the provision of individual-level behaviour change interventions. All these developments have been underpinned by numerous clinical trials, review articles, risk models, clinical guidelines and clinical standards of care, which mean that clinicians can now offer a number of evidence-based, preventive interventions to high-risk individuals. Governments at both the UK- and Wales-level have recently begun to systematise strategy for prevention in high-risk individuals with the announcement of programmes for primary prevention[282,283].

The focus of this thesis is the quantification of differences between social groups that arise from *agentic* or *individual-level* approaches – but, in the light of Rose's observations, such interventions ignore the low and moderate risk cases; because of the prevention paradox it is certain that a bulk of social differences in prevention of CHD between social groups must arise from the different distributions of risk factors within populations. While I acknowledge this important propensity from the outset (that is to say the phenomenon whereby effective population prevention requires a mass, rather than high-risk, approach), differences in mortality between socio-economic groups arising from systematic differences in the utilisation of agentic interventions might contribute to the development of some of the disparity seen. Moreover, I address in this thesis not just preventive approaches, but include also other components of management, as outlined below, which may contribute additionally to mortality differences. Thus, it is clear that the approach taken in this thesis cannot lead to the identification of the reasons for all of the disparity seen between socio-economic groups, but it may explain some of it. Furthermore, any such disparity identified, based as it is on differences in utilisation of agentic interventions, might be amenable to amelioration by a quite different set of strategies and policy approaches as compared to disparities arising from population risk factor distributions.

The focus of recent primary-prevention strategies at the individual level is in identifying individuals at a high risk – defined typically as a the risk of a disease event above a particular threshold, for example 20% risk of a cardiovascular event in the next 10 years – and offering those individuals interventions to mitigate that risk. For the high-risk subpopulation it has the potential to prevent disease onset, but such an approach is heavily dependent on the capacity to identify correctly those individuals that are at high risk; with a view to achieving this a number of risk models have been developed over recent decades.

Multivariate risk functions derived from cohort studies and randomised control trials underlie the development of such risk prediction functions and scores[284]. In principle, development of risk equations involves following over time groups of individuals on whom data are available on known and putative cardiovascular risk factors; during the follow-up period cardiovascular outcomes are recorded; these data then inform multivariate regression analyses, which produce the required risk equations (which contain coefficients for each of the risk factors found to be significant in predicting outcome and which allow calculation of a risk score). The extent to which such risk models are able to correctly predict cardiovascular outcomes is important; overestimating an individual's risk raises the possibility that they will be overtreated with the risk of adverse consequences without the concurrent benefit to justify such risk; underestimating individual risk can mean that individuals with a capacity to benefit from treatment miss out.

It is feasible that future developments, or even the systematic application of currently available technologies, might provide improved capacity to predict cardiovascular risk, for example by the use of imaging technologies to identify subclinical atheroma or by the use of more sophisticated biomarkers. Neither current UK practice nor UK guidelines advocate such approaches[260]. For the time being at least, designation of an individual as being at high risk is accomplished on the basis of the more traditional approach of using risk scores based on important known risk factors for CVD.

While each of the available risk scores is based on the same principles, the estimates that they produce vary[285]. A very large number of these tools are available to clinicians, with a NICE review of such tools from 2008 finding as many as 110 available[260]. The best known of such tools are the risk equations based on the Framingham cohort study. The first risk equations based on the study were published in 1976,

with further versions published in 1991, 1998 and 2008. Other risk scores include the QRISK 2 score, the European SCORE, and ASSIGN. The important characteristics of the major risk scores are summarised in table B.1; data in this table and in figure B.3 are taken from the 2011 paper by Liew et al[2]. The exact outcome events aand the time period over which these events occur vary between risk models.

Beyond the inherent limitation of a high-risk strategy articulated by Geoffrey Rose (namely its inability to prevent as many cases as a mass approach), other issues arise. Concerns have been raised over the capability of risk scores to predict accurately[284], and over the possibility that, though a risk score may be applicable in one population, it may perform poorly in another[286]. It is not clear the adequate comparison of different models in different populations has been carried out using appropriate methods[286]. A related concern with many of the risk scores available (particularly those based on more recent cohorts) is that they may not have taken adequate account of those beginning preventive treatment in the follow-up period, thus biasing the studies towards underestimating cardiovascular risk[2]. Furthermore, it has been argued that risk scores are unnecessary, because the use of age alone (because it is such a strong risk factor) provides sufficient information about risk[287]. Finally, even assuming an effective tool, it is not clear that clinicians are comfortable with using risk scores in practice; possibly due to difficulties using them or a perceived infringement of clinical autonomy[288]. While such concerns exist about the use of specific risk scores and about the wisdom of using risk scores at all, current UK guidelines advocate their use in clinical practice (though they do not specify a particular score)[260].

Potential problems related to risk scoring methods link to the wider problems with the high-risk approach to primary prevention of CVD. Although components of a high-risk prevention strategy have been subject to randomised trials (for example statins and antihypertensive medications), the overall effect of a high-risk strategy has not[289,290]. Even if a positive effect is assumed, it is not clear that the approach would be more cost effective than the equivalent expenditure on structural interventions. High-risk approaches offer 'treatments' to individuals to modify disease risk; but this brings with it the possibility of treatment failure, limited adherence to treatment, and medicalisation of healthy individuals (and depending on the nature of measures adopted, this may apply to large segments of the older population)[289]. At lower thresholds for treatment, more individuals need to be treated

to prevent a case of disease, but for these individuals there is no equivalent reduction in the risk of adverse effect; it is therefore difficult to be sure of an appropriate threshold for treatment[291]. Critics also point to the residual risk with which individuals are left – as the available preventive treatments do not eliminate risk, citing such treatments as simply 'sticking plasters' that do not address the underlying cause of the disease[291,292]. A further cause for concern is the possibility that a high-risk strategy using an agentic approach to prevention might distract from the potential merits of a structural approach that, for the reasons outlined by Rose, might have the capacity to substantially reduce disease[101,213,281,293]. Finally, and importantly for this thesis, a high-risk approach with its inherent emphasis on agentic intervention might *widen* rather than reduce socio-economic inequalities in CHD and CVD more generally[101,291,294]. Critics of a high-risk approach cite the operation of the inverse care law as evidence that more deprived individuals with reduced resource are less able to exploit the opportunities presented by agentic interventions[291,292,294].

Table B.1: Summary of risk models. All models have age, gender (where applicable), smoking and systolic blood pressure as predictors in addition to those shown in the table. Data are from Liew 2011[2]; The risk models are shown in order of the start of the time period during which they collected data

Study	Age group	Predictors	Event predicted
Framingham 1976[295]	35–64	Serum total cholesterol, blood/urine glucose, LVH on ECG	CVD events (death from CVD, MI, ischaemic stroke, angina, PAD, hypertensive congestive cardiac failure (CCF))
SCORE 2003[296]	45–64	Total cholesterol or ratio	Fatal CVD events
Framingham 1991[297]	30–74	Serum total cholesterol, blood glucose, LVH on ECG	CHD (death from CHD, MI, angina)
Framingham 1998[298]	30–74	Serum total cholesterol or LDL, blood glucose	CHD (death from CHD, MI, angina)
Framingham 2008[299]	30–74	Total cholesterol (or BMI in the non-lab score), antiplatelet medication	CVD events (CHD death, MI, ischaemic stroke, haemorrhagic stroke, TIA, angina, PAD, hypertensive CCF)
NHEFS 2008[300]	25–74	Diabetes, BMI	CVD events (CHD death, MI, ischaemic stroke, haemorrhagic stroke, revascularisation, hypertensive CCF)
PROCAM 2007[301]	20–75	LDL, fasting glucose, family history	CHD (death from CHD, MI)
PROCAM 2002[302]	35–65	LDL, fasting glucose, family history	CHD (death from CHD, MI)

Continued on next page

Table B.1 – *Continued from previous page*

Study	Age group	Predictors	Event predicted
Progetto CUORE 2004[303]	35–69	Total cholesterol, fasting blood glucose, antiplatelet	CVD events (death from CHD, MI, ischaemic stroke, haemorrhagic stroke, revascularisation)
USA-PRC 2006[304]	39–59	Total cholesterol, fasting glucose, BMI	CVD events (death from CHD, MI, ischaemic stroke)
ASSIGN 2007[305]	30–74	Total cholesterol, diabetes, family history, socio-economic deprivation	CVD events (death from CHD, MI, ischaemic stroke, haemorrhagic stroke, TIA, angina, revascularisation, hypertensive CCF
ARIC 2003[306]	45–64	Total cholesterol, fasting glucose, antiplatelet medication, ethinicity	CHD (death from CHD, MI)
Personal HEART 2007[307]	45–64	Hypercholesterolaemia, diabetes, family history (men), physical activity (men), BMI (women)	CHD (death from CHD, MI, revascularisation)
SHS 2006[308]	45–74	Total cholesterol or LDL, fasting glucose, antiplatelet medication, albuminuria	CHD (death from CHD, MI, angina, revascularisation)
Reynolds women 2007[309]	45+	Total cholesterol, family history, high-sensitivity C-reactive protein (hsCRP), HBA_{1c} in diabetics	CVD events (death from CHD, MI, ischaemic stroke, revascularisation)

Continued on next page

Table B.1 – *Continued from previous page*

Study	Age group	Predictors	Event predicted
QRISK 2 2008[182]	35–74	Total cholesterol/HDL ratio, antiplatelet, BMI, ethnicity, family history, Townsend deprivation, rheumatoid arthritis, chronic renal disease, atrial fibrillation	CVD events (CHD death, MI, ischaemic stroke, TIA, angina)
Reynolds men 2008[90]	50–80	Total cholesterol, family history, hsCRP; diabetics exluded at baseline	CVD events (death from CHD, MI, ischaemic stroke, haemorrhagic stroke, revascularisation)
QRISK 2007[310]	35–74	Total cholesterol/HDL ratio, antiplatelet, BMI, family history, Townsend deprivation. Diabetics excluded at baseline	CVD events (CHD death, MI, ischaemic stroke, haemorrhagic stroke, TIA, angina

Notwithstanding the issues and debates around approaches to primary prevention in high-risk individuals, current guidelines make a number of recommendations[183,260].

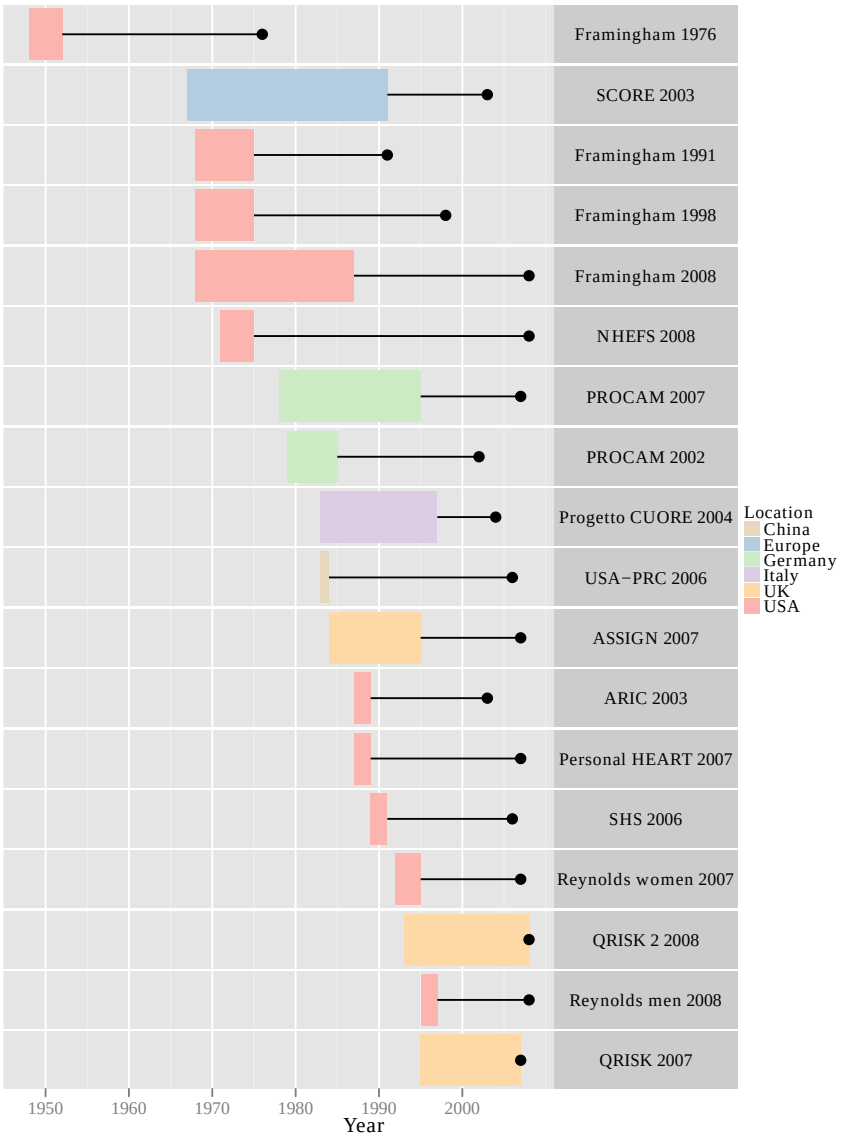
- A systematic strategy should be implemented with a view to identifying individuals in the 40–74 age range who are likely to be at high risk of CVD
- Risk equations should be used (where available) to carry out formal CVD risk assessments in such individuals, with a 20% or greater 10-year risk of CVD used as a threshold
- The balance of benefits and risks should be clearly explained to individuals
- In high-risk individuals, identified by formal risk assessment, modifiable CVD risk factors should be addressed by encouragement of lifestyle changes (cardioprotective diet, physical activity, weight management, reduction of alcohol consumption, smoking cessation) and referral to specialist services where appropriate
- Additionally such individuals should, where appropriate, be offered antihypertensives, lipid-lowering therapy, have their blood sugars managed, and their obesity addressed

When providing lipid-lowering therapy for primary prevention, simvastatin 40mg is the recommended dose; there is no target level for cholesterol. Other lipid-lowering agents can be considered in those who do not tolerate statins[260].

Individuals with a CVD risk greater than 20% should be offered antihypertensive therapy if they have either stage 1 or stage 2 hypertension[183]. It is now recommended that suspected hypertension (blood pressure reading greater than 140/90 mmHg) is confirmed by ambulatory blood pressure monitoring or home blood pressure monitoring[183]. Using these tests, the cut-offs used are slightly different, with a blood pressure greater than 135/85 mmHg indicating stage 1 hypertension; greater than 150/95 mmHg indicates stage 2 hypertension. A staged approach to treatment is recommended, with progression through stages based on response to therapy – the minimum number of medications requred to control blood pressure being employed[183].

1. In those aged under 55 offer a ACE inhibitor or, if this is not tolerated, an ARB (or beta-blocker as last resort); those over 55 or of afro-Caribbean ethnicity should be offered a CCB, or, if this is not tolerated, a thiazide-like diuretic (chlortalidon, indapamide)

Figure B.3: Risk models over time. Coloured rectanges indicate the period of recruitment; black lines show the period to publication; black points show publication year; rectangles are coloured by location. Studies are ordered by the start date of data collection



Source: adapted from safe Liew 2011 [2]

2. Progress to treatment with a CCB together with an ACE or ARB.
3. Add thiazide-like diuretic
4. Consider adding a fourth drug (spironolactone, beta blocker, alpha blocker), higher doses of a thiazide-like diuretic or obtaining specialist advice

The target for therapy is a blood pressure of 140/90 mmHg (using standard blood pressure readings) or lower in those aged under 80 years, and of 150/90 mmHg (using standard blood pressure readings) in those aged 80 and over[183].

Much attention has been paid in the preceding sections to the content of clinical guidelines that pertain to CHD. I feel that such an approach was necessary because, though guidelines are not universally applicable and are not universally agreed with, they are, for the purposes of this thesis, useful, in that they provide a coherent view of the standard of care that an individual might expect. Moreover, NICE guidelines outline the standard of care that an individual might expect to be offered from the NHS, regardless of their personal characteristics; such characteristics include an individual's socio-economic status and the level of deprivation of the area in which an individual lives; I discuss these issues next.

B.2.6 *Organisation of cardiac services in Wales*

Political responsibility for the control of cardiac services in Wales operates through the WAG. In 2001, it published NSF-2001, which set out the standard of cardiac care that should be provided for the Welsh population.[163] Subsequently this document has been updated with a revision that also includes non-CHD cardiac disease: NSF-2009.[163] Broadly, these documents set out the expectation that organisations responsible for the delivery of cardiac services should prepare a local plan to develop and deliver effective care, aiming to address issues throughout the 'patient journey' and that they should ensure that best practice is identified and transferred throughout the system.[164] To aid with the delivery of the NSFs, WAG set up three cardiac networks within Wales (North Wales; Mid and South West Wales; South East Wales), overseen by a Cardiac Networks Coordinating Group.[164]

The delivery of care for CHD for the population of Wales is undertaken by a number of different organisations, according to the type of care provided. Primary care is delivered by GPs in practices across

Wales, and for some patients living close to the border by practices in England. Such care involves the management of risk factors for CVD, the management of stable disease, and referral of complex cases to secondary care. Secondary care for CHD involves the management of complex cases in outpatient departments of District General Hospitals (or higher-level centres) as well as inpatient treatment of cases – particularly ACSs. Hospitals involved in the provision of secondary care for Welsh patients are located across Wales and in areas of England close to the Welsh border.

Only certain centres have the capacity to provide specialist cardiac services for Welsh patients. Diagnostic angiography for Welsh patients has been provided at eight Welsh centres: Ysbyty Glan Clwyd (YGC), Prince Charles Hospital, Royal Gwent Hospital (RGH), Nevil Hall Hospital, University Hospital of Wales (UHW), Royal Glamorgan Hospital, Morriston Hospital (MH), and the Princess of Wales Hospital. Two English centres across the border also provide the service: Liverpool Heart and Chest Hospital (LHCH), Countess of Chester Hospital.[165] PCI has traditionally been provided at three main centres in Wales (MH, UHW, YGC) as well as at LHCH in England; from June 2011 RGH has also begun providing the procedure.[165] Cardiac surgery for Welsh patients, including CABG, is carried out at three principal centres: MH, UHW, and LHCH.[165]

On the basis of original NSFs, target population rates for major procedures for the treatment of CHD have been set out.[166–168] It is notable that as of the financial year 2010/11, rates of PCI (1112 per million population) were lower than rates in England (1401 per million population), but higher than the recommended rates set out in the original NSF (750 per million population).[165] For primary PCI, the rate of 111 per million population in Wales was substantially lower than the rate in England (302 per million population).[165] For CABG, the overall rate was 270 per million population for Wales, lower than the target rate of 754 million population set out in the original NSF.[165]

B.3 ADDITIONAL BACKGROUND MATERIAL RELATING TO THESIS METHODS

B.3.1 *Clinical coding*

For the purposes of this thesis, three clinical coding systems are relevant:

1. ICD-10 – used in PEDW records to code diagnoses and mortality records to code cause of death
2. OPCS-4 – used in PEDW records to code procedures
3. Read codes – used in GP records to code all primary-care activity

B.3.1.1 *ICD-10*

ICD-10 is the 10th revision of the International Statistical Classification of Diseases and Related Health Problems. It is a medical classification system developed by the WHO.[311] The 10th revision was developed between 1983 and 1992, building on earlier versions of the classification.[311,312] The original function served by the International Statistical Classification of Diseases and Related Health Problems (ICD) was in classifying causes of death at registration.[312] It is now the international standard diagnostic classification for general epidemiological and many health-management purposes.[311,312] As well as classification of diseases, ICD can be used to classify signs, symptoms, abnormal findings, complaints, and social circumstances.[311,312]

ICD-10 can be used either at a three- or four-digit level, with three-digit codes providing the core classification, mandatory for reporting to the WHO mortality database, and four-digit codes allowing more detailed specification where required.[311,312] The classification itself is divided into 21 chapters.[311,312] The first character in each code is a letter associated with a chapter (except for letters 'D' and 'H', which are associated with more than one chapter).[311,312] Thus, chapter IX, entitled 'Diseases of the circulatory system', contains codes beginning with the letter 'I'.[311,312] Each of the chapters in the classification contains sufficient three-digit codes to cover all its content.[311,312] Not all available codes are used, to allow space for addition and revision.[311,312] Chapters themselves are divided into blocks of homogenous three-character subcategories.[312] For most of these three-character blocks, an additional, fourth numeric-character can be used to create up to 10 subcategories for that block.[312] The ICD-10 codes relevant to this thesis are shown in appendix E.

B.3.1.2 *OPCS-4*

Coding of procedures in PEDW is carried out using the OPCS-4 coding system. This is a procedural coding system for classifying operations, procedures, and interventions.[313] The original classification was developed by the Office of Population Censuses and Surveys in 1992.[313]

Since that time there have been a number of revisions; current responsibility for maintaining and revising the classification lies with NHS Connecting for Health.[313]

The coding system for OPCS-4 uses a four-character alphanumeric system, similar to that employed by the ICD-10.[313] Codes are composed of a letter and three numeric characters.[313] Codes in the OPCS-4 are divided into chapters as with ICD-10, though the chapters in the two systems do not correspond.[313] The OPCS-4 codes relevant to this thesis are shown in appendix E.

B.3.1.3 *Read codes*

Read codes are the standard clinical terminology used in primary care in the UK to encode primary-care activity.[314,315] Multiple patient phenomena can be captured using the system, including patient characteristics, signs, symptoms, observations, laboratory tests and results, diagnoses, procedures, and administrative items.[315] The first version of the Read code system was developed by a Loughborough GP, Dr James Read. Two further versions of the Read code system have subsequently been developed, version 2 and version 3.[314,315]

The vast majority of primary care data used for this thesis were coded using Read code version 2.[314,315] This version was released in the early 1990s. It uses an alphanumeric code with five digits.[314,315] The TRUD maintains the Read code version 2 classification system, as well as providing NHS Data Migration datasets, which allow the conversion of version 2 Read codes into version 3 Read codes and SNOMED CT codes (which was necessary in this thesis – see chapter 4).[316] Recent releases of Read codes version 2 contain in excess of 80,000 codes.[316] A co-publication with Read codes version 2 is the drug and appliance dictionary, which contains in excess of 50,000 codes relating to medications and medical devices, organised along the same lines as Read codes version 2. This additional set of codes is used to record the use of medications and medical devices in primary care.

C

LITERATURE REVIEW TABLES

On the following pages, we include tables relevant to the literature review presented in a chapter 3. The format of the tables that follow is equivalent to that used in table 3.1. We include these tables here with a view to providing necessary supporting detail for chapter 3 while at the same time seeking to avoid overloading the reader with information.

Table C.1: Summary of papers examining inequity of provision of antihypertensives for primary prevention

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Pears 2003[108]; Scotland, 1998	Carstairs and Morris Index of deprivation 1991	Cross-sectional study using GP administrative data. 19,352 patients with hypertension-related Read code could be assigned deprivation category. Outcome was 'under-review', 'treated' or 'not-followed-up'. Multiple logistic regression	Patients from deprived areas less likely to be under review, adjusted odds ratio 0.7 (95% CIs 0.7, 0.8), compared to least deprived patients. Odds ratios adjusted for sex age, and comorbidities for most deprived compared to least deprived (reference group): thiazide diuretics 0.7 (95% CIs 0.7, 0.8); ACE inhibitors 1.2 (95% CIs 1.0, 1.3); calcium-channel blockers 1.3 (95% CIs 1.2, 1.4)	The odds of being on *any* treatment for hypertension are not available from the study. More deprived hypertension patients are less likely to be on thiazide diuretics, as likely to be on beta-blockers, and more likely to be on ACE inhibitors and calcium-channel blockers compared to the least deprived patients
Edwards 2003[111]; Salford, UK, 1993-4 and 2000-1	Townsend deprivation 1991	Data from Diabetes Information System used to analyse individuals for attainments of targets for diabetes treatment at two time-points.	In 1993-4, 30.5% in the least deprived quintile met SBP target; compared to 31.1% in the most deprived quintile ; p-value for trend across fifths 0.862. In 2000-1, 47.1% (least deprived); 46.5% (most) met SBP target; p-value for trend 0.466. In 1993-4, 18.9% (least deprived); 19.8% (most) received anti-hypertensive treatment; p-value for trend 0.810. In 2000-1, 50.5% (least deprived); 51.1% (most) received anti-hypertensives; p-value for trend 0.0071	Diabetic patients only. No evidence of differential achievement of BP targets. No evidence of differencial BP treatment

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Table C.1 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Chen 2003[113]; Scotland, 1986 to 1995	Carstairs and Morris Index of deprivation 1991	Data from the Glasgow MONICA study – cross-sectional surveys. Study examined the difference in proportion of individuals with hypertension identified, treated and controlled. Multivariate logistic regression	Multivariate analysis hypertension control was not significantly related to socio-economic deprivation in this population (p-value 0.238)	No evidence of association between deprivation status and quality of BP control
Bachman 2003[114]; Avon and Somerset, UK, 1998 to 2000	Income	Questionnaire of patients with diabetes. 74% response rate	No significant difference between income groups in the mean SBP. Adjusted slope index of inequality -0.25 (95% CIs -5.1, 4.6)	Diabetic patients only
Ward 2004[109]; Four Primary Care Trusts (PCTs) in North-West England, 1999 and 2000	Age; ethnicity; LISI score (deprivation); Townsend score	Ecological study at practice level. Univariate relationships between LISI score and prescribing rate. Associations examined using Spearman's rank correlations	Townsend score correlation coefficient for ACE inhibitors -0.405 (significant at the 0.01 level) across all PCTs and for bendrofluazide -0.275 (significant at the 0.01 level). Correlation coefficients for beta-blockers not significant	Univariate analysis does not take account of each of the different proxies of need when considering their relationships with prescribing rates

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Table C.1 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Hippisley-Cox 2004[115]; UK, 2004	Townsend 2001	QRESEARCH database. 54180 patients with diabetes. Outcome was adjusted odds ratio for main outcome indicators from general medical services contract. Comparisons between most deprived and least deprived fifths of deprivation	Achievement of blood pressure target (<145/85 mmHg) not statistically different between the two most extreme deprivation groups. Odds ratio (most deprived compared to least deprived) 0.96 (95% CIs 0.90, 1.03)	Diabetic patients only. No systematic difference in achievement of blood pressure target between deprivation categories
Ward 2005[110]; Four PCTs in North-West England, 1999; 2000	Age; ethnicity; LISI score	Ecological: prescribing rates for practices, modelled on a number of proxies for CHD need for practices	Multivariate regression analysis. No association between LISI score ACE inhibitors or between LISI score and beta-blockers. Negative association between LISI score and bendrofluazide prescription rate, implying that increased bendrofluazide prescribing is associated with less deprived practices. Beta coefficient in regression model -0.261; R^2 x 100 = 13.1, suggesting that 13.1% of the prescribing rate for bendrofluazide can be attributed to this relationship	Does not consider need at an individual level; uses a limited list of cardiovascular drugs; not possible to differentiate between primary prevention and secondary prevention in this study

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Table C.1 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
McLean 2006[117]; Scotland, 2005	SIMD 2004 – income domain; Practice-level analysis using average deprivation	Retrospective analysis of GP QOF data. 1024 general practices. Examined relationship between practice deprivation and delivered care. Linear regression	The regression coefficient for control of hypertension was -0.05 (p-value 0.14) for payment quality and -0.08 (p-value 0.01) for delivered quality. For diabetic blood-pressure control the payment quality regression coefficient was 0.31 (p-value <0.001) and the delivered quality regression coefficient was 0.16 (p-value <0.001)	Regression coefficients in this study indicate the change in quality associated with a one-point increase in the percentage of deprived individuals. Payment quality analysis removes individuals who, for various reasons, are excluded from payment calculations. Delivered quality includes these individuals. The regression coefficient suggests a non-significant decline in the management of hypertension generally as deprivation increases; for diabetic patients, management of hypertension improves as deprivation increases
Patel 2006[118]; UK, 1998 to 2001	Social class (manual verses non-manual)	Data from British Women's Heart and Health Study and the British Regional Heart Study. Cross-setional analysis. Multiple logistic regression	Social class is not associated with a difference in the quality of blood pressure control in multivariate analysis, odd ratio manual vs non-manual 1.19 (95% CIs 0.94, 1.50)	Suggests manual group may have better blood pressure control, though not statistically significant.

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Table C.1 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Gray 2006[116]; Wandsworth, London, 2003	IMD	Population-based cross-sectional survey using electronic GP records. Examined success rate for diabetes quality indicators. Logistic regression. n=6035	Patients in the most deprived groups were less likely to meet the target for blood pressure, but this result did not reach statistical significance – odds ratio of achieving target least deprived compared to most deprived (1.18 (95% CIs 0.92, 1.52)	Diabetic patients only
Millett, Car et al 2007[119]; England and Scotland, 2004	IMD linked to practices via postcode	Study uses QOF data from England and Scotland. Practice-level data. Studies the effect, at practice-level, of deprivation on achievement scores	In the most deprived group of practices 69.5% of patients met BP control targets; in the intermediate practices 72.2% and in the least deprived practices 71.4% of patients met targets. No CIs presented	This study only considers diabetic patients. Ecological study using QOF data
Saxena 2007[104]; UK, 2004, 2005	IMD 2004. Grouped into three bands	Ecological study using QOF data. Large number of GP practices in the UK. Examination of practice performance in relation to a number of practice characteristics, including practice size, deprivation	Some indication of a gradient of increased proportion of hypertensive patients meeting target blood pressure with decreased deprivation. Groups statistically different using Kruskal Wallis exact test p-value <0.0001	Ecological data

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Table C.1 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
McGovern 2008[120]; Scotland, UK, 2004, 2005	Carstairs and Morris Index of deprivation 1991	Study of a number of quality indicators of diabetic care in diabetic patients. Logistic regression with covariates gender, age, diabetes co-morbidities and deprivation category	In the logistic regression, deprivation was not a significant covariate for blood pressure control in 2004, with adjusted odds ratio 1.10 (95% CIs 0.94, 1.30), or 2005, with adjusted odds ratio 1.13 (95% CIs 0.98, 1.31)	Multiple comparisons were made; in most comparisons deprivation was not a statistically significant covariate. This study looks only at diabetic patients
Ashworth 2008[121]; England, 2005 to 2007	IMD	Retrospective longitudinal survey. Deprivation analysed at practice level. Practice-level analysis. Relationship between deprivation and six QOF indicators related to blood pressure.	In those with hypertension, the gap between the least and most deprived in the proportion with blood pressure controlled narrowed over the study period. In 2004-5, 72.4 (95% CIs 71.9, 72.9) in the least deprived group met control targets compared to 69.1 (95% CIs 68.6, 69.6); in 2006-7, the percentages were for least deprived 78.0 (95% CIs 75.5, 76.3) and for the most deprived 77.4 (95% CIs 77.1, 77.7)	This study suggest that there may be a narrowing in the disparity in control of blood pressure and those with hypertension over the study period. Practice-level analysis

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Table C.1 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Hamilton 2010; UK, 1997 and 2005	IMD 2004	Patients with type 1 or type 2 diabetes. Study looked at achievement of HbA_{1C} <7.0%, blood pressure <140/80 mmHg, and total cholesterol (<5 mmol/L)	In 1997, adjusted odd ratio (for age and sex) for achievement of BP target (most versus least deprved quintile) was 1.03 (95% CIs 1.01, 1.05). Fourth most deprived quintile versus least deprived quintile 1.04 (95% CIs 1.02, 1.06). Other quintile comparisons not significant. By 2005 the adjusted odds ratio (most versus least) was 1.03 (95% CIs 0.99, 1.06). Other quintile comparisons not statistically significant	Diabetic patients only. Some suggestion that more deprived patients are more likely to achieve BP target
Hammouche 2011[123]; 18 general practices in Norfolk, UK, 2003 and 2005	IMD	Individual level data extracted from general practice records. 304 patients. Achievement of quality for indications by deprivation assessed in univariate and multivariate analysis	The achievement of quality indicators for hypertension either did not vary with geographic deprivation, or was higher in patients from more deprived localities.	Individual level data. Small numbers.

Table C.2: Summary of papers examining inequity of provision of lipid-lowering medications for primary prevention

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Bradshaw 1998[124]; Gwent, Wales, 1997	Townsend 1991	Ward-level analysis. Correlation coefficient for ward-level deprivation and statin-prescribing rate.	No association at ward-level between the rate of statin prescribing and the Townsend deprivation quintile (r = -0.15; p-value = 0.09)	The papers argues that patients in areas of greater deprivation are likely to have greater need for statins; the absence of a correlation might represent evidence of inequity of provision of statins
Packham 1999[125]; Nottingham, UK, 1996	Townsend 1991; Jarman 'Under-privileged Area Score'	Statin prescribing in relation to deprivation in general practices. Ecological analysis at practice level	There was a statistically significant inverse relationship between the rate of statin prescribing and deprivation score, with p-value <0.0001	This study does not directly take account of the level of need for lipid-lowering medications in the different practices examined, but assumes that there will be a higher level of need in more deprived areas, which, in an equitable situation, ought to be reflected in higher prescribing rates
Packham 2000[126]; Nottingham, UK, 1996 to 1998	Townsend 1991	Analysis of general practice data looking for practice-level relationships between statin-prescribing and practice-level deprivation. Multiple linear regression adjusting for other practice characteristics	In each year practices in the most deprived areas had lower rates of statin prescribing. In 1996 this relationship was statistically significant (p-value <0.0005. In 1997 and 1998, proportionately larger increases in the more deprived practices meant that no significant relationship existed between deprivation and practice prescribing	Initial relationship between deprivation and statin-prescribing is not statistically significant after 1996

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Table C.2 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Edwards 2003[111]; Salford, UK, 1993-4 and 2000-1	Townsend deprivation 1991	Data from Diabetes Information System used to analyse individuals for attainments of targets for diabetes treatment at two time-points.	No evidence of significant trend across deprivation fifths in treatment with lipid-lowering medication or in achievement of cholesterol targets in either 1993-4 or 2000-1	Diabetic patients only. No indication of systematic difference based on deprivation
Bachman 2003[114]; Avon and Somerset, UK, 1998 to 2000	Income	Questionnaire of patients with diabetes. 74% response rate	Results for this paper seem inconsistent. The adjusted slope index of inequality (derived from the linear regression line) is 0.6 (95% CIs 0.2, 0.9), with a P-value of 0.39	Diabetic patients only
Ward 2004[109]; Four PCTs in North-West England, 1999 and 2000	Age; ethnicity; LISI score (deprivation); Townsend score	Ecological study at practice level. Univariate relationships between LISI score and prescribing rate. Associations examined using Spearman's rank correlations	The Spearman's rank correlation coefficient for the association between prescribing rates for statins and the Townsend score was -0.237, which was statistically significant at the 0.01 level. When the LISI score was used instead of Townsend, the correlation coefficient was -0.326, and was statistically significant at the 0.01 level.	The findings suggest that as deprivation increases the prescribing rate for statins decreases. Methodological limitations of this study, including the ecological nature, and the failure to correct for important covariates limit the weight that can be given to this finding

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Table C.2 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Hippisley-Cox 2004[115]; UK, 2004	Townsend 2001	QRESEARCH database. 54180 patients with diabetes. Outcome was adjusted odds ratio for main outcome indicators from general medical services contract. Comparisons between most deprived and least deprived fifths of deprivation	Cholesterol target <5 mmol/L achievement does not differ between deprivation fifths. Odds ratio (most deprived to least deprived) 0.99 (95% CIs 0.92, 1.06)	Diabetic patients only. No suggestion that the achievement of cholesterol target is systematically different between deprivation groups. Statin prescription is not analysed in this study
Ward 2005[110]; Four PCTs in North-West England, 1999; 2000	Age; ethnicity; LISI score	Ecological: prescribing rates for practices, modelled on a number of proxies for CHD need for practices	This study used multivariate regression modelling and examined whether deprivation (represented by LISI score) was a predictor of statin prescribing. Deprivation dropped out of the model as is was not a significant predictor of statin prescribing	No evidence of a relationship between deprivation and statin prescribing. Not possible to separate analysis by primary and secondary prevention. Individual need is not considered.
McLean 2006[117]; Scotland, 2005	SIMD 2004 – income domain; Practice-level analysis using average deprivation	Retrospective analysis of GP QOF data. 1024 general practices. Examined relationship between practice deprivation and delivered care. Linear regression	The regression coefficient for achievement of cholesterol control was -0.13 (p = 0.01) for payment quality; for delivered quality the regression coefficient was -0.12 (p = 0.01)	Regression coefficients in this study indicate the change in quality associated with a one-point increase in the percentage of deprived individuals. Payment quality analysis removes individuals who, for various reasons, are excluded from payment calculations. Delivered quality includes these individuals. Increasing practice-level deprivation is reflected in poorer levels of cholesterol control in those with CHD, both for payment and delivered quality.

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Table C.2 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Gray 2006[116]; Wandsworth, London, 2003	IMD	Population-based cross-sectional survey using electronic GP records. Examined success rate for diabetes quality indicators. Logistic regression. n=6035	No significant difference in achievement of cholesterol target of less than or equal to 5mmol/L, odds ratio least deprived versus most deprived 1.02 (95% CIs 0.81, 1.28)	There is no information in this study on prescribing of cholesterol-lowering medication
Millett, Car et al 2007[119]; England and Scotland, 2004	IMD linked to practices via postcode	Study uses QOF data from England and Scotland. Practice-level data. Studies the effect, at practice-level, of deprivation on achievement scores	In most deprived practices, 69.9% of patients met cholesterol targets; in the intermediate group of practies 72.7%; in the least deprived practices 73.3% of patients met the cholesterol target. CIs not presented.	This is a study using QOF data. Diabetic patients only.
Ashworth 2007[128]; England, 2004-5	IMD	Practice-level analysis of prescribing of statins in general practice, looking at covariates associated with increased prescribing	Statin prescribing was higher in more deprived communities. IMD was statistically significant in predicting statin prescribing, with increased deprivation associated with increased prescribing in univariate and multivariate analysis with p-values <0.001	Ecological study at practice level.

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Table C.2 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Ward 2007[127]; Four PCTs in North-West England, 1999, 2000	LISI score	Cross-sectional ecological study at practice level to look at possible inequity in provision of statins in primary care. Multivariate regression analysis looking at practice-prescribing rate as dependent variable. LISI score is a covariate in the model	LISI score explained 11% of the variation in prescribing rates seen between practices, with a beta-coefficient of -0.327, for only one of the PCT. Overall, LISI score was not significant in predicting practice-prescribing rate for statins and dropped out of the multiple regression model	Some suggestion of reduced prescribing of statins with increased deprivation in one PCT, but no overall relationship. Ecological study
McGovern 2008[120]; Scotland, UK, 2004, 2005	Carstairs and Morris Index of deprivation 1991	Study of a number of quality indicators of diabetic care in diabetic patients. Logistic regression with covariates gender, age, diabetes co-morbidities and deprivation category	In 2004 , prior to introduction of the new contract, the adjusted odds ratio for management of cholesterol less than or equal to 5 mmol/l was 1.17 (95% CIs 0.93, 1.46). After the new contract (in 2005), the odds ratio was 1.17 (95% CIs 1.02,1.34), suggesting that diabetics from deprived areas had better cholesterol control	Multiple comparisons were made; in most comparisons deprivation was not a statistically significant covariate. This study looks only at diabetic patients

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Table C.2 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Crawley 2009[112]; England, 2003; 2006	Social class (collapsed to manual and non-manual groups)	Health Survey for England data, 2003 and 2006; patient groups: diabetics (n= 611 in 2003), CHD (n=861 in 2003), hypertensives (n= 3717 in 2003). Management and prescribing targets for hypertension, diabetes and cholesterol. Logistic regression; adjusted for age, gender, BMI, disease duration and treatment	For diabetic patients, the manual to non-manual adjusted odds ratio for reducing cholesterol below 5 was 1.13 (95% CIs 0.68, 1.87) in 2003 and 0.86 (95% CIs 0.48, 1.54) in 2006. The manual to non-manual adjusted odds ratio for lipid-lowering prescription was 1.30 (95% CIs 0.87, 1.91) in 2003 and 0.96 (95% CIs 0.70, 1.31) in 2006.	These findings suggest that the management of cholesterol and the prescription of lipid-lowering agents does not vary significantly across social class groups. This study only used two groups for comparison of deprivation, collapsing analysis into manual and non-manual. This may masked differences in outcome between respondents at either end of the spectrum. The relatively small number of individuals with diabetes examined in this study may mean that numbers were insufficient to demonstrate an effect of social class in 2006.
Hamilton 2010; UK, 1997 and 2005	IMD 2004	Patients with type 1 or type 2 diabetes. Study looked at achievement of HbA_{1C} <7.0%, blood pressure <140/80 mmHg, and total cholesterol (<5 mmol/L)	In 1997, the adjusted odd ratio (for age and sex) for meeting the cholesterol target (most deprived versus least deprived quintile) was 1.03 (95% CIs 0.99, 1.07). Other comparisons between quintiles not significant either. In 2005, most versus least adjusted odds ratio was 1.14 (95% CIs 1.02, 1.28)	Diabeteic patients only. In 2005, more deprived patients were more likely to achieve the cholesterol target

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Table C.2 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Forde 2011 [129]; Whitehall civil servants, 2005–2007	Socio-economic group (British civil service grade); ethnicity	Whitehall II, prospective cohort study; nearly 7000 participants at baseline;	No difference in prescribed lipid-lowering drug use between employment grades in either moderate or low risk groups. Odds ratio adjusted for age and sex for those at moderate risk was for the intermediate to high employment grade 0.74 (95% CIs 0.55, 1.01) and for the low to high employment grade 0.89 (95% CIs 0.49,1.75). In those at high risk, the odds rate for the intermediate to high employment grade was 0.99 (95% CIs 0.83, 1.19) and for the low to hight employment grade was 1.06 (95% CIs 0.78, 1.43)	Prospective cohort study does not suggest inequity in provision. Does not include extreme deprivation groups, for example those not in employment. Detailed and repeated assessments of clinical need

Table C.3: Summary of papers examining inequity of provision of anti-platelet medications for primary prevention

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Bedson 2001[132]; North Staffordshire, UK, Not clear	Townsend 1991	Cross-sectional analysis, using individual-level GP data. 5983 patients with cardiovascular disease identified	Some suggestion that more affluent individuals were taking more aspirin, but the trend across the deprivation categories is not statistically significant (p-value 0.445). Odds ratio moderately deprived to most deprived 1.05 (95% CIs 0.89, 1.24); moderately affluent to most deprived 1.10 (95% CIs 0.93, 1.31); most afflent to most deprived 1.06 (95% CIs 0.90, 1.26)	
Edwards 2003[111]; Salford, UK, 1993-4 and 2000-1	Townsend deprivation 1991	Data from Diabetes Information System used to analyse individuals for attainments of targets for diabetes treatment at two time-points.	The p-value for trend across deprivation fifths not significant in 1993-4 or 2000-1. Substantial improvement over study period. By 2000-1 24.9% of least deprived and 25.5% of most deprived quintile were treated with anti-platelet drug	Diabetic patients only.
Ward 2004[109]; Four PCTs in North-West England, 1999 and 2000	Age; ethnicity; LISI score (deprivation); Townsend score	Ecological study at practice level. Univariate relationships between LISI score and prescribing rate. Associations examined using Spearman's rank correlations	Spearman's rank correlation coefficient between aspirin and Townsend score was 0.041; the result was not statistically significant at the 0.05 level. When the LISI score was used as an alternative to the Townsend score, the Spearman's rank correlation coefficient was -0.128; again not significant at the 0.05 level	No evidence of a relationship between aspirin prescribing and deprivation level. Does not take account of individual need. Univariate analysis does not take account of each of the different proxies of need when considering their relationships with prescribing rates. This study is largely superseded by Ward 2005, which used similar methodology and data sources but employed multivariate analysis.

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Table C.3 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Ward 2005[110]; Four PCTs in North-West England, 1999; 2000	Age; ethnicity; LISI score	Ecological: prescribing rates for practices, modelled on a number of proxies for CHD need for practices	In the multivariate regression model, the LISI score was a significant predictor of aspirin prescribing. The beta coefficient was -0.261 (suggesting that increased deprivation is associated with decreased prescribing), with 10.4% of the variation explained.	Not possible to separate into primary and secondary prevention. The need of individuals for aspirin is not considered; the analysis is amalgamated to practice level. Aspirin alternatives are not considered.
Elwood 2005[130]; Wales, 2003	Social class (manual, non-manual)	Stratified sample of 16 general medical practices in Wales. Cross-sectional study of individuals with high vascular-risk or cardio-vascular conditions	The proportion of patients in manual social classes who stated that they were taking aspirin regularly (59%) was significantly greater ($p < 0.025$) than the proportion in non-manual classes (53%)	Primary and secondary prevention were indistinguishable in this study
Saxena 2007[104]; UK, 2004, 2005	IMD 2004. Grouped into three bands	Ecological study using QOF data. Large number of GP practices in the UK. Examination of practice performance in relation to a number of practice characteristics, including practice size, deprivation	Weak association with increased deprivation of practice associated with decreased proportion of patients being prescribed anti-platelet medication. Groups statistically different using Kruskal Wallis exact test p-value <0.0001	Ecological data. In this comparison, patients all had a previous history of CVA; provision of antiplatelet therapies in this group might not legitimately be regarded as primary prevention of CHD
Petty 2008[131]; 152 PCTs in the UK, 2006	IMD at PCT level	PCT-level analysis using precribing data. Ecological study	Deprivation was a statistically significant explanatory variable for the level of clopidogrel prescribing at PCT level.	Ecological study; results hard to intepret. Need for clopidogrel is inferred from population characteristics rather than from individual-level data

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Table C.3 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Vinogradova 2009 [133]; UK, 2003 to 2007	Townsend deprivation 2001	QRESEARCH database to examine aspirin in use in relation to deprivation and co-morbidity. 459 GP practices	Use was higher in deprived compared to affluent areas (11.8% in lowest quintile versus 8.6% in highest quintile in 2003, 15.9% and 12.5% in 2007)	There is also a increased risk of gastrointestinal bleeding associated with increased aspirin use in more deprived groups. Aspirin use increased between 2003 and 2007
Elwood 2011 [134]; Caerphilly, South Wales, 2008	Social class (manual and non-manual)	Representative sample of population on the NHS Administrative Register (NHSAR). 4558 respondents (53% response rate). Looking at aspirin prescribing rates in those with and without a history of vascular events	In those respondents without a previous vascular event, 26% (95% CIs 24, 28) in the manual social classes and 21% (95% CIs 19, 23) in the non-manual were taking aspirin	Cross-sectional analysis. Representative sample of population. Includes over-the-counter and presribed medication. Clopidogrel not considered in responses

Table C.4: Summary of papers examining inequity of diabetes managment in patients without coronary heart disease requiring primary prevention

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Weng 2000[136]; London, 1995	Jarman 'Under-privileged Area Score'	Outcomes of diabetes care for Cohort recruited between 1982 and 1985 were examined in 1995. Analysed relationship between diabetes care and material deprivation score	Mean HbA_{1C} for patients in deprived wards was significantly higher than that of patients from less deprived wards. For most deprived wards, the mean was 10.5 (95% CIs 10.1, 10.9); for intermediate it was 9.9 (95% CIs 9.5, 10.4); for least deprived it was 9.1 (95% CIs 8.2, 10.0); p-value for trend 0.003. This difference arose primarily from a difference in glycaemic control across groups for those treated with insulin	The patients in the study were recruited in the 1980s
Edwards 2003[111]; Salford, UK, 1993-4 and 2000-1	Townsend deprivation 1991	Data from Diabetes Information System used to analyse individuals for attainments of targets for diabetes treatment at two time-points.	The percentage of diabetic patients achieving the HbA_{1C} target in 1993-4 was 30.5% in the least deprived and 31.1% in the most deprived quintile with p-value for trend across quintiles 0.862. In 2000-1 for the least deprived quintile this rose to 28.1% and for the most 25.8%, with a p-value for the trend across fifths of 0.420	No evidence of differential achievement of HbA_{1C} target across deprivation quintiles
Bachman 2003[114]; Avon and Somerset, UK, 1998 to 2000	Income	Questionnaire of patients with diabetes. 74% response rate	No significant difference in the mean HbA_{1C} between the income groups; p-value 0.22 for adjusted estimate of slope index of inequality	

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Table C.4 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Hippisley-Cox 2004[115]; UK, 2004	Townsend 2001	QRESEARCH database. 54180 patients with diabetes. Outcome was adjusted odds ratio for main outcome indicators from general medical services contract. Comparisons between most deprived and least deprived fifths of deprivation	The odds ratio (most deprived compared to least deprived) of achieving the <7.5% target for HbA_{1C} was 0.88 (95% CIs 0.82, 0.95). For the <10% target, the odds ratio was 0.70 (95% CIs 0.64, 0.77)	Statistically significant worse achievement of glycaemic control targets in most deprived category compared to least deprived
Bebb 2005[137]; Nottingham, UK, 2001 and 2002	Townsend 2001	1534 patients with type 2 diabetes from general practices. Patient characteristics assessed by a clinical interview, case note review; practice characteristics by questionnaire. Outcome measure HbA_{1C}. Two-level random effects linear regression	Patients registered at the most deprived practices had higher HbA_{1C} values than those in the least deprived practices (mean difference 0.42%, 95% CIs 0.14, 0.71)	The authors note a 'threshold effect' rather than a 'dose-response effect', noting 'the effect of deprivation only becoming important where deprivation is most extreme'

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Table C.4 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
McLean 2006[117]; Scotland, 2005	SIMD 2004 – income domain; Practice-level analysis using average deprivation	Retrospective analysis of GP QOF data. 1024 general practices. Examined relationship between practice deprivation and delivered care. Linear regression	For those with diabetes, the regression coefficient was 0.21, with the p-value less than 0.001 for achievement of HbA_{1C} less than 7.4% for payment quality. For delivered quality, the regression coefficient was -0.15 with p-value less than 0.001.	Regression coefficients in this study indicate the change in quality associated with a one-point increase in the percentage of deprived individuals. Payment quality analysis removes individuals who, for various reasons, are excluded from payment calculations. Delivered quality includes these individuals. These results for diabetes management suggest that in those practices with a higher proportions of deprived patients, a higher percentage of patients achieve criteria for payment, but when exclusions are taken account of the percentage of patients achieving targets is actually worse.
Gray 2006[116]; Wandsworth, London, 2003	IMD	Population-based cross-sectional survey using electronic GP records. Examined success rate for diabetes quality indicators. Logistic regression. n=6035	Patients in the least deprived group may be more likely to achieve HbA_{1C} targets though the differences are not statistically significant. Odds ratio least deprived compared to most deprived for less than 7.4% HbA_{1C} target 1.10 (95% CIs 0.87,1.38); odds ratio for less than 10.0% target 1.27 (95% CIs 0.97, 1.65)	Some suggestion of worse diabetic control in those from more deprived areas.

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Table C.4 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Millett, Car et al 2007[119]; England and Scotland, 2004	IMD linked to practices via postcode	Study uses QOF data from England and Scotland. Practice-level data. Studies the effect, at practice-level, of deprivation on achievement scores	Practices located in deprived areas performed less well on quality measures. The proportions of patients reaching the target for diabetics of an HbA_{1C} less than or equal to 7.4% was 57.3% in the most deprived group of practices, 59.1% in the intermediate group, and 60.1% in the least deprived group. CIs not presented. The effect of deprivation was more pronounced in smaller practices	This is an ecological study using QOF data.
Millett, Saxena et al 2007[135]; England, 1998 to 2004	Social class (manual, non-manual)	Secondary analysis of the HSE. Comparing national treatment targets for blood glucose, blood pressure and cholesterol and use of medications in survey respondents with diabetes.	No evidence of adverse gradient of insulin or oral diabetic medication between diabetics from the two social classes groups. In 1998, 59.6% of the manual group and 57.9% of the non-manual group were on oral dabetic medication. In 2003 this had risen to 65.8% in the manual group and 64.2%in the non-manual group. In 1998, 17.7% in the manual group were on insulin, compared to 17.5% in a manual groups; by 2003 this rose to 23.3% in the manual group and 18.8% in the non-manual group	Individual-level data from HSE. CIs not available

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Author Year; Setting	Inequity dimension	Study type	Results	Comment
McGovern 2008[120]; Scotland, UK, 2004, 2005	Carstairs and Morris Index of deprivation 1991	Study of a number of quality indicators of diabetic care in diabetic patients. Logistic regression with covariates gender, age, diabetes co-morbidities and deprivation category	In 2004, the odds ratio for deprivation fifth 5 (compared to 1) of achieving HbA_{1C} target less than or equal to 7.4% was 0.90 (95% CIs 0.71, 1.15). The odds ratio of achieving target less than or equal to 10.0% 0.57 (95% CIs 0.37, 0.87) In 2005, the odds ratio for the less than 7.4% target was 0.87 (95% CIs 0.76, 1.00) and for the less than 10.0% target was 0.58 (95% CIs 0.39, 0.84)	Multiple comparisons were made; in most comparisons deprivation was not a statistically significant covariate
Wild 2008[138]; Glasgow and Lothian, UK, 2005 and 2006	SIMD	Cross-sectional study of 52280 people in diabetes registers linked to hospital admissions data. Logistic regression	Diabetes more prevalent in the most deprived quintile 3.3% versus 2.3% age-adjusted prevalence. There was a gradient of increasing HbA_{1C} (>7.5%) with increasing deprivation: least deprived quintile 46%, most deprived quintile 47%, p-value 0.01 The study also finds that, beyond the mild gradient in glucose control, most deprived groups are more likely to smoke compared to least deprived (32% versus 13%, p-value <0.0001) and to be overweight (51% versus 38%, p-value <0.0001) and obese (9.8% versus 4.9% <0.0001)	This study also includes individuals with CHD. Individual level data

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Table C.4 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Crawley 2009[112]; England, 2003; 2006	Social class (collapsed to manual and non-manual groups)	Health Survey for England data, 2003 and 2006; patient groups: diabetics (n= 611 in 2003), CHD (n=861 in 2003), hypertensives (n= 3717 in 2003). Management and prescribing targets for hypertension, diabetes and cholesterol. Logistic regression; adjusted for age, gender, BMI, disease duration and treatment	In diabetic patients comparison was made between manual and non-manual groups for achievement of HbA_{1C} less than 7.5%. Here the manual to non-manual adjusted odds ratio was 0.47 (95% CIs 0.28, 0.80) in 2003 and was 0.66 (95% CIs 0.37, 1.15) in 2006. Comparison was also made for prescription of oral hypoglycaemic agents. The manual to non-manual adjusted odds ratio was 1.18 (95% CIs 0.84, 1.66) in 2003 and 1.34 (95% CIs 0.68, 1.23) in 2006	This study only used two groups for comparison of deprivation, collapsing analysis into manual and non-manual. This may have masked differences in outcome between respondents at either end of the spectrum. Findings from the study show that the difference in prescribing of oral hypoglycaemic agents between social classes is not significant. The achievement of HbA_{1C} targets was significantly less likely in the manual group in 2003. The odds ratio and confidence intervals for 2006 suggest a possible effect might exist that the study may be insufficiently powered to uncover.
Millett 2009[140]; Southwest London, 2000 and 2005	Primarily ethnicity; IMD	Longitudinal model studying the quality of diabetes care. Outcome measures were HbA_{1C} and mean blood pressure. Multilevel regression model	The impact of pay for performance on blood pressure and blood glucose levels was not found to vary significantly with neighbourhood socio-economic status (SES), either at the patient or practice level.	Individual level data. Looks primarily at the impact of pay-for-performance on disparities in ethnic groups
O'Kane 2010[139]; Northern Ireland, UK, 2003	N. Ireland income deprivation measure; educational achievement	Cross-section study of stratified random sample of patients diabetes service database. 685 patients. Individual questionnaire interview. Linear regression	HbA_{1C} level not significantly related to deprivation in regression.	Individual level data; area-level deprivation. Fairly small study. No evidence of worse diabetes care in more deprived groups

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Table C.4 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Hamilton 2010; UK, 1997 and 2005	IMD 2004	Patients with type 1 or type 2 diabetes. Study looked at achievement of HbA_{1C} <7.0%, blood pressure <140/80 mmHg, and total cholesterol (<5 mmol/L)	In 1997, the adjusted odd ratio (for age and sex) for achieving the HbA_{1c} target (most deprived versus least deprived quintile) was 0.96 (95% CIs 0.90, 1.01). Other comparisons between quintiles not significant either. In 2005, most versus least adjusted odds ratio was 1.06 (95% CIs 0.94, 1.21)	No evidence of differential glycaemic control between deprivation groups

Table C.5: Summary of papers examining inequity of provision of antihypertensives for secondary prevention

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Britton 2004[141]; 20 civil service departments in the UK, 1985 to 1999	Civil service employment grade	Prospective study with follow up over 15 years. 10308 participants at baseline. Need for cardiac care was determined by the presence of angina, myocardial infarction, and coronary risk factors. Outcome: cardiac procedures and drugs.	Age adjusted prevalence of use of beta-blockers among participants who attended phase 5 and had a history of myocardial infarction or angina were similar across three grades (low 18%, medium 16%, high 14%), with p-value for trend 0.22 For ACE inhibitors, prescription rates were again similar across grades (low 10%, medium 10%, high 10%), with p-value for trend 0.91	No suggestion of differencial use of beta-blockers or ACE inhibitors across social class groups in those who have a history of MI or angina. Does not include more extreme social class groups
Harding 2005[143]; English Midlands, 1999 – 2000	Census based deprivation at community level	Comparison of prescribing between communities with contrasting levels of deprivation (based on census data). Baseline analysis of deprivation, and age, sex, and burden of CHD. Prescribing information from NHS prescription analysis and cost (PACT) data. Chi-squared test to compare proportions; t-tests for continuous measures	Patients in the more deprived community were less likely to be prescribed calcium channel blockers, odds ratio 0.43 (95% CIs 0.24, 0.79), and a diuretic, odds ratio 0.57 (95% CIs 0.34, 0.96). Comparisons for beta-blockers, 32% prescribed among more deprived compared to 39% for less deprived (p-value 0.18) and ACE inhibitors, 18% prescribed in the more deprived compared to 28% in the less deprived (p-value 0.07), were not significant	Patients in the more deprived community were less likely to be prescribed calcium-channel blockers and diuretics, and received on average fewer hypertension drugs. The greater burden of CHD that might be expected in the more deprived community was not found; possible under-ascertainment of cases in the more deprived community. Non-significant results for ACE inhibitors and beta-blockers may reflect a lack of power. Analyses relating to antihypertensive medications include all cardiovascular disease, not just CHD

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Table C.5 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Ramsay 2005 [144]; UK, 1998 to 2000 and 2003	Social class (manual and non-manual)	Prospective cohort study using patient information on medication use. Subjects had a diagnosis of myocardial infarction or angina. British Regional Heart Study data. Response rate appoximately 80%.	For angina, in 2000, the prevalence ratio (manual to non-manual) for taking an ACE inhibitor was 0.72 (95% CIs 0.48, 1.08); for beta-blockers, 0.99 (0.75, 1.32). In 2003, for ACE inhibitors 0.78 (0.60, 1.03); beta-blockers 1.07 (0.85, 1.36) For MI, in 2000, for ACE inhibitors the ratio was 1.17 (0.81, 1.69); for beta-blockers 0.73 (0.54, 0.99). In 2003, for ACE inhibitors 0.98 (0.76, 1.25); beta-blockers 1.07 (0.85, 1.36)	Multiple comparisons were made. Most of which were not statistically significant. The finding that in those who have had an MI those in the manual social class are less likely to take a beta-blocker needs to be considered in the light of the numbers of comparisons made
Simpson 2005 [142]; Scotland, 1997 and 2002	Carstairs and Morris Index of deprivation 1991	Cross-sectional study based on GP morbidity and prescribing data (continuous morbidity recording project). 14425 patients with CHD	No difference between deprivation groups in the prescribing of ACE inhibitors or beta-blockers	Individual-level data

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Table C.5 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
McLean 2006[117]; Scotland, 2005	SIMD 2004 – income domain; Practice-level analysis using average deprivation	Retrospective analysis of GP QOF data. 1024 general practices. Examined relationship between practice deprivation and delivered care. Linear regression	The regression coefficient in those with CHD having their blood pressure controlled was -0.02 with a p-value of 0.53 for payment quality. For delivered quality, the regression coefficient was -0.04 with a p-value of 0.28. The regression coefficient for those with CHD being treated with a beta-blocker was -0.06 with a p-value of 0.21 for payment quality and 0.03 with a p-value of 0.2 for delivered quality	Regression coefficients in this study indicate the change in quality associated with a one-point increase in the percentage of deprived individuals. Payment quality analysis removes individuals who, for various reasons, are excluded from payment calculations. Delivered quality includes these individuals. In relation to both the control of blood pressure achieved and the prescription of a beta-blocker (which controls blood pressure among other effects) this paper does not find a statistically significant relationship between practice-level deprivation and practice-level performance

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Author Year; Setting	Inequity dimension	Study type	Results	Comment
Strong 2006[106]; Rotherham Primary Care Trust, United Kingdom, 2003 – 2004 data	Mean IMD (England) 2004; calculated at practice level	Practice-level analysis; mean practice-level index of multiple deprivation. Looks at the Quality and Outcomes Framework CHD registered patients, standardised indirectly for age and sex. Spearman's rank correlation coefficient for standardised CHD against practice deprivation for quality-of-care indicators	This study examined three measures of blood pressure management quality, and for each looked at the correlation between these measures and the mean practice level deprivation. The percentage of patients with the last blood pressure reading less than 150/90 mmHg increased with increased deprivation with a Spearman's rank correlation coefficient of 0.19, the result was not statistically significant. Spearman's rank correlation coefficient for the percentage of patients treated with beta-blocker and deprivation was 0.13, and again the result was not statistically significant. The Spearman's rank correlation coefficient for patients with previous MI treated with an ACE inhibitor was 0.10; the result was not statistically significant	This study suggest that there is, at a practice level, no evidence of increased quality of hypertension management in those with CHD and no evidence of increased prescribing of beta-blockers and ACE inhibitors as levels of deprivation decrease

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Author Year; Setting	Inequity dimension	Study type	Results	Comment
Murphy 2006[145]; Scotland, 2001 to 2002	Carstairs and Morris Index of deprivation 1991	General morbidity and prescribing data in the Continuous Morbidity Recording database. Study examined individuals with angina. Logistic regression to examine prescribing of drugs	In univariate analysis, with increasing deprivation, patients with angina were less likely to be prescribed a beta-blocker (p-value for trend 0.018), but more likely to be presribed an ACE inhibitor (p-value for trend 0.02) In multivariate analysis, patients in most deprived category were 25% more likely to be prescribed a calcium-channel blocker; 51% more likely to be prescribed an ACE inhibitor, angiotensin-receptor blocker or both. The difference in beta-blocker precription was not significant	No suggestion of inequity in provision according to need, with those in more deprived groups prescribed more (other than for beta-blockers)
Saxena 2007[104]; UK, 2004, 2005	IMD 2004. Grouped into three bands	Ecological study using QOF data. Large number of GP practices in the UK. Examination of practice performance in relation to a number of practice characteristics, including practice size, deprivation	Weak association with increased deprivation of practice associated with decreased ACE inhibitor and beta-blocker prescribing, and with decreased proportion of patients meeting target BP. Groups statistically different using Kruskal Wallis exact test p-value <0.0001	Ecological data

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Table C.5 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
McGovern 2008[317]; Scotland, 2004 and 2005	Carstairs and Morris Index of deprivation 1991	Individuals with CHD were identified from GP records. Individual-level data. Logistic regression.	More deprived groups were more likely to receive ACE inhibitors: in 2004 the odds ratio (most deprived compared to least deprived) was 1.64 (95% CIs 1.18, 2.28); in 2005 the odds ratio was 1.67 (95% CIs 1.34, 2.10). More deprived groups were less likely to receive beta-blockers: in 2004 the odds ratio was 0.87 (95% CIs 0.77, 0.97); in 2005 the ratio was 0.84 (95% CIs 0.76, 0.92)	Multiple comparisons related to deprivation, only some of which are statistically significant.
Ashworth 2008[121]; England, 2005 to 2007	IMD	Retrospective longitudinal survey. Deprivation analysed at practice level. Practice-level analysis. Relationship between deprivation and six QOF indicators related to blood pressure.	Over the study period the gap between the least and most deprived groups decreased for those with CHD. In the least deprived group in 2004-5 85.1% (95% CIs 84.7, 85.6) met BP targets compared to 81.8% (95% CIs 81.3, 82.3) in the most deprived group. By 2006-7 the least deprived figure was 89.4% (95% CIs 89.1, 89.7) and the most deprived figure was 88.4% (88.2, 80.7)	Initial evidence of a disparity in blood pressure control between deprivation groups in the first year of the study subsequently disappeared. Practice-level analysis

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Author Year; Setting	Inequity dimension	Study type	Results	Comment
Crawley 2009[112]; England, 2003; 2006	Social class (collapsed to manual and non-manual groups)	Health Survey for England data, 2003 and 2006; patient groups: diabetics (n= 611 in 2003), CHD (n=861 in 2003), hypertensives (n= 3717 in 2003). Management and prescribing targets for hypertension, diabetes and cholesterol. Logistic regression; adjusted for age, gender, BMI, disease duration and treatment	In patients diagnosed with CHD, the manual to non-manual adjusted odds ratio for successful management of SBP to less than 150/90 mmHg was 0.95 (95% CIs 0.26, 3.51) in 2003 and 0.44 (95% CIs 0.21, 0.90) in 2006. For prescription of antihypertensives, the odds ratios were 1.28 (95% CIs 0.97, 1.70) in 2003, and 0.80 (95% CIs 0.64, 1.00) in 2006	This study only used two groups for comparison of deprivation, collapsing analysis into manual and non-manual. This may mask differences in outcome between respondents at either end of the spectrum. The odds ratios presented suggest no significant effect of social class on anti-hypertensive prescribing. In 2006, the manual group was significantly less likely to achieve the target blood pressure, though in 2003 this difference had not been significant. This study carried out 24 comparisons between social classes and found only two to be statistically significant. This multiple comparison may mean that random effects explain this and the other statistically significant result from this study.
Mathur 2011[146]; East London, 2009 – 2010	Area-level socio-economic deprivation	Routinely collected data from 98 GP practices. Cross-sectional study. 10933 patients with CHD. Logistic regression looking at prescribing of CHD drugs by age, sex, ethnicity, socio-economic deprivation, co-morbidity and contra-indications	No difference in prescribing rates by social deprivation was found. Adjusted odds ratio for beta-blockers most deprived compared to least deprived 0.90 (95% CIs 0.75, 1.09). Comparisons with other deprivation quintiles were also not significant. For ACE inhibitors the most to least adjusted odds ratio was 1.10 (95% CIs 0.91, 1.32); again comparisons with other deprivation were not statistically significant	No evidence of inequity in utilisation of beta-blockers or ACE inhibitors for secondary prevention

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Table C.5 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Hawkins 2013 [103]; England, 1999; 2003; 2007	IMD; comparisons by quintile	Cross-section observational analysis using data from MINAP and the General Practice Research Database (GPRD). Looked at provision of intervention into three groups: MI patients, examined using data from MINAP; patients requiring secondary prevention – including patients with previous MI or revascularisation (GPRD); chronic angina (GPRD).	In comparison of ACE inhibitors and ARBs, there was no statistically significant difference in the comparison of age-sex-standardised rates between quintile 5 and quintile 1, either in 2003 or in 2007 – rate ratio 1.00 (95% CIs 0.92; 1.10) in 2003 and 1.08 (95% CIs 0.98; 1.19) in 2007 . Likewise, in the secondary prevention group there was no difference in 1999 – rate ratio 1.08 (95% CIs 0.84; 1.37) – or in 2007 – rate ratio 1.02 (95% CIs 0.79; 1.32). In the stable angina group, the rate ratio favoured quintile 5 (most deprived) in 2007, at 1.25 (95% CIs 1.09;1.43), but not in 1999, rate ratio 1.11 (95% CIs 0.94; 1.30). Using the same method to compare beta-blocker prescription, there were no statistically significant differences between groups. The rate ratios in the MI group were 1.00 (95% CIs 0.94; 1.06) in 2003 and 1.05 (95% CIs 0.96; 1.14) in 2007. For the secondary prevention group, the rate ratio was 1.02 (95% CIs 0.55; 1.90) in 1999 and 1.06 (95% CIs 0.80; 1.39) in 2007	Comparison between quintiles and three distinct groups. In the MI group, initiation of treatment as an inpatient following MI was examined. In the secondary prevention and stable angina groups, prescription in primary care in the same calendar year as the diagnosis was examined

Table C.6: Summary of papers examining inequity of provision of lipid-lowering medications for secondary prevention

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Reid 2002[147]; England, 1998	Social class (non-manual and manual)	Cross-sectional analysis of HSE data. Outcome was treatment with lipid-lowering therapy	Adjusted odd ratio of lipid-lowering treatment in those with CHD (non-manual versus manual) 1.24 (95% CIs 0.85, 1.82)	No association between lipid-lowering therapy and social class.
Britton 2004[141]; 20 civil service departments in the UK, 1985 to 1999	Civil service employment grade	Prospective study with follow up over 15 years. 10308 participants at baseline. Need for cardiac care was determined by the presence of angina, myocardial infarction, and coronary risk factors. Outcome: cardiac procedures and drugs.	Age adjusted prevalence of use of lipid-lowering agents among participants who attended phase 5 and had a history of myocardial infarction or angina were similar across three grades (low 19%, medium 14%, high 14%), with p-value for trend 0.41	No suggestion of differential use of lipid-lowering agents across social class groups in those who have a history of MI or angina. Does not include more extreme social class groups
Harding 2005[143]; English Midlands, 1999 – 2000	Census based deprivation at community level	Comparison of prescribing between communities with contrasting levels of deprivation (based on census data). Baseline analysis of deprivation, and age, sex, and burden of CHD. Prescribing information from PACT data. Chi-squared test to compare proportions; t-tests for continuous measures	Results for statin prescription only presented for those less than 74 years of age. In those with a history of MI, 52.8% were prescribed a statin in the more deprived community compared to 47.5% in the less deprived community. The p-value for the difference was 0.65. For those with angina, 48.2% of those in the more deprived community were prescribed a statin, compared to 39.3% in less deprived community. The p-value for the difference was 0.72	No evidence from the study of an increased prescription of lipid-lowering medications to less deprived communities for individuals with a history of MI or angina

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Table C.6 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Ramsay 2005[144]; UK, 1998 to 2000 and 2003	Social class (manual and non-manual)	Prospective cohort study using patient information on medication use. Subjects had a diagnosis of myocardial infarction or angina. British Regional Heart Study data. Response rate appoximately 80%.	For patients with angina, in the year 2000 the prevalence ratio (manual compared to non-manual) for taking a statin was 0.64 (95% CIs 0.45, 0.91); in 2003, it was 0.91 (95% CIs 0.76, 1.09) For patients with MI, in 2000, the prevalence ratio was 1.08 (95% CIs 0.77, 1.52); in 2003 it was 1.14 (95% CIs 0.97, 1.35)	For those who have had an MI, there is some suggestion that the manual group is more likely to take a statin, though the results do not achieve statistical significance. For those with angina, there is a statistically significant reduced likelihood of taking a statin in the manual social class in 2000, but this association is no longer statistically significant in 2003
Simpson 2005[142]; Scotland, 1997 and 2002	Carstairs and Morris Index of deprivation 1991	Cross-sectional study based on GP morbidity and prescribing data (continuous morbidity recording project). 14425 patients with CHD	Comparisons were made in multivariate analysis for multiple years. 1997–2002. In 1998, the most deprived group received significantly less statin treatment than the most deprived, odds ratio 0.6 (95% CIs 0.5, 0.8); this difference continued until 2000, odds ratio 0.6 (95% CIs 0.5, 0.8). In other years there was no difference between most and least deprived quartiles	The apparent different between most extreme deprivation groups between 1998 and 2000 disappears by 2001. Individual-level data

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Table C.6 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Strong 2006[106]; Rotherham Primary Care Trust, United Kingdom, 2003 – 2004 data	Mean IMD (England) 2004; calculated at practice level	Practice-level analysis; mean practice-level index of multiple deprivation. Looks at the Quality and Outcomes Framework CHD registered patients, standardised indirectly for age and sex. Spearman's rank correlation coefficient for standardised CHD against practice deprivation for quality-of-care indicators	The Spearman's rank correlation coefficient between the percentage of patients in a practice with CHD with total cholesterol less than 5 mmol/l and the mean practice deprivation score was -0.07. This result was not statistically significant, though an exact p-value is not given	Evidence from this study suggest that there is no statistically significant difference in the quality of lipid-lowering management according to deprivation and practice level. Information on the correlation between the percentage of these patients prescribed a statin and mean deprivation score is not available
Murphy 2006[145]; Scotland, 2001 to 2002	Carstairs and Morris Index of deprivation 1991	General morbidity and prescribing data in the Continuous Morbidity Recording database. Study examined individuals with angina. Logistic regression to examine prescribing of drugs	There were no differences in prescribing of statins, with the odds ratio in the most deprived compared to the least deprived group 0.92 (95% CIs 0.77, 1.10)	No inequity in statin prescription

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Table C.6 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Crawley 2009[112]; England, 2003; 2006	Social class (collapsed to manual and non-manual groups)	Health Survey for England data, 2003 and 2006; patient groups: diabetics (n= 611 in 2003), CHD (n=861 in 2003), hypertensives (n= 3717 in 2003). Management and prescribing targets for hypertension, diabetes and cholesterol. Logistic regression; adjusted for age, gender, BMI, disease duration and treatment	In patients diagnosed with CHD, the manual to non-manual adjusted odds ratios for successful management of cholesterol to less than 5 were 0.71 (95% CIs 0.18, 2.81) in 2003 and 0.86 (95% CIs 0.36, 2.05) in 2006. For prescription of lipid-lowering drugs, the odds ratio was 0.80 (95% CIs 0.56, 1.10) in 2003 and 0.85 (95% CIs 0.64, 1.14) in 2006.	This study only used two groups for comparison of deprivation, collapsing analysis into manual and non-manual. This may have masked differences in outcome between respondents at either end of the spectrum. The evidence presented suggests no statistically significant difference in the mangement of cholesterol or in prescribing rates between social classes. Outcomes inproved significantly in all groups between 2003 and 2006, with manual groups having a better increase in statin prescribing.
Mathur 2011[146]; East London, 2009 – 2010	Area-level socio-economic deprivation	Routinely collected data from 98 GP practices. Cross-sectional study. 10933 patients with CHD. Logistic regression looking at prescribing of CHD drugs by age, sex, ethnicity, socio-economic deprivation, co-morbidity and contra-indications	Odds ratio of treatment with lipid-modifying drug in most versus least deprived quintile 1.03 (95% CIs 0.78, 1.36). Comparisons with other quintiles were also not statistically significant	No evidence of inequity of provision of lipid-lowering therapy for secondary provision in this study

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Table C.6 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Hawkins 2013 [103]; England, 1999; 2003; 2007	IMD; comparisons by quintile	Cross-section observational analysis using data from MINAP and the GPRD. Looked at provision of intervention into three groups: MI patients, examined using data from MINAP; patients requiring secondary prevention – including patients with previous MI or revascularisation (GPRD); chronic angina (GPRD).	Statin prescription was compared for the secondary prevention and stable angina groups in 1999 and 2007. In the secondary prevention group, there was no evidence of a significant difference in prescription between quintile 5 and quintile 1, with the rate ratio 0.67 (95% CI 0.45; 1.01) in 1999 and 0.91 (95% CIs 0.71; 1.17) in 2007. In the stable angina group, prescribing favoured quintile 5 at both time points: rate ratio 1.18 (95% CI 1.02; 1.36) in 1999; rate ratio 1.37 (95% CIs 1.25; 1.50) in 2007	Comparison of rate ratios of age-sex-standardised rates between quintile 5 (most deprived) in quintile 1 (least deprived)

Table C.7: Summary of papers examining inequity of provision of anti-platelet medications for secondary prevention

Author Year; Setting	Inequity dimension	Study type	Results	Comment
McCallum 1997[318]; UK, 1992	Social class (manual and non-manual)	British Regional Heart Study data. 5751 men with cardiovascular disease completing questionnaires on aspirin use	The proportion of individuals with cardiovascular disease was very similar in the manual and non-manual groups (39%)	No difference between social class groups in the proportion taking aspirin.
Trinder 2003[148]; North Stafford-shire, UK, Not clear	Townsend	Cross-sectional population study carried out on a stratified random sample of 10000 adults aged over 35. Response rate 67%. Examined aspirin prescription	The chance of being on aspirin was increased for those living in more deprived areas, though the result was not statistically significant. The adjusted odds ratio most deprived to least deprived was 1.69 (95% CIs 0.99, 2.89); for intermediate group compared to least deprived the adjusted odds ratio was 1.48 (95% CIs 0.87, 2.53)	Some suggestion that more deprived individuals with cardio-vascular disease are more likely to take aspirin, though this is not statistically significant.
Britton 2004[141]; 20 civil service departments in the UK, 1985 to 1999	Civil service employment grade	Prospective study with follow up over 15 years. 10308 participants at baseline. Need for cardiac care was determined by the presence of angina, myocardial infarction, and coronary risk factors. Outcome: cardiac procedures and drugs.	Age adjusted prevalence of use of aspirin among participants who attended phase 5 and had a history of myocardial infarction or angina were similar across three grades (low 31%, medium 26%, high 24%), with p-value for trend 0.33	No suggestion of differencial use of aspirin across social class groups in those who have a history of MI or angina. Does not include more extreme social class groups

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Table C.7 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Harding 2005 [143]; English Midlands, 1999 – 2000	Census based deprivation at community level	Comparison of prescribing between communities with contrasting levels of deprivation (based on census data). Baseline analysis of deprivation, and age, sex, and burden of CHD. Prescribing information from PACT data. Chi-squared test to compare proportions; t-tests for continuous measures	In the more deprived community 83.1% of those with a history of MI were prescribed antithrombotic medication compared to 84.3% in the less deprived community. The p-value for the chi squared test was 0.85. In those with a history of angina, 70.0% were prescribed an antithrombotic medication in more the deprived community compared to 70.9% in the less deprived community. The p-value for the difference was 0.54	This study provides no evidence of a difference in antithrombotic prescribing rates between the more and less deprived community in either those with a history of MI or angina
Ramsay 2005 [144]; UK, 1998 to 2000 and 2003	Social class (manual and non-manual)	Prospective cohort study using patient information on medication use. Subjects had a diagnosis of myocardial infarction or angina. British Regional Heart Study data. Response rate appoximately 80%.	For patients with angina, in 2000 the prevalence ratio (manual versus non-manual) was 0.91 (95% CIs 0.80, 1.04); in 2003 it was 0.93 (95% CIs 0.84, 1.04) For patients with MI, in the 2000 the prevalence ratio was 0.93 (95% CIs 0.84, 1.03); in 2003 it was 0.97 (95% CIs 0.88, 1.06)	Some suggestion that more deprived groups take less aspirin, but the results do not attain statistical significance
Simpson 2005 [142]; Scotland, 1997 and 2002	Carstairs and Morris Index of deprivation 1991	Cross-sectional study based on GP morbidity and prescribing data (continuous morbidity recording project). 14425 patients with CHD	No significant difference between deprivation groups in the presciption of secondary anti-platelet medication.	Individual-level data

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Table C.7 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Elwood 2005[130]; Wales, 2003	Social class (manual, non-manual)	Stratified sample of 16 general medical practices in Wales. Cross-sectional study of individuals with high vascular-risk or cardio-vascular conditions	The proportion of patients in manual social classes who stated that they were taking aspirin regularly (59%) was significantly greater (P <0.025) than the proportion in non-manual classes (53%)	Not possible to tell if there are social class differences in primary and secondary preventative treatment with aspirin
McLean 2006[117]; Scotland, 2005	SIMD 2004 – income domain; Practice-level analysis using average deprivation	Retrospective analysis of GP QOF data. 1024 general practices. Examined relationship between practice deprivation and delivered care. Linear regression	The regression coefficient for prescribing aspirin or equivalent medication for those with CHD was 0.01, p-value 0.78 for payment quality. For delivered quality the regression coefficient was 0.03, with p-value 0.2	Regression coefficients in this study indicate the change in quality associated with a one-point increase in the percentage of deprived individuals. Payment quality analysis removes individuals who, for various reasons, are excluded from payment calculations. Delivered quality includes these individuals. These result suggest that there is not a statistically significant trend of prescribing of anti-platelet medications in more deprived practices.

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Table C.7 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Strong 2006[106]; Rotherham Primary Care Trust, United Kingdom, 2003 – 2004 data	Mean IMD (England) 2004; calculated at practice level	Practice-level analysis; mean practice-level index of multiple deprivation. Looks at the Quality and Outcomes Framework CHD registered patients, standardised indirectly for age and sex. Spearman's rank correlation coefficient for standardised CHD against practice deprivation for quality-of-care indicators	The Spearman's rank correlation coefficient between practice-level mean deprivation and the percentage of patients with CHD treated with anti-platelet medication or anticoagulant was -0.04. This result was not statistically significant, though an exact p-value is not given	Results suggest that there is no relationship at a practice level between increased deprivation and decreased provision of anti-platelet medication in those diagnosed with CHD
Murphy 2006[145]; Scotland, 2001 to 2002	Carstairs and Morris Index of deprivation 1991	General morbidity and prescribing data in the Continuous Morbidity Recording database. Study examined individuals with angina. Logistic regression to examine prescribing of drugs	In multivariate analysis, the odds ratio (most deprived groups compared to least deprived group) of anti-platelet treatment was 1.08 (95% CIs 0.89, 1.32)	No evidence of inequity of antiplatelet prescribing in those with angina
Saxena 2007[104]; UK, 2004, 2005	IMD 2004. Grouped into three bands	Ecological study using QOF data. Large number of GP practices in the UK. Examination of practice performance in relation to a number of practice characteristics, including practice size, deprivation	Weak association with increased deprivation of practice associated with decreased use of anti-platelet medications. Groups statistically different using Kruskal Wallis exact test p-value <0.0001	Ecological data

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Table C.7 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
McGovern 2008[317]; Scotland, 2004 and 2005	Carstairs and Morris Index of deprivation 1991	Individuals with CHD were identified from GP records. Individual-level data. Logistic regression.	More deprived groups with CHD were more likely to be treated with antiplatelet medications. In 2004, the odds ratio (most deprived quintile versus least deprived quintile) was 1.11 (95% CIs 0.95, 1.28); in 2005, the odds ratio was 1.14 (95% CIs 1.00, 1.22)	Multiple comparisons related to deprivation, only some of which are statistically significant.
Elwood 2011[134]; Caerphilly, South Wales, 2008	Social class (manual and non-manual)	Representative sample of population on the NHSAR. 4558 respondents (53% response rate). Looking at aspirin prescribing rates in those with and without a history of vascular events	Sixty-seven percent of those in manual social classes were taking aspirin, compared to 56% in the non-manual social classes	Cross-sectional analysis. Representative sample of population. Includes over-the-counter and presribed medication. Clopidogrel not considered in responses
Mathur 2011[146]; East London, 2009 – 2010	Area-level socio-economic deprivation	Routinely collected data from 98 GP practices. Cross-sectional study. 10933 patients with CHD. Logistic regression looking at prescribing of CHD drugs by age, sex, ethnicity, socio-economic deprivation, co-morbidity and contra-indications	Odds ratio of treatment with aspirin in the most versus least deprived quintile 1.20 (95% CIs 0.96, 1.50). Comparisons with other quintiles were also not statistically significant	No evidence from this study of inequity of aspirin use for secondary prevention

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Table C.7 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Hawkins 2013 [103]; England, 1999; 2003; 2007	IMD; comparisons by quintile	Cross-section observational analysis using data from MINAP and the GPRD. Looked at provision of intervention into three groups: MI patients, examined using data from MINAP; patients requiring secondary prevention – including patients with previous MI or revascularisation (GPRD); chronic angina (GPRD).	In the MI group, there were no significant differences in the rate ratios of prescribing rates for either aspirin or clopidogrel at either time point. For aspirin, the rate ratio was 1.00 (95% CIs 0.96; 1.04) in 2003 and 0.98 (95% CIs 0.97; 1.00) in 2007; for clopidogrel, the rate ratio was 0.94 (95% CIs 0.70; 1.25) in 2003 and 0.96 (95% CIs 0.93; 1.00) in 2007. Rate ratios suggested increased relative aspirin prescription in the secondary prevention group favouring quintile 5 in 1999, with the rate ratio 1.28 (95% CIs 1.08; 1.53), but not in 2007, 1.01 (95% CIs 0.76; 1.34). For the stable angina group, relatively higher aspirin prescription was observed both in 1999 – 1.63 (95% CIs 1.46; 1.82) – and in 2007 – 1.65 (95% CIs 1.48; 1.83).	Comparison of rate ratios of age-sex-standardised rates between quintile 5 (most deprived) in quintile 1 (least deprived). The increased relative provision of aspirin to angina patients was particularly pronounced in younger age groups

Table C.8: Summary of papers examining inequity of provision of revascularisation

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Ben-Shlomo 1995[157]; London, 1991	Townsend 1981	Ecological comparison of operation rates for CABG for 1991 with CHD mortality 1981-85	CHD mortality showed steady, significant increase with increasing area deprivaiton score. For women, CABG rate ratios increased as deprivation increased. For men, there was a U-shaped relationship, with lowest values for the second and third quartiles	Some suggestion of inequity of revascularisation provision in men
Kee 1995[158]; Nothern Ireland, 1993	Townsend 1991	Analysis of waiting times for revascularisation surgery in patients undergoing angiography	Townsend deprivation was not associated with waiting time for coronary artery surgery	No evidence of an association. Individual-level data. Waiting times
Black 1995[159]; UK, 1992-93	Jarman; Department of the Environment social deprivation index	Cross-sectional ecological study	More socially deprived districts had higher rates of revascularisation procedures	The authors note that this finding may be confounded by the proximity of more deprived patients to specialist centres. Includes private hospitals. Univariate analysis which did not correct for distance from specialist centre
Payne 1997[150]; Sheffield, UK, 1991 to 1995	Townsend deprivation 1991	A stratified random sample of patients registered with GPs (12240 respondents; 79% response rate) was used to determine the proportion of patients with symptoms of angina. Ward-level analysis	There was a relationship between the prevalence of angina symtoms and deprivation (r = 0.79; p-value <0.001). No relationship between the revascularisation rate and deprivation. There was a relationship between the ratio of revascularisations to the number in an electoral ward estimated to have symptoms of angina (r= -0.67; p-value <0.001)	Ecological analysis at ward level; suggests that the supply of revascularisations is inequitable

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Table C.8 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Manson-Siddle 1998[151]; Yorkshire, UK, 1992 to 1994	Super Profile multidimensional categorisation of socio-economic disadvantage	Cross-sectional ecological study at enumeration-district level. CHD standardised mortality ratio as a proxy for need. Subjects with a primary diagnosis of CHD aged 25 and over	Gradient in the utilisation of revascularisation procedures across the deprivation groups, though the gradient does not reflect the gradient in standardised mortality ratio. This effect is more pronounced in those aged 65 to 74 than in those <65	Ecological evidence of an inequity in supply between deprivation groups
Manson-Siddle 1999[152]; South Humberside, UK, 1992 to 1994	Super Profile multidimensional categorisation of socio-economic disadvantage	Cross sectional ecological study of revascularisation rates, using the Super Profile classification of enumeration districts and CHD standardised mortality ratios as a proxy for need. Analysis was performed before and after resource investment in cardiac services in the area	Decreasing trend for revascularisation across the Super Profile Lifestyle groups, with more deprived groups having lower rates of procedures (the ratio of revascularisation rates in the least to most deprived groups was 1.53 : 1 (CIs not provided). After investment, the apparent inequity in provision diminished, with the ratio of revascularisation rates 0.71 : 1, though the trend across all the deprivation categories was not improved	Investment in cardiac services, with an overall increased in revascularisation rates, reduced the inquity between the most extreme deprivation groups; a trend of increased provision with increased affluence remained
MacLeod 1999[156]; Scotland, 1991 to 1995	Carstairs and Morris Index of deprivation 1991	Individual-level analysis of the proportion of patients admitted with MI undergoing PTCA and CABG over the following two years. 36838 patients. Multiple logistic regression.	Socio-economic deprivation was associated with a reduced likelihood of CABG. Adjusted odd ratio for the most deprived versus the least deprived group was 0.70 (95% CIs 0.53, 0.92). The difference between deprivation groups in progression to PTCA was not significant.	Small numbers of PTCAs may mean that this study was underpowered to demonstrate a genuine association

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Table C.8 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Hippisley-Cox 2000[153]; Nottinghamshire, 1997	Jarman 'Underprivalaged Area Score'	Practice-level analysis. Poisson regression, examining utilisation rates with deprivation as a covariate (as well as admission rates for CHD)	In multivarate Poisson regression, adjusted for a number of practice characteristics, increased deprivation was associated with reduced utilisation of revascularisation procedures; adjusted rate ratio 0.955 (95% CIs 0.985, 0.991)	Practice-level analysis. CHD admission rate as a proxy of need
Pell 2000[149]; Scotland, 1986 to 1997	Carstairs deprivation category	Retrospective analysis of waiting list data in Scotland. 26642 patients. Multivariate logistic regression	Patients in the most deprived categories waited about three weeks longer for surgery than those in the least deprived category: mean difference 24 days (95% CIs 15, 32). Deprived patients had an odds ratio of 0.5 (95% CIs 0.46, 0.61) for having operations classified as urgent compared with the least deprived. When urgent and routine cases were considered separately, there was no significant difference in waiting times between the most and least deprived categories	This study looks at waiting times, not revascularisation rates
Gatrell 2002[160]; North-West England, 1993–1996	Carstairs and Morris Index of deprivation 1991	Small-area level analysis of rates of utilisation of angiography, angioplasty and bypass surgery. Poisson regression to examine explanatory variables, including deprivation. CHD mortality was used as a proxy for need	For CABG, the risk ratios (adjusted for need and travel time) for treatment rose across deprivation quartiles, indicating that those living in more deprived areas were receiving more treatments. The trends across quartiles were statistically significant. Numbers for PTCA were too small to allow precision of estimates, but showed increased provision with increased material deprivation	Small-area level study; no suggestion of inequity of provision at small area level. CHD mortality used as a proxy for need

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Table C.8 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Lester 2004[154]; Wales, 2000 to 2002	Townsend deprivation from 2001	Cross-sectional ecological study involving a retrospective analysis of routinely collected hospital activity statistics in relation to need	Persons in the most deprived fifth are less likely to undergo investigation by coronary angiogram compared to least deprived fifth (OR 0.88, 95% CI 0.83-0.92); Persons in the most deprived fifth are less likely to undergo treatment by coronary revascularisation compared to least deprived fifth (OR 0.84, 95% CI 0.79-0.89)	For persons living in the most socio-economically deprived fifth of electoral divisions in Wales, provision of coronary angiography and revascularisation is inequitable. Ecological study; does not take account of co-morbidity and other covariates. Not a peer-reviewed study
Britton 2004[141]; 20 civil service departments in the UK, 1985 to 1999	Civil service employment grade	Prospective study with follow up over 15 years. 10308 participants at baseline. Need for cardiac care was determined by the presence of angina, myocardial infarction, and coronary risk factors. Outcome: cardiac procedures and drugs.	After correction for smoking, systolic and diastolic blood pressure, total cholesterol, body mass index, diabetes, ethnicity, and family history using logistic regression the odds ratio for revascularisation in those with CHD in the low employment grade group compared to high was 1.14 (95% CIs 0.57, 2.30); for medium employment grade the figure was 1.24 (95% CI CIs 0.83, 1.85)	Reverse gradient in use of revascularisation after correction for risk factors. Does not take account of extremes of social groups. Small numbers in some groups
Morris 2005[161]; 24 medium sized British towns, 1992 to 1996	Registrar general's classification of social class	Prospective population based study. British Regional Heart Study	In multifactorial analysis, which included adjustment for incidence of major coronary heart disease or angina, a lower incidence of revascularisation was found among men with manual occupations (0.73, 95% CIs 0.53 to 1.02)	Evidence of lower incidence in men with manual occupations; not statistically significant

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Table C.8 – *Continued from previous page*

Author Year; Setting	Inequity dimension	Study type	Results	Comment
Cosh 2008[155]; Wales, 1992 to 2006	Townsend deprivation 2001	Ecological database analysis comparing revascularisation rates with proxies of need (CHD deaths and admissions)	Fewer angiographies per 1000 admissions in the more deprived groups. Flat gradient of revascularisation across deprivation fifths, despite the gradient of increased (proxy) level of need as deprivation increases	Overall pattern of apparent horizontal inequity in CHD investigation and treatment across Wales. Not a peer-reviewed study
Mindell 2008[162]; London, 2001 to 2003	2004 IMD; Gini coefficients	Analyses of hospital episodes statistics and private-sector data by age, sex and primary care trust of residence. Gini coefficients were derived to provide an index of inequality across subpopulations, with parametric bootstrapping to estimate confidence intervals.	NHS-funded admission rates were not related to deprivation or age-standardised deaths rates from CHD. Privately funded admission rates were lower in more deprived PCTs. NHS provision was significantly more egalitarian (Gini coefficient 0.12) than the private sector (0.35). Including all procedures was significantly less equal (0.13) than NHS funded care alone.	Suggests the NHS funded provision is more equitable than privately-funded care

D

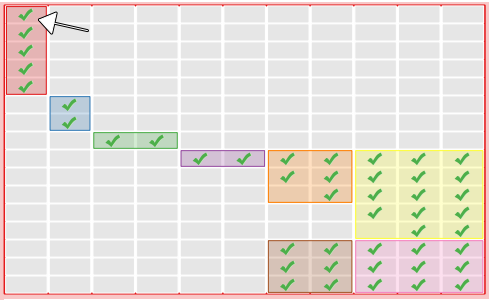
ADDITIONAL RESULTS

D.1 MAIN ANALYSIS

In the analysis in the following pages, I present to graphics for each of the points in the pathway of care for CHD using the same means of presentation as that employed in chapter 8. I provide at each point in the pathway:

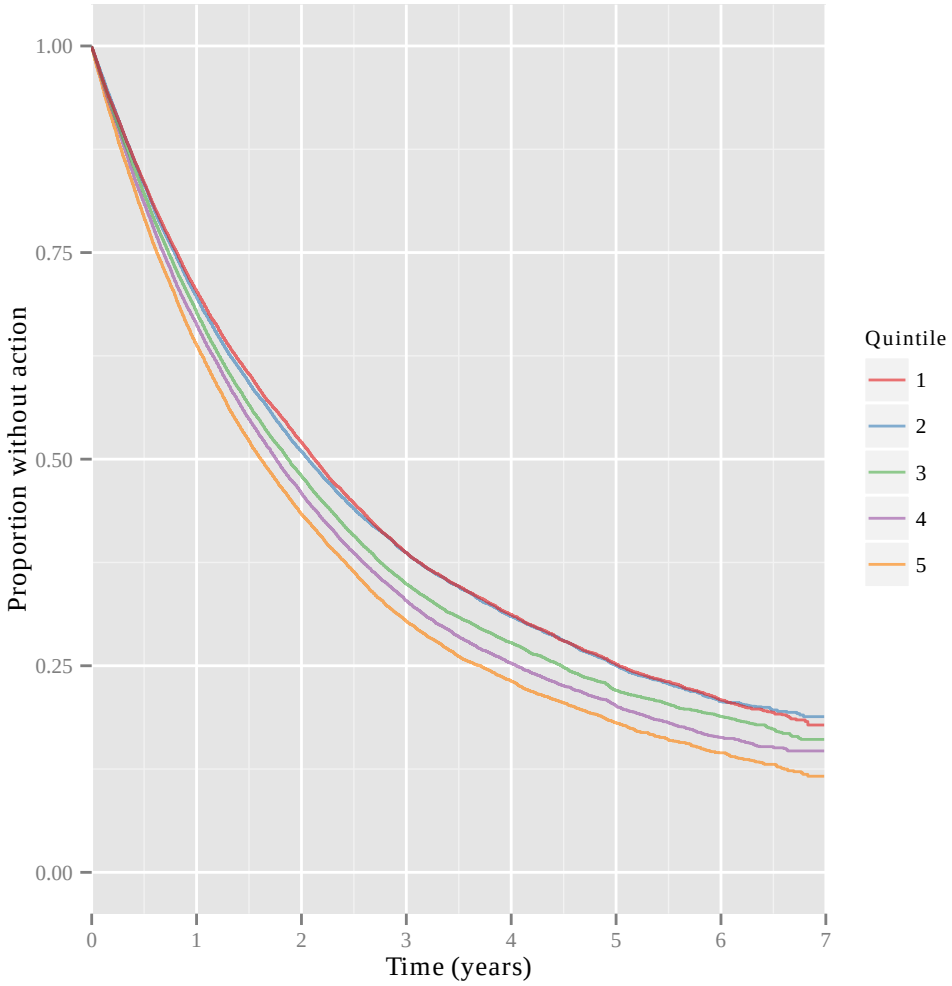
- A Kaplan-Meier plot for that clinical trigger-action
- The results of the 'fully-adjusted model' for that clinical trigger-action

These figures correspond to figures 8.5 and 8.8 in chapter 8. On request, I can make available additional graphics relating to these points in the pathway, again corresponding to each of the figures presented in chapter 8. These graphics are currently contained in the SAIL Gateway, so providing them would entail delays while they were exported, and would be subject to review by HIRU in line with information governance procedures.



Risk and risk factor attainment

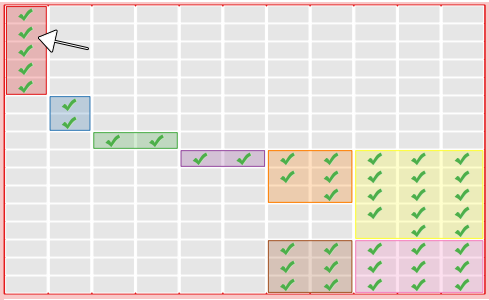
Kaplan−Meier plot for 'aged 40+ with no high risk diagnosis' and 'ascertainment of smoking status'. Incident clinical trigger (triggers = 122486; actions = 72291)



Mixed−effects model for 'aged 40+ with no high risk diagnosis' and 'ascertainment of smoking status'. Incident clinical trigger

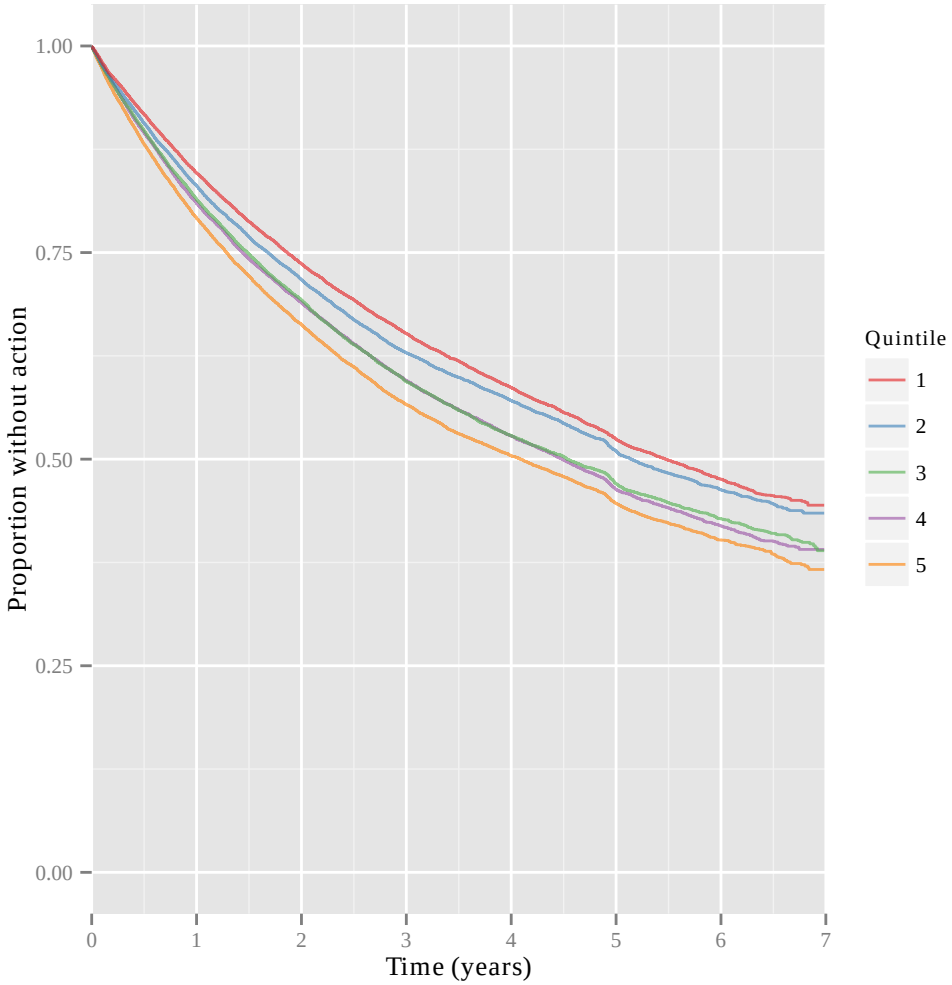
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.02	(1.00; 1.05)
Quintile 3	1.09	(1.06; 1.12)
Quintile 4	1.13	(1.10; 1.16)
Quintile 5	1.20	(1.17; 1.24)
Male	1	(Reference)
Female	1.51	(1.49; 1.54)
No hyp.	1	(Reference)
Hyp. contr.	1.86	(1.79; 1.93)
Hyp. uncontr.	1.87	(1.75; 2.00)
Untreat. hyp.	1.28	(1.22; 1.36)
No oth. co.	1	(Reference)
Other co.	1.65	(1.59; 1.70)

Number of clinical triggers 122486; Number of clinical actions 72291. ICC for practice = 0.041. Missing values imputed using MICE.



Risk and risk factor attainment

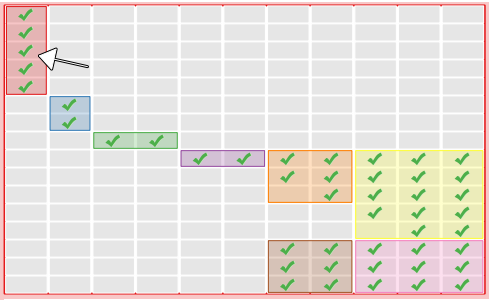
Kaplan−Meier plot for 'aged 40+ with no high risk diagnosis' and 'measurement of BMI'. Incident clinical trigger (triggers = 122486; actions = 46235)



Mixed−effects model for 'aged 40+ with no high risk diagnosis' and 'measurement of BMI'. Incident clinical trigger

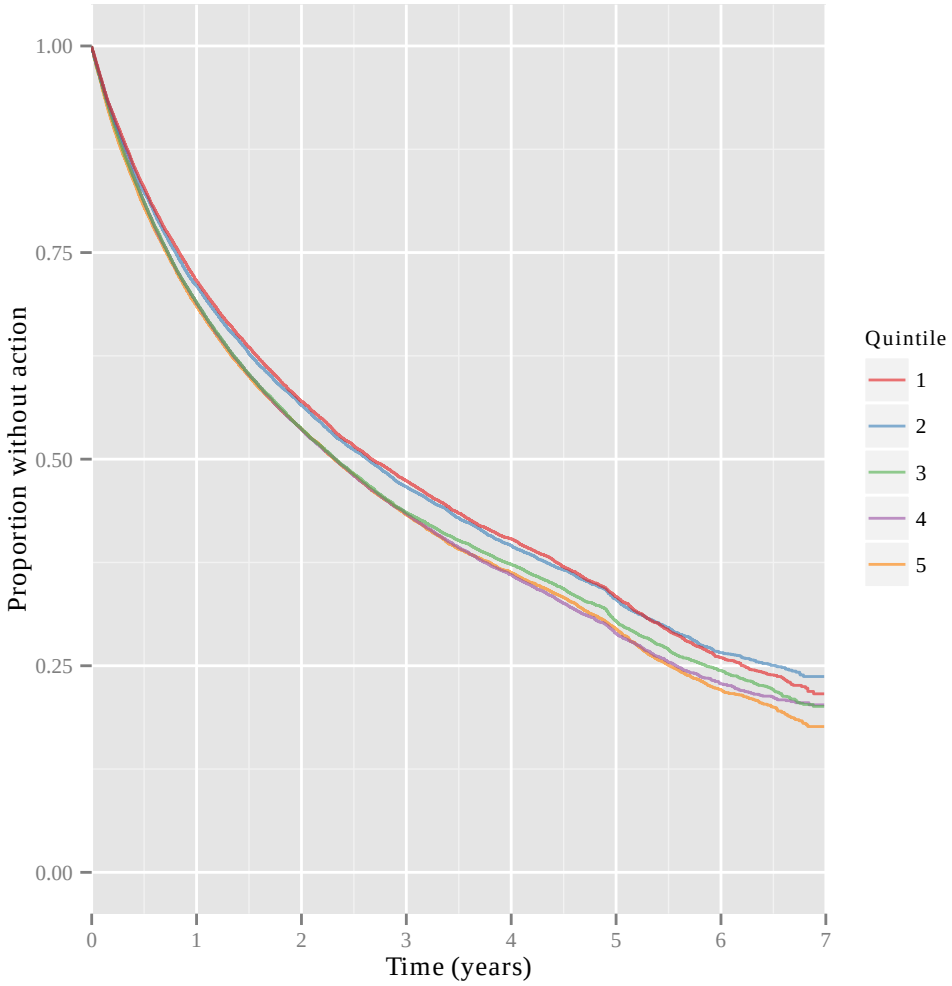
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.04	(1.01; 1.08)
Quintile 3	1.09	(1.05; 1.12)
Quintile 4	1.08	(1.04; 1.12)
Quintile 5	1.12	(1.08; 1.16)
Male	1	(Reference)
Female	1.91	(1.88; 1.95)
No hyp.	1	(Reference)
Hyp. contr.	2.39	(2.29; 2.49)
Hyp. uncontr.	2.62	(2.43; 2.82)
Untreat. hyp.	1.61	(1.51; 1.72)
No oth. co.	1	(Reference)
Other co.	1.58	(1.52; 1.65)

Number of clinical triggers 122486; Number of clinical actions 46235. ICC for practice = 0.133. Missing values imputed using MICE.



Risk and risk factor attainment

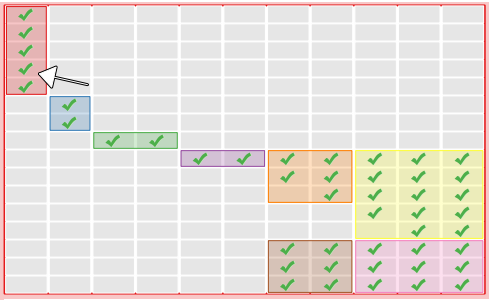
Kaplan−Meier plot for 'aged 40+ with no high risk diagnosis' and 'measurement of BP'. Incident clinical trigger (triggers = 122486; actions = 64312)



Mixed−effects model for 'aged 40+ with no high risk diagnosis' and 'measurement of BP'. Incident clinical trigger

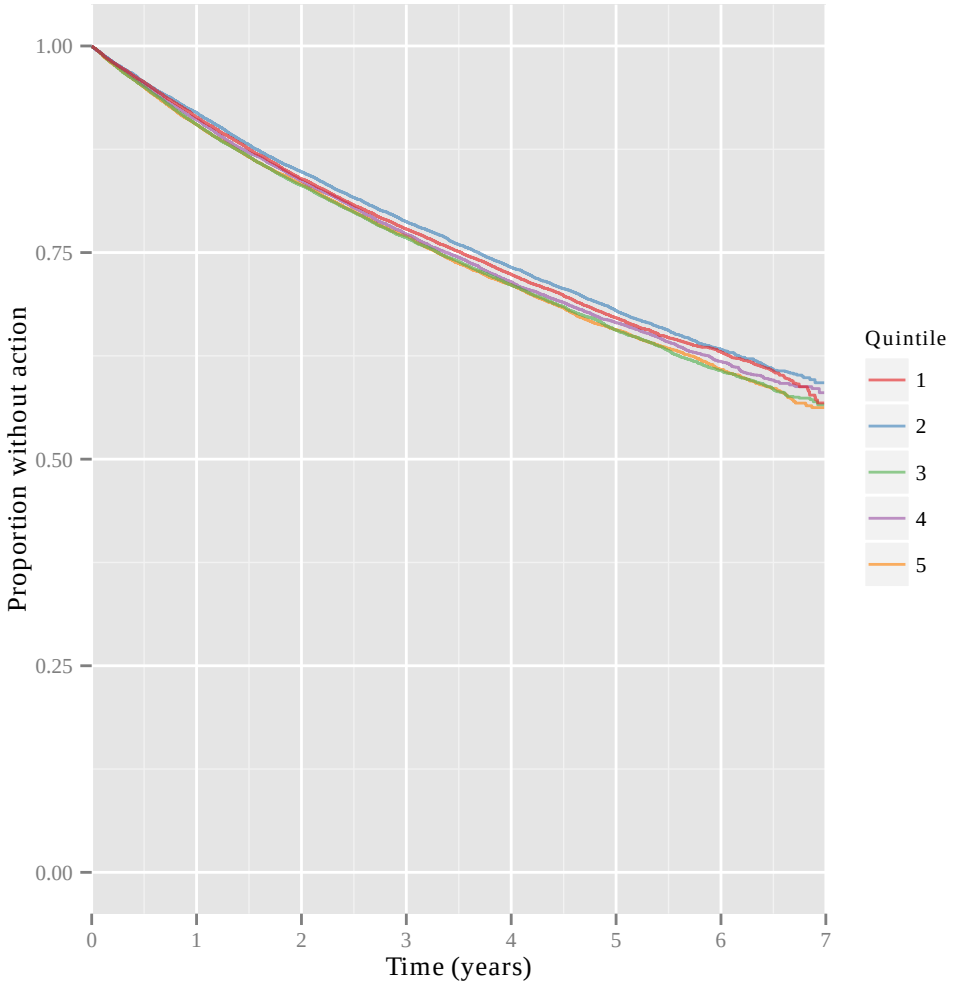
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.00	(0.97; 1.03)
Quintile 3	1.03	(1.00; 1.06)
Quintile 4	1.02	(0.99; 1.05)
Quintile 5	1.03	(1.00; 1.06)
Male	1	(Reference)
Female	1.92	(1.89; 1.95)
No hyp.	1	(Reference)
Hyp. contr.	3.88	(3.74; 4.02)
Hyp. uncontr.	5.18	(4.86; 5.51)
Untreat. hyp.	1.65	(1.57; 1.75)
No oth. co.	1	(Reference)
Other co.	1.38	(1.33; 1.43)

Number of clinical triggers 122486; Number of clinical actions 64312. ICC for practice = 0.125. Missing values imputed using MICE.



Risk and risk factor attainment

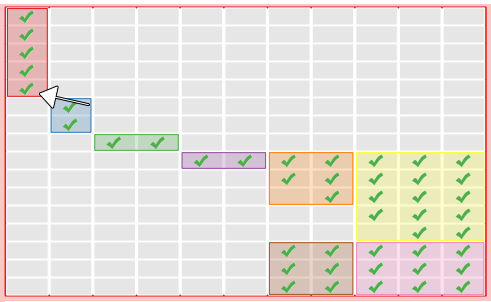
Kaplan−Meier plot for 'aged 40+ with no high risk diagnosis' and 'measurement of cholesterol'. Incident clinical trigger (triggers = 122486; actions = 28652)



Mixed−effects model for 'aged 40+ with no high risk diagnosis' and 'measurement of cholesterol'. Incident clinical trigger

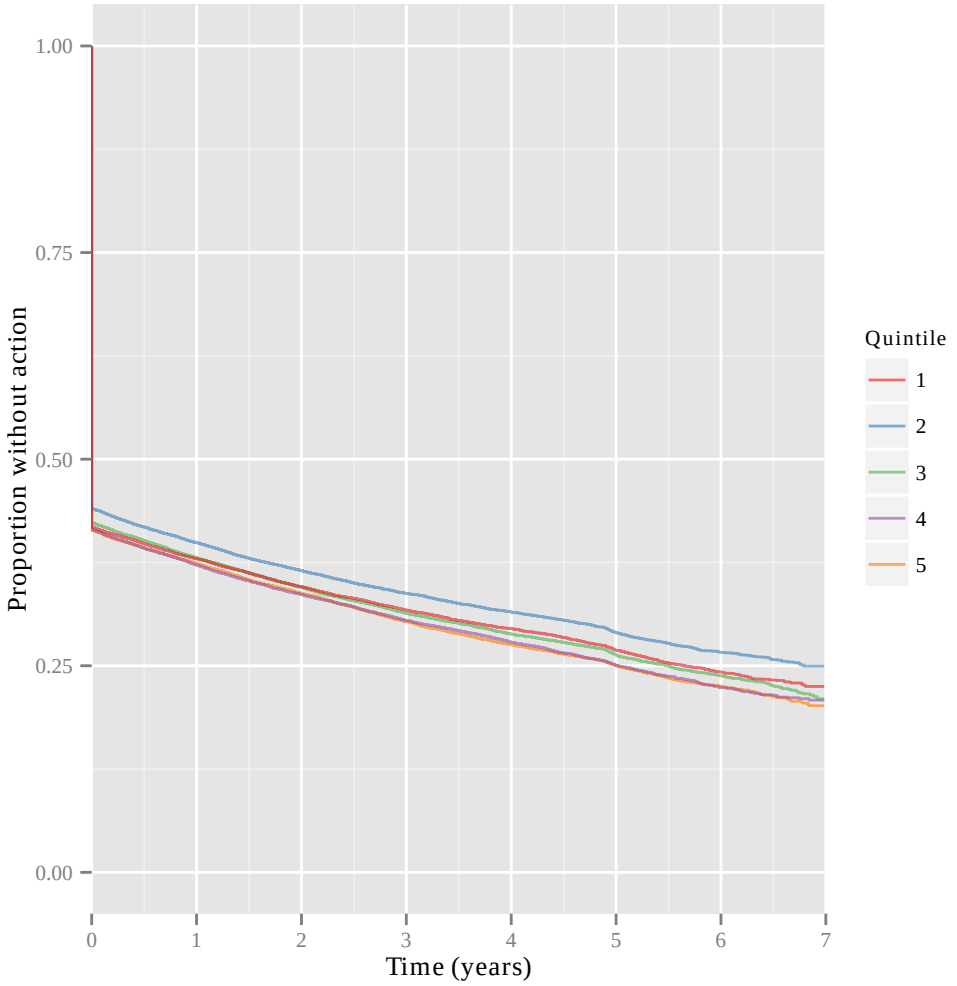
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.95	(0.91; 0.99)
Quintile 3	1.01	(0.97; 1.05)
Quintile 4	0.97	(0.93; 1.02)
Quintile 5	0.97	(0.93; 1.01)
Male	1	(Reference)
Female	1.00	(0.98; 1.02)
No hyp.	1	(Reference)
Hyp. contr.	4.62	(4.42; 4.83)
Hyp. uncontr.	5.03	(4.66; 5.42)
Untreat. hyp.	2.16	(2.02; 2.32)
No oth. co.	1	(Reference)
Other co.	1.23	(1.17; 1.30)

Number of clinical triggers 122486; Number of clinical actions 28652. ICC for practice = 0.055. Missing values imputed using MICE.



Risk and risk factor attainment

Kaplan−Meier plot for 'aged 40+ with no high risk diagnosis' and 'full cardiovascular risk assessment'. Incident clinical trigger (triggers = 122486; actions = 84969)



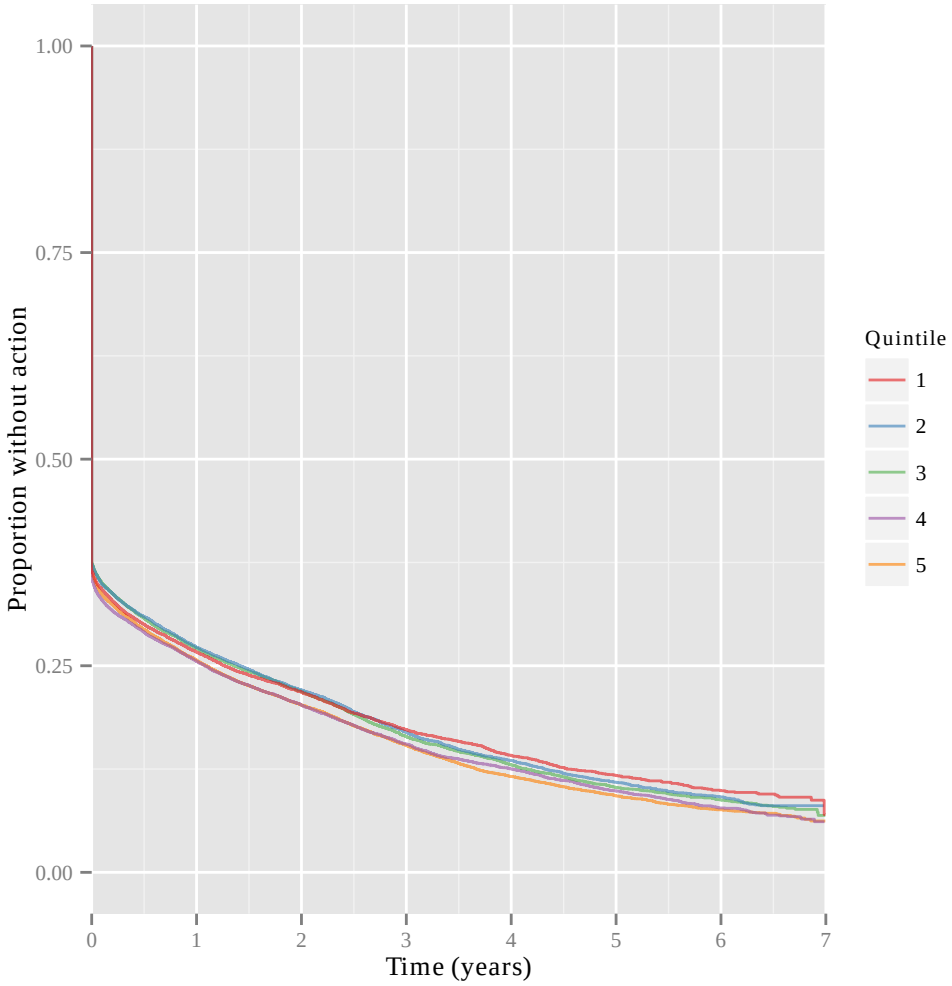
Mixed−effects model for 'aged 40+ with no high risk diagnosis' and 'full cardiovascular risk assessment'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.00	(0.98; 1.03)
Quintile 3	1.00	(0.97; 1.02)
Quintile 4	0.98	(0.95; 1.00)
Quintile 5	0.97	(0.95; 1.00)
Male	1	(Reference)
Female	2.21	(2.18; 2.24)
No hyp.	1	(Reference)
Hyp. contr.	1.96	(1.89; 2.02)
Hyp. uncontr.	2.24	(2.11; 2.37)
Untreat. hyp.	2.22	(2.12; 2.32)
No oth. co.	1	(Reference)
Other co.	1.38	(1.34; 1.42)

Number of clinical triggers 122486; Number of clinical actions 84969. ICC for practice = 0.166. Missing values imputed using MICE.

Smoking management

Kaplan−Meier plot for 'first identified as smoker' and 'provision of smoking−cessation advice'. Incident clinical trigger (triggers = 55161; actions = 45926)



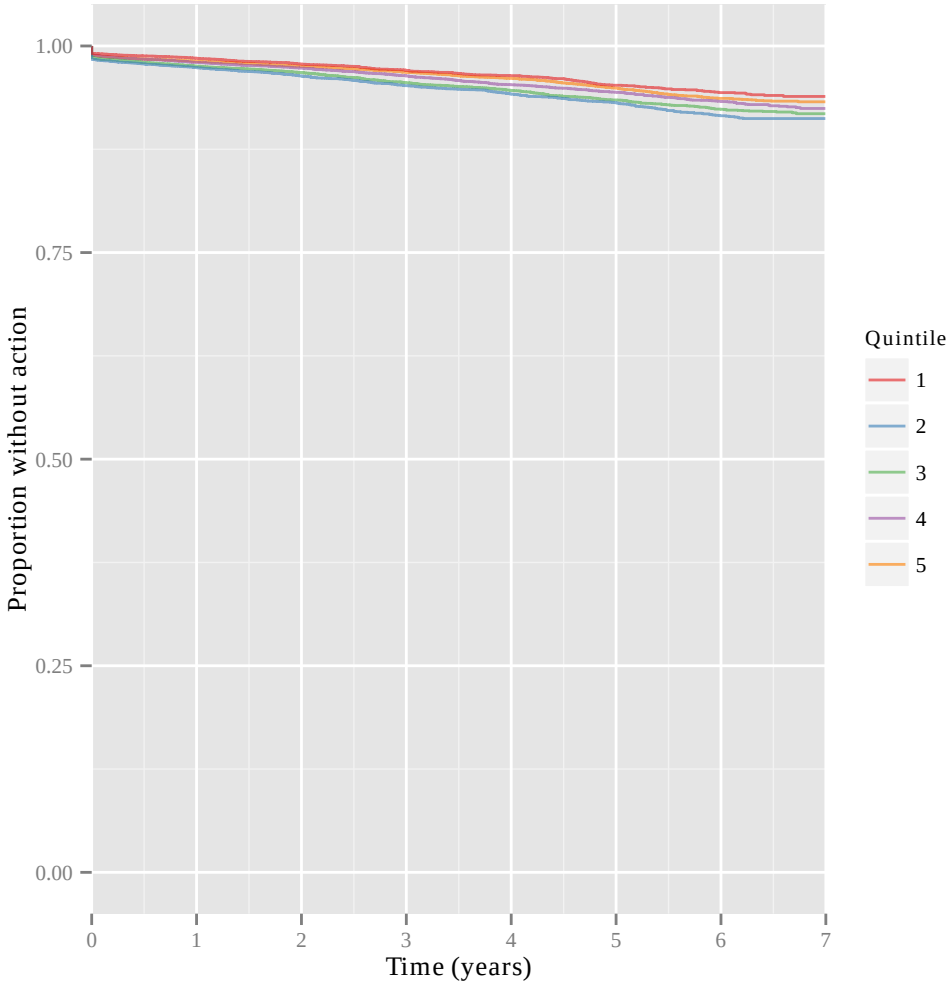
Mixed−effects model for 'first identified as smoker' and 'provision of smoking−cessation advice'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.02	(0.99; 1.06)
Quintile 3	1.05	(1.02; 1.09)
Quintile 4	1.08	(1.05; 1.12)
Quintile 5	1.10	(1.06; 1.14)
Age 35 to 39	0.96	(0.92; 0.99)
Age 40 to 44	0.98	(0.95; 1.02)
Age 45 to 49	1.02	(0.99; 1.06)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.01	(0.98; 1.05)
Age 60 to 64	1.01	(0.97; 1.05)
Age 65 to 69	0.98	(0.94; 1.03)
Age 70 to 74	0.93	(0.88; 0.98)
Age 75 to 79	0.92	(0.86; 0.97)
Age 80 to 84	0.82	(0.77; 0.89)
Age 85+	0.80	(0.73; 0.88)
Male	1	(Reference)
Female	1.06	(1.03; 1.08)
BMI low / norm.	1	(Reference)
Overweight	0.99	(0.96; 1.01)
Obese	1.01	(0.98; 1.04)
No hyp.	1	(Reference)
Hyp. contr.	1.19	(1.15; 1.23)
Hyp. uncontr.	1.22	(1.16; 1.28)
Untreat. hyp.	1.02	(0.97; 1.08)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.08	(1.03; 1.13)
No CVA	1	(Reference)
CVA	1.10	(1.04; 1.17)
No oth. co.	1	(Reference)
Other co.	1.06	(1.02; 1.10)
No diabetes	1	(Reference)
Diabetes	1.03	(0.98; 1.08)

Number of clinical triggers 55161; Number of clinical actions 45926. ICC for practice = 0.056. Missing values imputed using MICE.

Smoking management

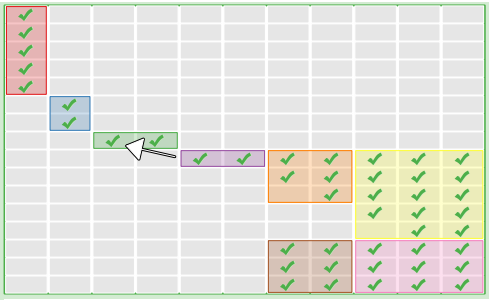
Kaplan−Meier plot for 'first identified as smoker' and 'referral to smoking−cessation services'. Incident clinical trigger (triggers = 55161; actions = 2514)



Mixed−effects model for 'first identified as smoker' and 'referral to smoking−cessation services'. Incident clinical trigger

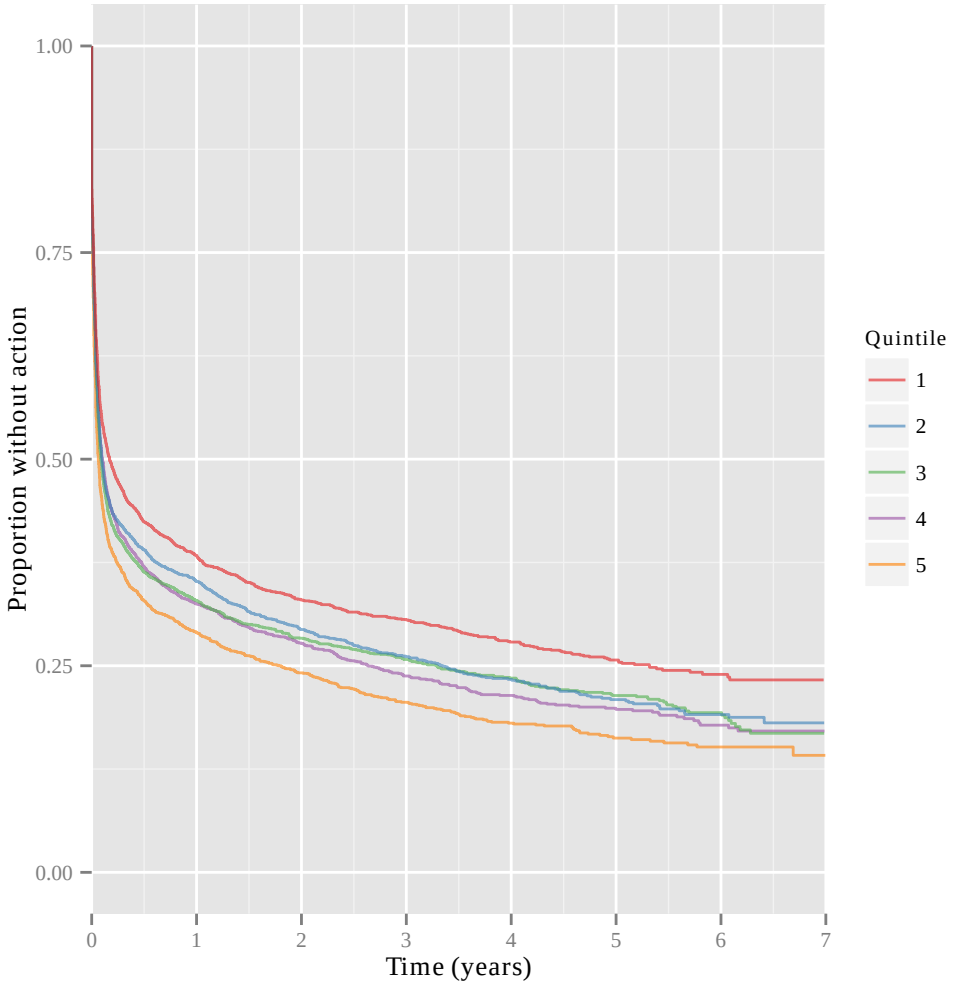
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.06	(0.90; 1.23)
Quintile 3	1.10	(0.93; 1.29)
Quintile 4	1.14	(0.97; 1.33)
Quintile 5	1.17	(0.99; 1.38)
Age 35 to 39	0.97	(0.85; 1.12)
Age 40 to 44	1.02	(0.89; 1.18)
Age 45 to 49	0.98	(0.85; 1.13)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.99	(0.85; 1.15)
Age 60 to 64	1.01	(0.85; 1.19)
Age 65 to 69	0.99	(0.81; 1.20)
Age 70 to 74	0.66	(0.52; 0.85)
Age 75 to 79	0.41	(0.29; 0.58)
Age 80 to 84	0.17	(0.09; 0.33)
Age 85+	0.13	(0.05; 0.34)
Male	1	(Reference)
Female	1.12	(1.02; 1.23)
BMI low / norm.	1	(Reference)
Overweight	0.99	(0.90; 1.10)
Obese	1.05	(0.93; 1.19)
No hyp.	1	(Reference)
Hyp. contr.	1.43	(1.25; 1.64)
Hyp. uncontr.	1.27	(1.03; 1.57)
Untreat. hyp.	1.10	(0.86; 1.40)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.11	(0.75; 1.65)
No CVA	1	(Reference)
CVA	1.02	(0.77; 1.37)
No oth. co.	1	(Reference)
Other co.	1.46	(1.26; 1.69)
No diabetes	1	(Reference)
Diabetes	1.20	(0.99; 1.46)

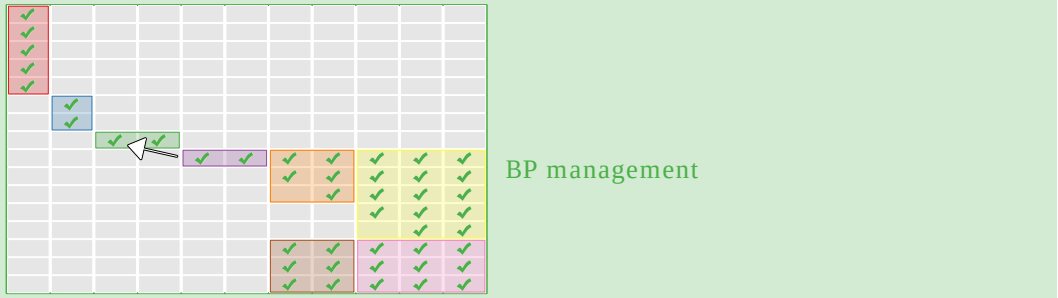
Number of clinical triggers 55161; Number of clinical actions 2514. ICC for practice = 0.533. Missing values imputed using MICE.



BP management

Kaplan−Meier plot for 'BP raised and low−risk' and 'treatment with antihypertensive medication'. Incident clinical trigger (triggers = 13814; actions = 9899)

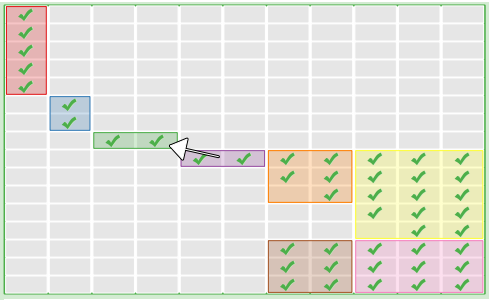




Mixed−effects model for 'BP raised and low−risk' and 'treatment with antihypertensive medication'. Incident clinical trigger

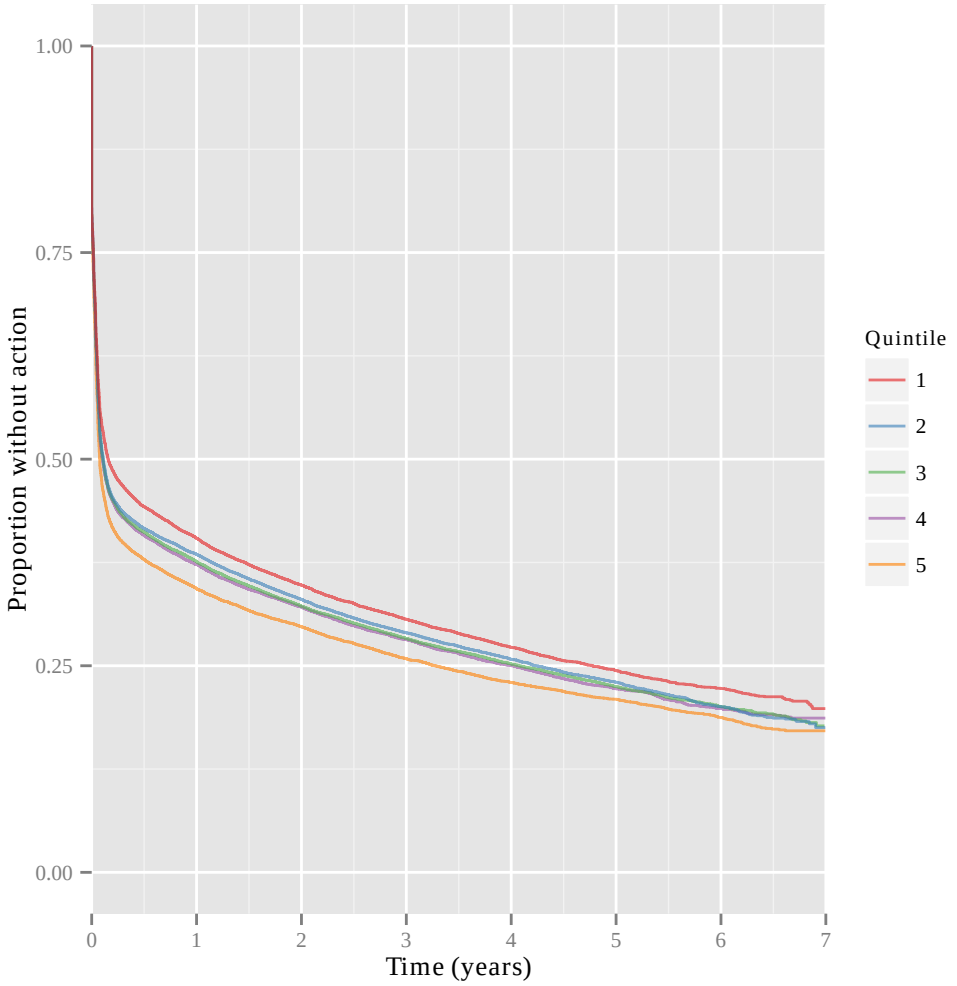
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.08	(1.00; 1.15)
Quintile 3	1.14	(1.06; 1.22)
Quintile 4	1.11	(1.04; 1.20)
Quintile 5	1.22	(1.13; 1.31)
Age 35 to 39	0.96	(0.87; 1.06)
Age 40 to 44	1.16	(1.07; 1.25)
Age 45 to 49	1.09	(1.01; 1.17)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.89	(0.82; 0.95)
Age 60 to 64	0.80	(0.74; 0.87)
Age 65 to 69	0.95	(0.87; 1.05)
Age 70 to 74	1.08	(0.98; 1.19)
Age 75 to 79	1.09	(0.99; 1.20)
Age 80 to 84	1.15	(1.04; 1.28)
Age 85+	0.93	(0.83; 1.05)
Male	1	(Reference)
Female	0.95	(0.90; 0.99)
BMI low / norm.	1	(Reference)
Overweight	1.03	(0.97; 1.09)
Obese	1.03	(0.96; 1.11)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.08	(0.99; 1.17)
No oth. co.	1	(Reference)
Other co.	1.08	(1.00; 1.17)

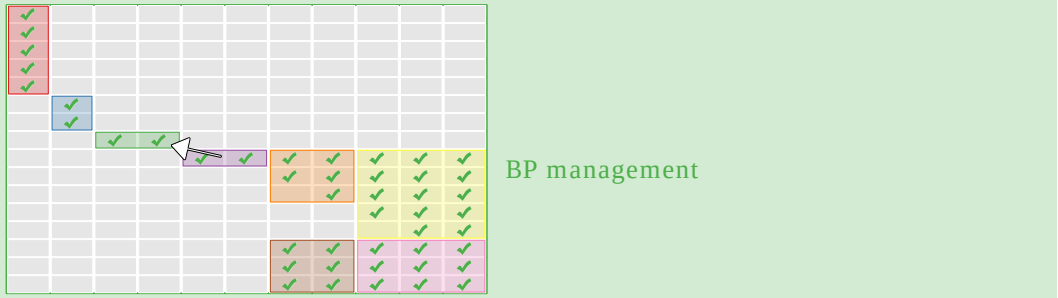
Number of clinical triggers 13814; Number of clinical actions 9899. ICC for practice = 0.052. Missing values imputed using MICE.



BP management

Kaplan−Meier plot for 'BP raised and high−risk' and 'treatment with antihypertensive medication'. Incident clinical trigger (triggers = 106079; actions = 75797)

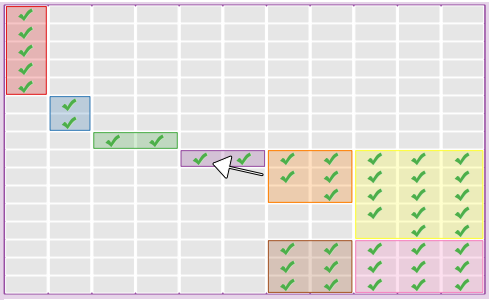




Mixed−effects model for 'BP raised and high−risk' and 'treatment with antihypertensive medication'. Incident clinical trigger

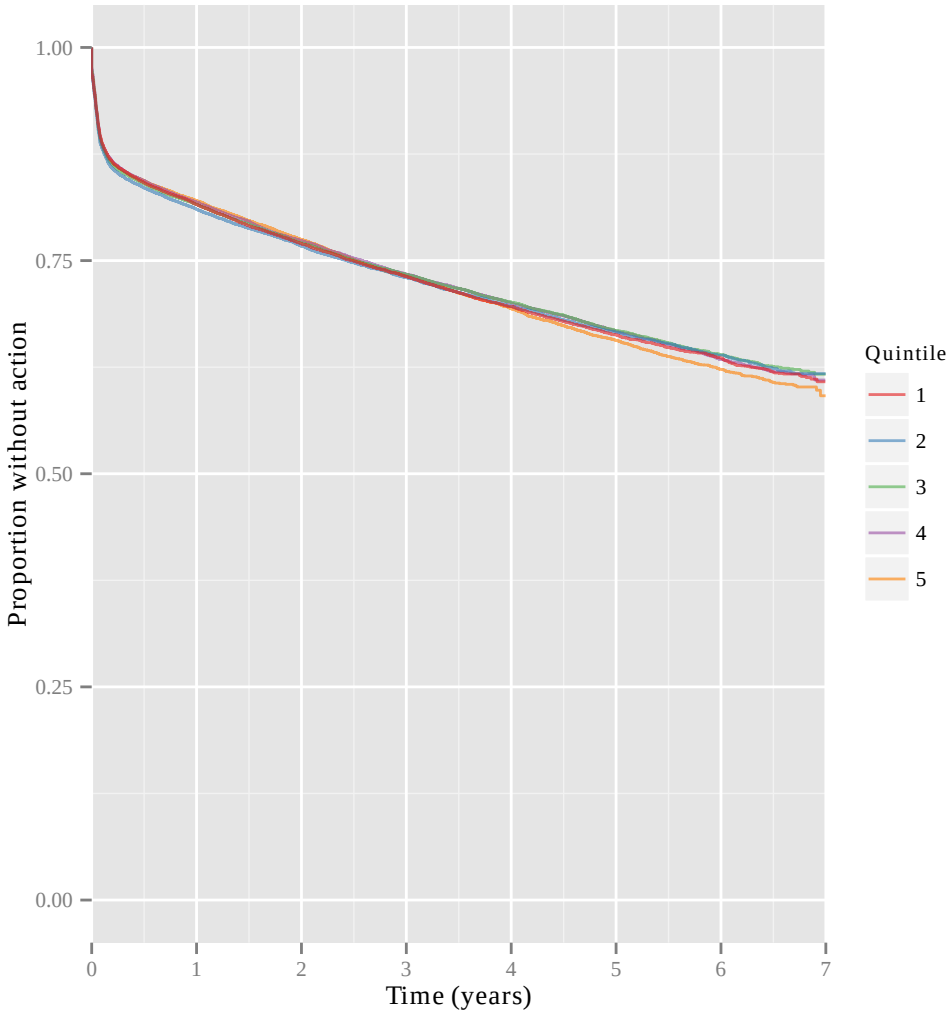
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.01	(0.99; 1.04)
Quintile 3	1.00	(0.97; 1.02)
Quintile 4	1.00	(0.97; 1.03)
Quintile 5	1.00	(0.98; 1.03)
Age 35 to 39	0.88	(0.81; 0.96)
Age 40 to 44	1.09	(1.03; 1.15)
Age 45 to 49	1.06	(1.02; 1.10)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.83	(0.80; 0.85)
Age 60 to 64	0.71	(0.69; 0.73)
Age 65 to 69	0.64	(0.62; 0.65)
Age 70 to 74	0.60	(0.58; 0.62)
Age 75 to 79	0.57	(0.55; 0.59)
Age 80 to 84	0.55	(0.53; 0.57)
Age 85+	0.51	(0.49; 0.53)
Male	1	(Reference)
Female	1.30	(1.28; 1.32)
BMI low / norm.	1	(Reference)
Overweight	1.10	(1.08; 1.12)
Obese	1.17	(1.15; 1.19)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.97	(0.96; 0.99)
No oth. co.	1	(Reference)
Other co.	0.95	(0.93; 0.97)
Indication 1	1	(Reference)
Indication 2	1.93	(1.85; 2.00)
Indic. years	1.01	(1.01; 1.02)

Number of clinical triggers 106079; Number of clinical actions 75797. ICC for practice = 0.046. Missing values imputed using MICE.



High risk statin management

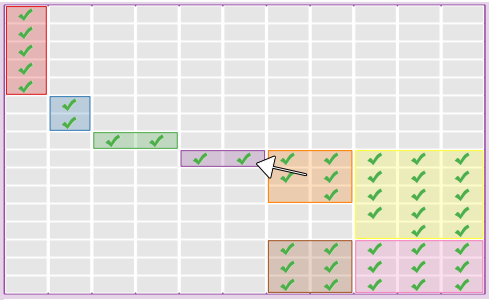
Kaplan−Meier plot for 'risk assessed high' and 'statin'. Incident clinical trigger (triggers = 120459; actions = 33226)



Mixed−effects model for 'risk assessed high' and 'statin'. Incident clinical trigger

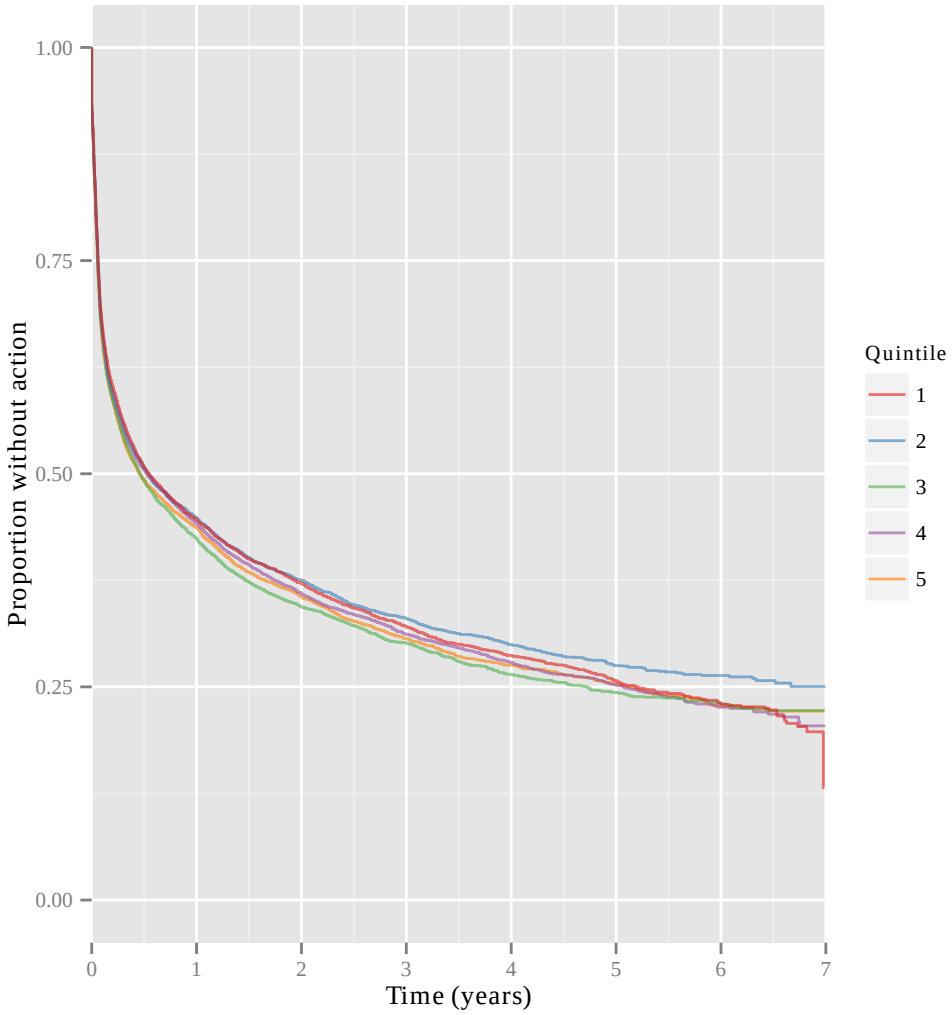
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.01	(0.96; 1.06)
Quintile 3	0.99	(0.94; 1.04)
Quintile 4	1.01	(0.96; 1.06)
Quintile 5	1.01	(0.95; 1.07)
Age 35 to 39	0.77	(0.58; 1.03)
Age 40 to 44	0.94	(0.84; 1.06)
Age 45 to 49	0.90	(0.84; 0.96)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.20	(1.14; 1.26)
Age 60 to 64	1.30	(1.24; 1.37)
Age 65 to 69	1.31	(1.24; 1.39)
Age 70 to 74	1.19	(1.12; 1.27)
Age 75 to 79	0.82	(0.75; 0.88)
Age 80 to 84	0.56	(0.51; 0.62)
Age 85+	0.34	(0.29; 0.40)
Male	1	(Reference)
Female	1.28	(1.24; 1.32)
Non−smoker	1	(Reference)
Smoker	1.00	(0.96; 1.03)
BMI low / norm.	1	(Reference)
Overweight	1.05	(1.01; 1.09)
Obese	0.92	(0.88; 0.96)
No hyp.	1	(Reference)
Hyp. contr.	1.80	(1.73; 1.88)
Hyp. uncontr.	1.79	(1.71; 1.87)
Untreat. hyp.	1.43	(1.36; 1.49)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	2.35	(2.21; 2.51)
No oth. co.	1	(Reference)
Other co.	0.90	(0.85; 0.95)

Number of clinical triggers 105301; Number of clinical actions 20661. ICC for practice = 0.089. Missing values imputed using MICE.



High risk statin management

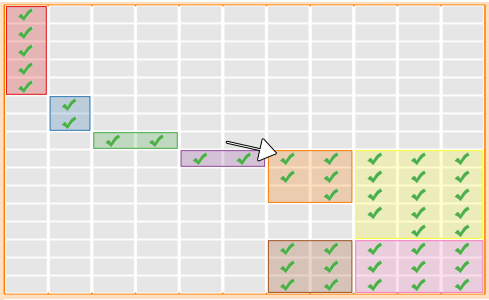
Kaplan−Meier plot for 'high−risk diagnosis' and 'statin'. Incident clinical trigger (triggers = 45601; actions = 29135)



Mixed−effects model for 'high−risk diagnosis' and 'statin'. Incident clinical trigger

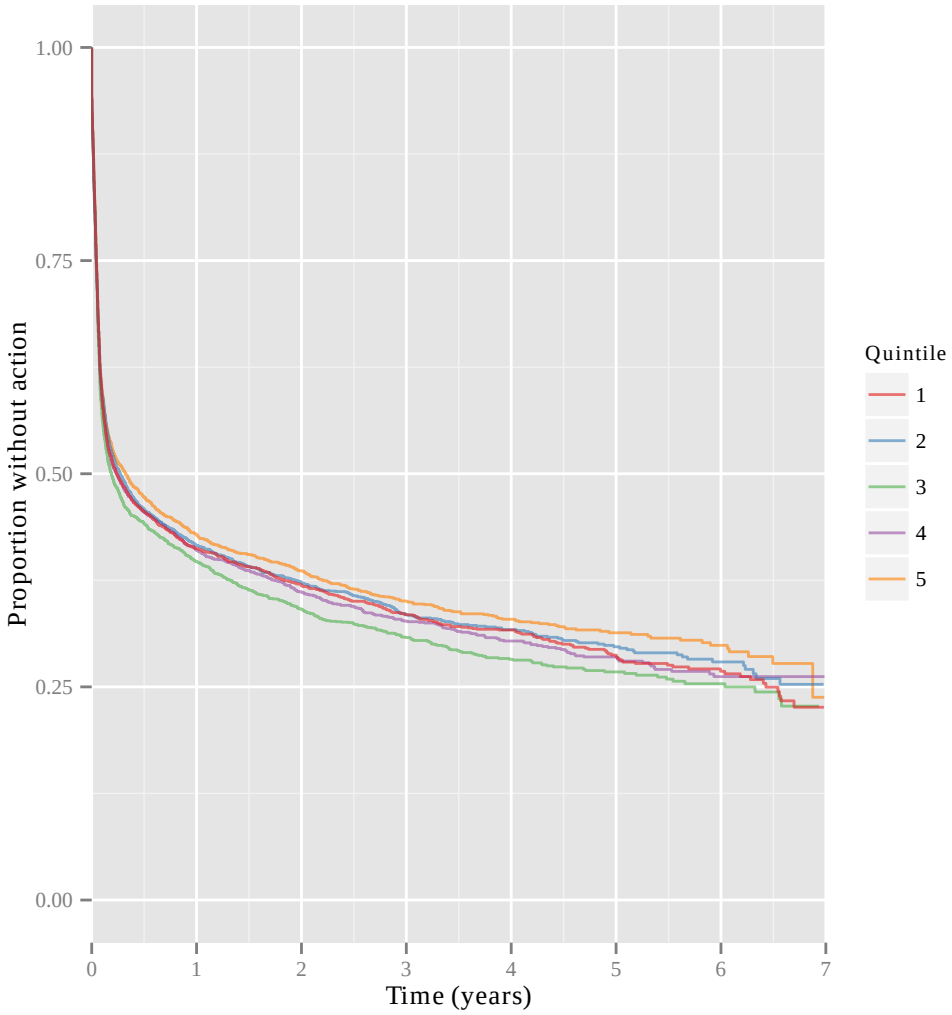
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.97	(0.92; 1.02)
Quintile 3	1.01	(0.96; 1.07)
Quintile 4	1.02	(0.97; 1.08)
Quintile 5	1.01	(0.96; 1.07)
Age 35 to 39	0.55	(0.50; 0.61)
Age 40 to 44	0.79	(0.73; 0.85)
Age 45 to 49	0.92	(0.86; 0.98)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.06	(1.00; 1.13)
Age 60 to 64	1.11	(1.04; 1.18)
Age 65 to 69	1.10	(1.04; 1.18)
Age 70 to 74	1.10	(1.02; 1.17)
Age 75 to 79	0.96	(0.90; 1.03)
Age 80 to 84	0.74	(0.68; 0.80)
Age 85+	0.48	(0.44; 0.52)
Male	1	(Reference)
Female	1.09	(1.06; 1.13)
Non−smoker	1	(Reference)
Smoker	1.12	(1.08; 1.17)
BMI low / norm.	1	(Reference)
Overweight	1.06	(1.01; 1.11)
Obese	0.99	(0.93; 1.04)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.49	(1.40; 1.59)
No oth. co.	1	(Reference)
Other co.	0.72	(0.70; 0.75)
Indication 1	1	(Reference)
Indication 2	1.15	(1.10; 1.20)
Indic. years	1.00	(1.00; 1.01)

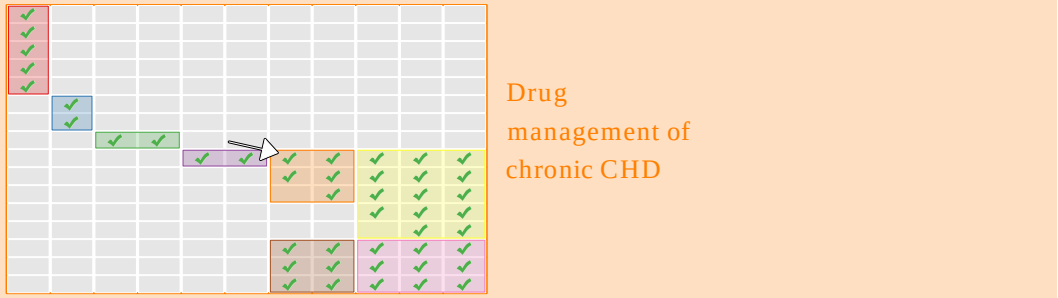
Number of clinical triggers 34387; Number of clinical actions 19389. ICC for practice = 0.062. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina' and 'statin'. Incident clinical trigger (triggers = 18934; actions = 11230)

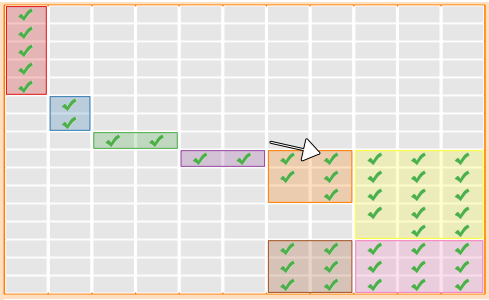




Mixed−effects model for 'stable angina' and 'statin'. Incident clinical trigger

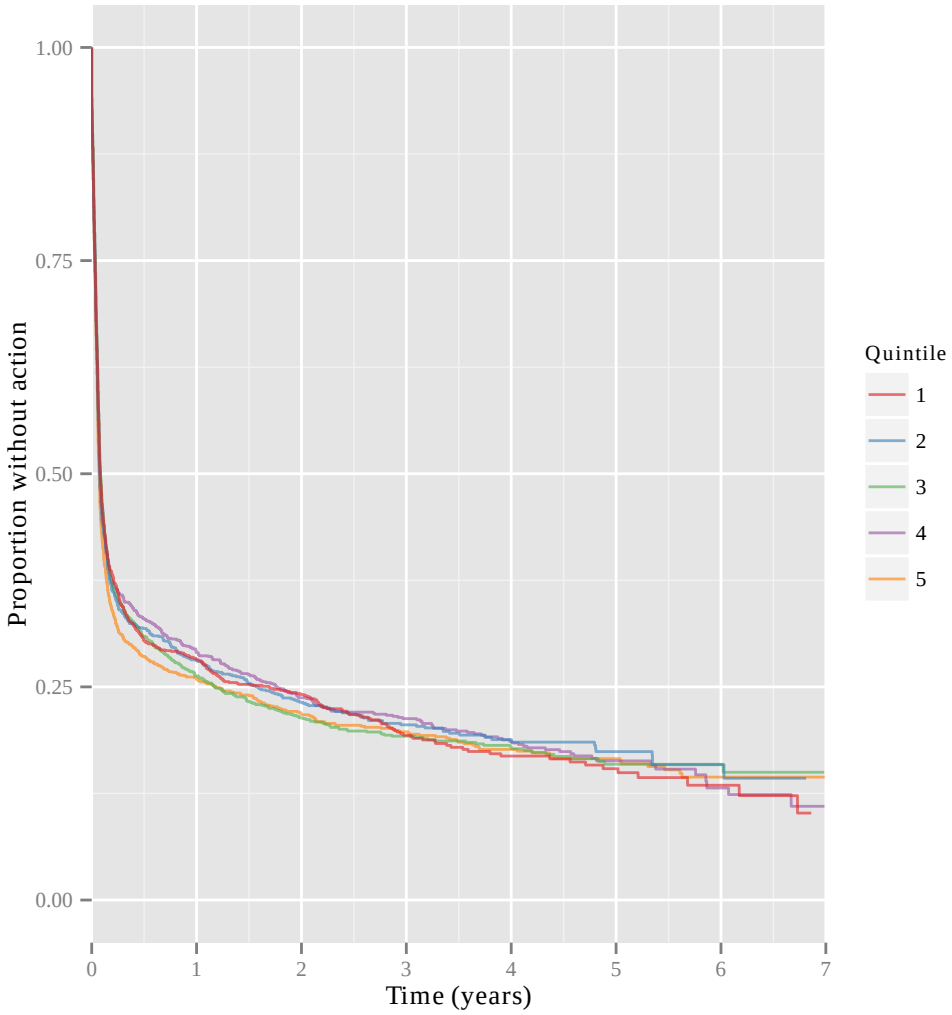
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.96	(0.87; 1.07)
Quintile 3	1.04	(0.94; 1.15)
Quintile 4	0.99	(0.89; 1.10)
Quintile 5	0.87	(0.79; 0.97)
Age 35 to 39	0.40	(0.27; 0.58)
Age 40 to 44	0.67	(0.54; 0.84)
Age 45 to 49	0.87	(0.74; 1.03)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.08	(0.95; 1.23)
Age 60 to 64	1.08	(0.95; 1.24)
Age 65 to 69	1.00	(0.88; 1.14)
Age 70 to 74	0.85	(0.74; 0.97)
Age 75 to 79	0.66	(0.57; 0.76)
Age 80 to 84	0.50	(0.43; 0.58)
Age 85+	0.24	(0.20; 0.29)
Male	1	(Reference)
Female	0.96	(0.90; 1.03)
Non−smoker	1	(Reference)
Smoker	0.95	(0.88; 1.03)
BMI low / norm.	1	(Reference)
Overweight	1.06	(0.98; 1.15)
Obese	0.88	(0.80; 0.97)
No hyp.	1	(Reference)
Hyp. contr.	0.91	(0.85; 0.98)
Hyp. uncontr.	1.09	(0.99; 1.19)
Untreat. hyp.	1.28	(1.15; 1.44)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.44	(1.27; 1.63)
No CVA	1	(Reference)
CVA	1.13	(0.99; 1.30)
No oth. co.	1	(Reference)
Other co.	0.63	(0.59; 0.68)
Indication 1	1	(Reference)
Indication 2	1.21	(1.11; 1.31)
Indication 3	1.10	(0.85; 1.42)
Indic. years	1.00	(0.99; 1.01)

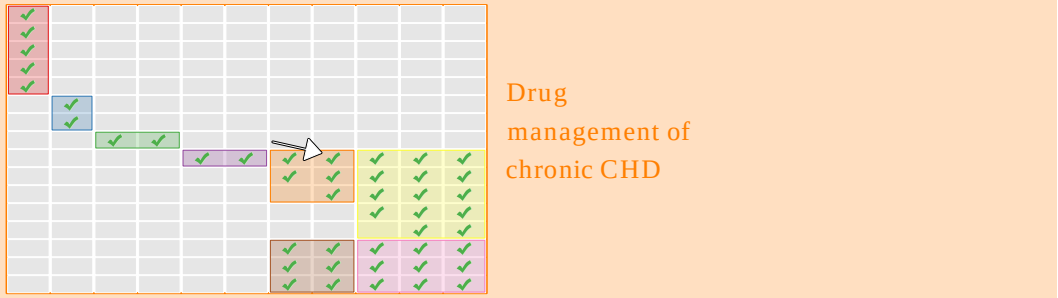
Number of clinical triggers 11104; Number of clinical actions 4660. ICC for practice = 0.04. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina and diabetes' and 'statin'. Incident clinical trigger (triggers = 8956; actions = 6588)



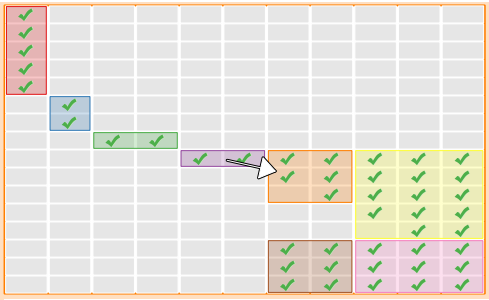


Mixed−effects model for 'stable angina and diabetes' and 'statin'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.96	(0.75; 1.21)
Quintile 3	1.09	(0.86; 1.36)
Quintile 4	1.07	(0.85; 1.35)
Quintile 5	0.97	(0.77; 1.23)
Age 35 to 39	0.94	(0.52; 1.71)
Age 40 to 44	0.96	(0.56; 1.65)
Age 45 to 49	1.15	(0.76; 1.72)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.88	(0.63; 1.24)
Age 60 to 64	0.88	(0.64; 1.21)
Age 65 to 69	0.83	(0.60; 1.13)
Age 70 to 74	0.76	(0.56; 1.04)
Age 75 to 79	0.64	(0.47; 0.88)
Age 80 to 84	0.50	(0.36; 0.70)
Age 85+	0.24	(0.16; 0.36)
Male	1	(Reference)
Female	1.08	(0.94; 1.24)
Non−smoker	1	(Reference)
Smoker	0.93	(0.77; 1.12)
BMI low / norm.	1	(Reference)
Overweight	1.01	(0.82; 1.24)
Obese	0.96	(0.79; 1.16)
No hyp.	1	(Reference)
Hyp. contr.	1.01	(0.86; 1.19)
Hyp. uncontr.	1.38	(1.13; 1.68)
Untreat. hyp.	1.34	(0.99; 1.82)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.52	(1.29; 1.78)
No CVA	1	(Reference)
CVA	0.98	(0.78; 1.23)
No oth. co.	1	(Reference)
Other co.	0.73	(0.63; 0.84)
Indication 1	1	(Reference)
Indication 2	2.34	(1.51; 3.63)
Indication 3	2.41	(1.53; 3.79)
Indication 4	1.15	(0.38; 3.49)

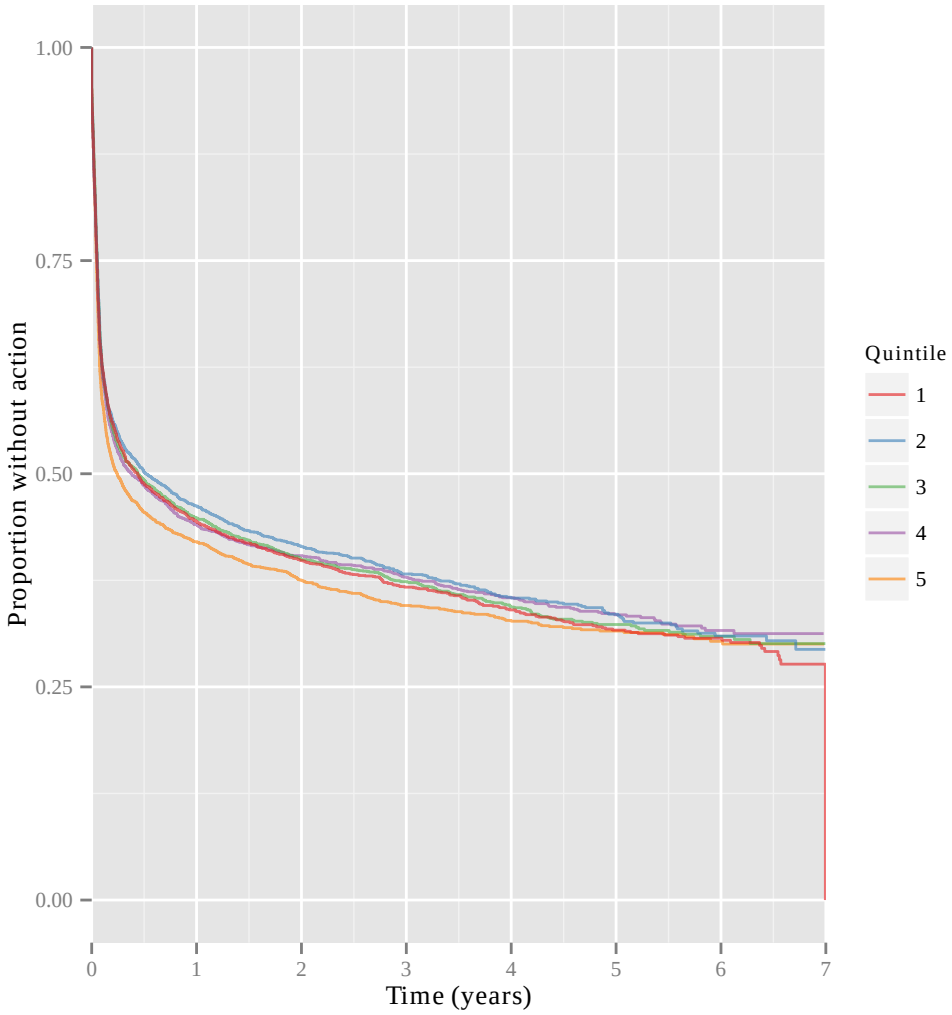
	HR	95% CI
Indic. years	1.00	(0.99; 1.01)

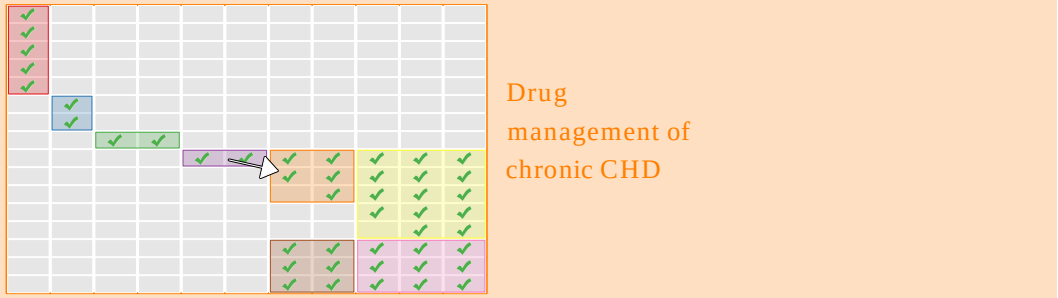
Number of clinical triggers 2457; Number of clinical actions 968. ICC for practice = 0.067. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina' and 'aspirin'. Incident clinical trigger (triggers = 18934; actions = 10703)

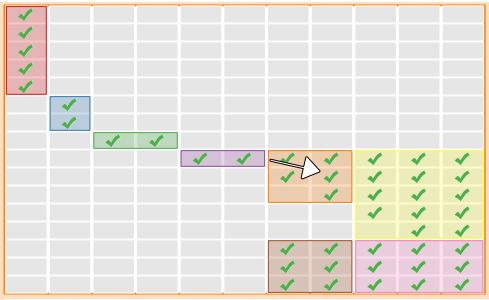




Mixed−effects model for 'stable angina' and 'aspirin'. Incident clinical trigger

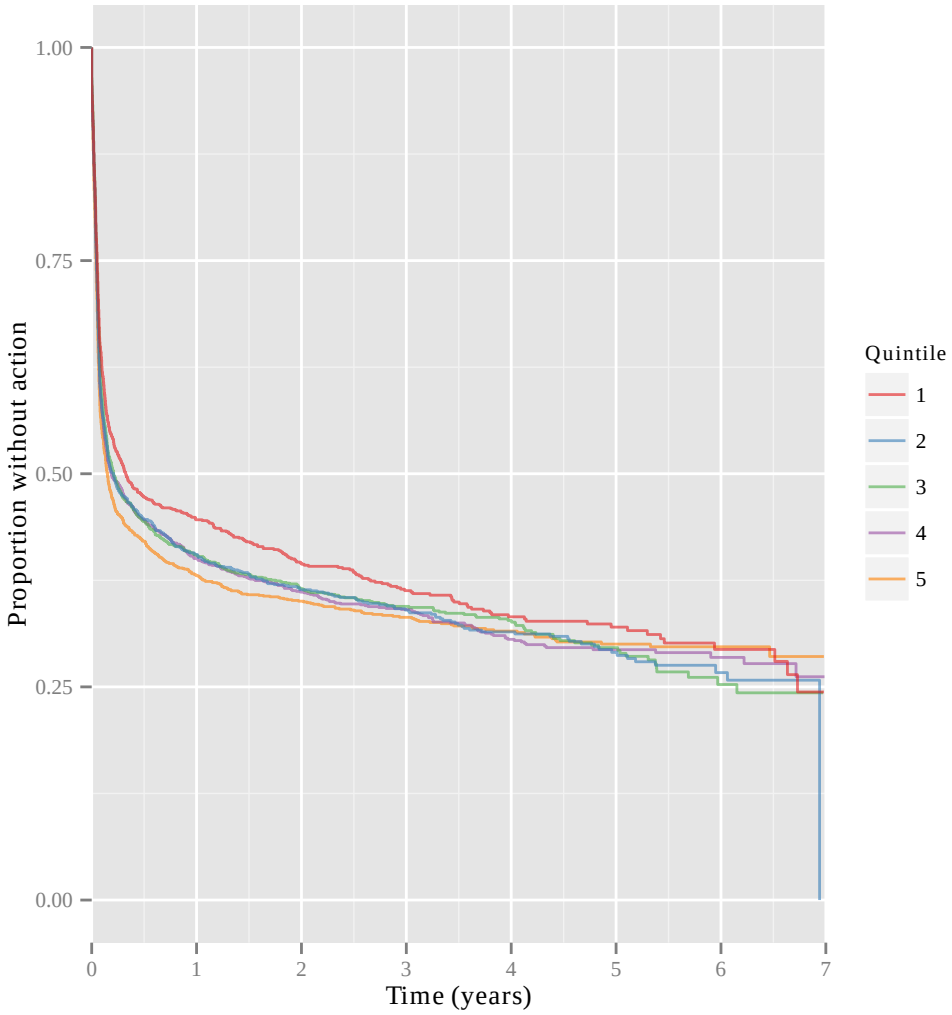
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.95	(0.85; 1.06)
Quintile 3	1.02	(0.91; 1.14)
Quintile 4	1.00	(0.89; 1.12)
Quintile 5	0.98	(0.88; 1.10)
Age 35 to 39	0.49	(0.34; 0.72)
Age 40 to 44	0.95	(0.76; 1.18)
Age 45 to 49	0.97	(0.81; 1.15)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.18	(1.03; 1.35)
Age 60 to 64	1.19	(1.04; 1.36)
Age 65 to 69	1.06	(0.92; 1.22)
Age 70 to 74	0.96	(0.83; 1.12)
Age 75 to 79	0.90	(0.77; 1.04)
Age 80 to 84	0.89	(0.76; 1.05)
Age 85+	0.71	(0.59; 0.85)
Male	1	(Reference)
Female	0.86	(0.80; 0.92)
Non−smoker	1	(Reference)
Smoker	1.06	(0.97; 1.16)
BMI low / norm.	1	(Reference)
Overweight	1.00	(0.93; 1.09)
Obese	0.90	(0.82; 0.98)
No hyp.	1	(Reference)
Hyp. contr.	0.91	(0.84; 0.98)
Hyp. uncontr.	1.03	(0.93; 1.13)
Untreat. hyp.	1.26	(1.11; 1.44)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.13	(0.99; 1.28)
No CVA	1	(Reference)
CVA	0.81	(0.70; 0.94)
No oth. co.	1	(Reference)
Other co.	0.64	(0.59; 0.69)

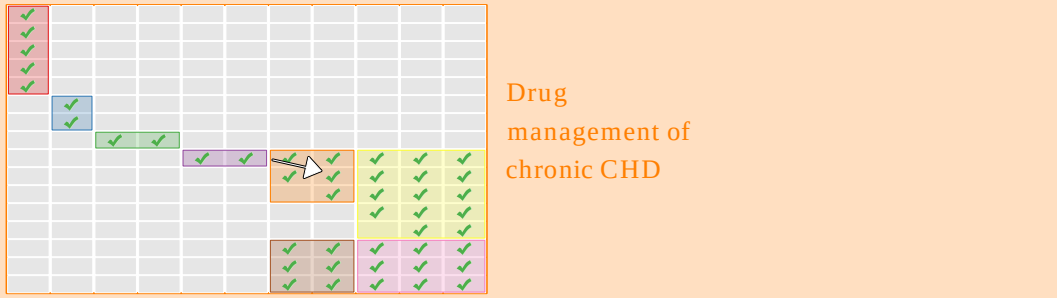
Number of clinical triggers 9433; Number of clinical actions 3923. ICC for practice = 0.056. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina and diabetes' and 'aspirin'. Incident clinical trigger (triggers = 8956; actions = 5472)

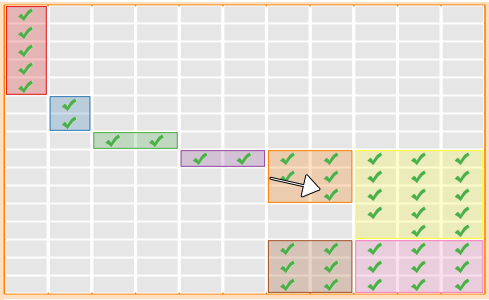




Mixed−effects model for 'stable angina and diabetes' and 'aspirin'. Incident clinical trigger

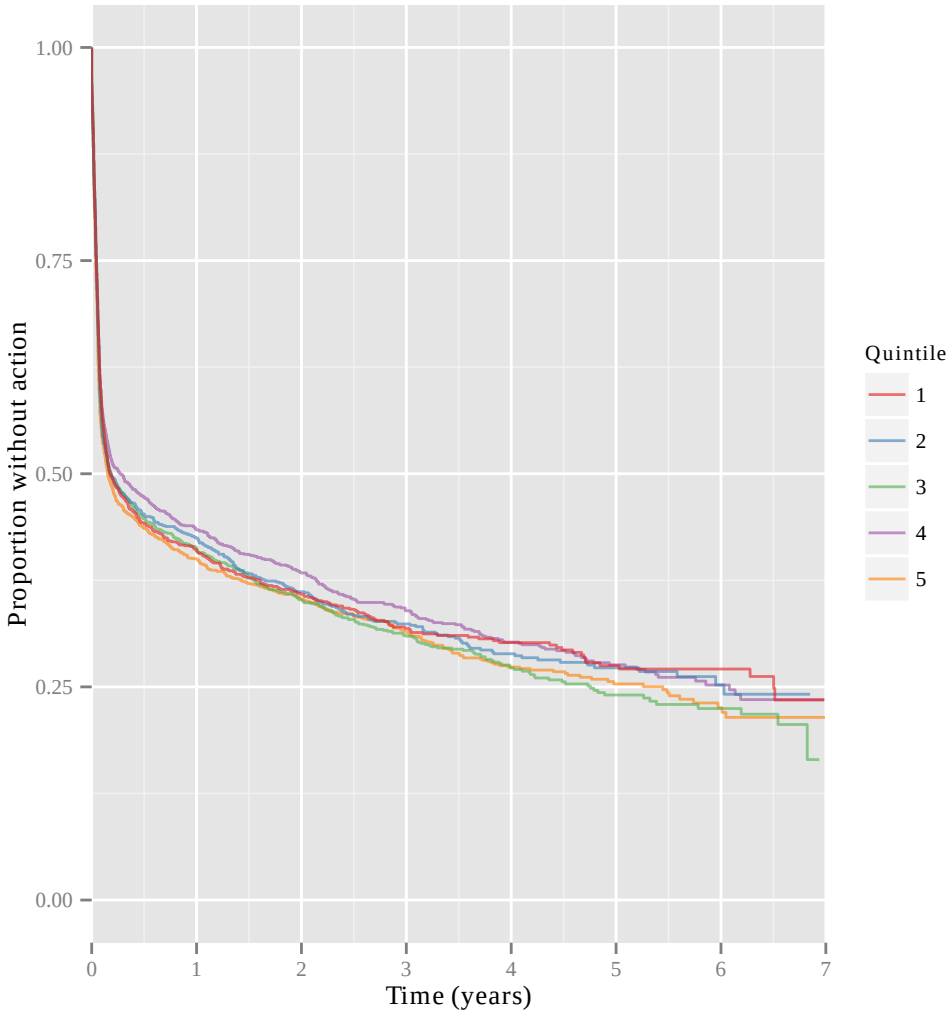
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.88	(0.70; 1.12)
Quintile 3	1.09	(0.87; 1.37)
Quintile 4	0.96	(0.77; 1.20)
Quintile 5	1.01	(0.81; 1.27)
Age 35 to 39	1.12	(0.60; 2.10)
Age 40 to 44	1.14	(0.72; 1.81)
Age 45 to 49	1.07	(0.71; 1.59)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.10	(0.80; 1.50)
Age 60 to 64	1.00	(0.74; 1.36)
Age 65 to 69	0.88	(0.65; 1.20)
Age 70 to 74	0.94	(0.69; 1.27)
Age 75 to 79	0.93	(0.68; 1.28)
Age 80 to 84	0.99	(0.70; 1.39)
Age 85+	0.81	(0.55; 1.20)
Male	1	(Reference)
Female	0.87	(0.75; 0.99)
Non−smoker	1	(Reference)
Smoker	1.00	(0.83; 1.21)
BMI low / norm.	1	(Reference)
Overweight	1.11	(0.90; 1.38)
Obese	0.99	(0.80; 1.22)
No hyp.	1	(Reference)
Hyp. contr.	0.93	(0.79; 1.10)
Hyp. uncontr.	1.18	(0.97; 1.44)
Untreat. hyp.	1.22	(0.87; 1.73)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.21	(1.00; 1.47)
No CVA	1	(Reference)
CVA	0.90	(0.71; 1.16)
No oth. co.	1	(Reference)
Other co.	0.69	(0.60; 0.80)
Indication 1	1	(Reference)
Indication 2	0.44	(0.36; 0.54)
Indic. years	1.01	(0.99; 1.03)

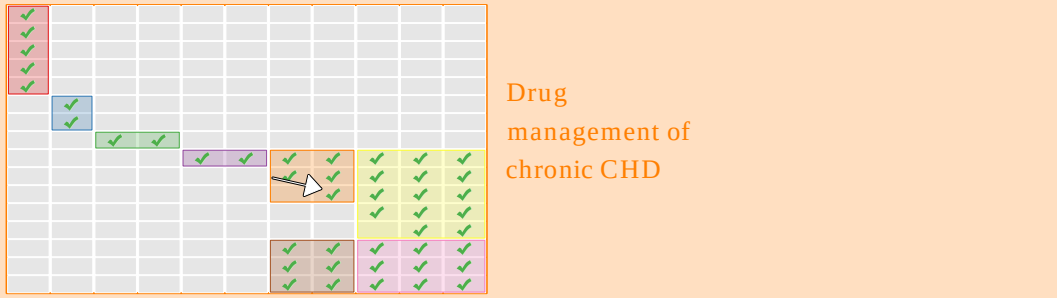
Number of clinical triggers 2736; Number of clinical actions 919. ICC for practice = 0.066. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina and diabetes' and 'ACE inhibitor'. Incident clinical trigger (triggers = 8956; actions = 5619)

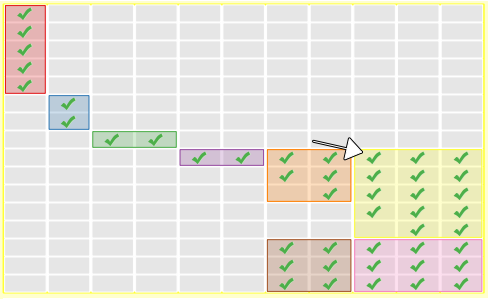




Mixed−effects model for 'stable angina and diabetes' and 'ACE inhibitor'. Incident clinical trigger

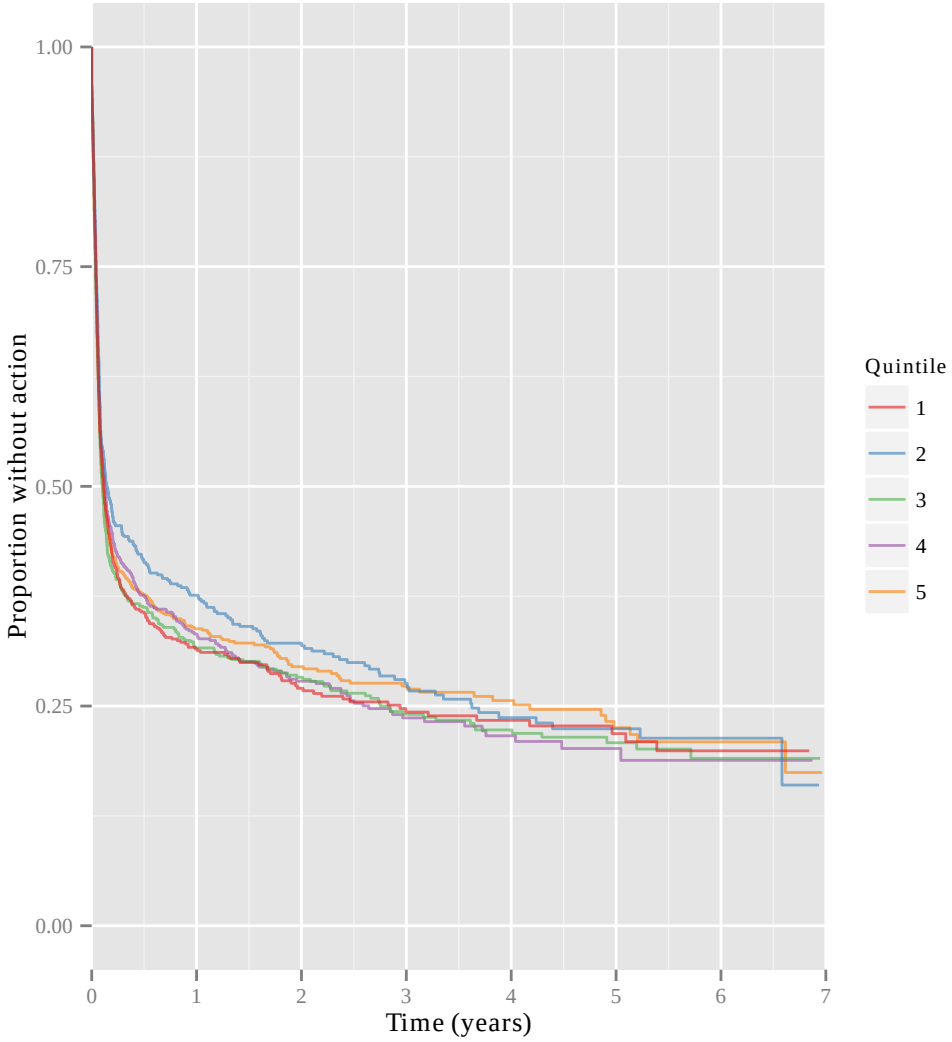
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.12	(0.89; 1.40)
Quintile 3	1.20	(0.97; 1.48)
Quintile 4	1.06	(0.86; 1.31)
Quintile 5	1.12	(0.91; 1.39)
Age 35 to 39	0.87	(0.41; 1.82)
Age 40 to 44	0.70	(0.42; 1.19)
Age 45 to 49	0.74	(0.49; 1.13)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.81	(0.60; 1.10)
Age 60 to 64	0.82	(0.61; 1.09)
Age 65 to 69	0.88	(0.66; 1.16)
Age 70 to 74	0.92	(0.70; 1.23)
Age 75 to 79	0.73	(0.54; 0.99)
Age 80 to 84	0.88	(0.64; 1.21)
Age 85+	0.60	(0.42; 0.88)
Male	1	(Reference)
Female	0.91	(0.80; 1.03)
Non−smoker	1	(Reference)
Smoker	0.92	(0.77; 1.09)
BMI low / norm.	1	(Reference)
Overweight	1.10	(0.90; 1.34)
Obese	1.27	(1.05; 1.54)
No hyp.	1	(Reference)
Hyp. contr.	1.36	(1.18; 1.57)
Hyp. uncontr.	2.72	(2.27; 3.26)
Untreat. hyp.	1.61	(1.26; 2.05)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.21	(1.05; 1.39)
No CVA	1	(Reference)
CVA	1.16	(0.96; 1.40)
No oth. co.	1	(Reference)
Other co.	0.88	(0.77; 1.01)

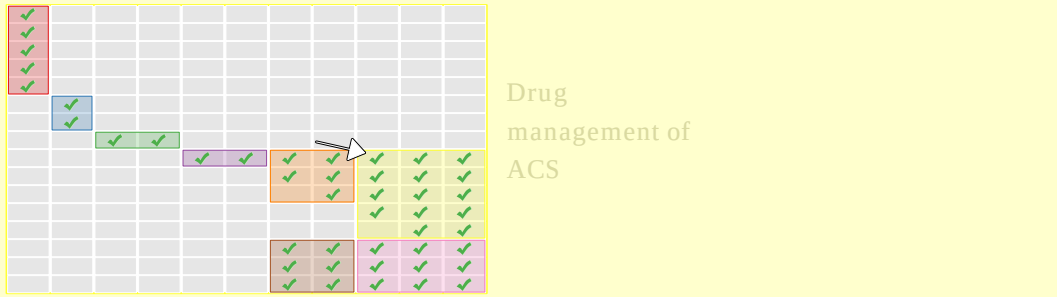
Number of clinical triggers 3361; Number of clinical actions 1092. ICC for practice = 0.03. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'old ACS' and 'statin'. Incident clinical trigger (triggers = 4256; actions = 2763)

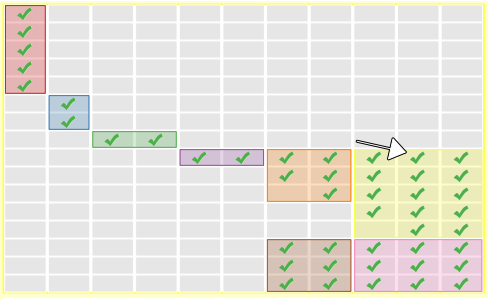




Mixed−effects model for 'old ACS' and 'statin'. Incident clinical trigger

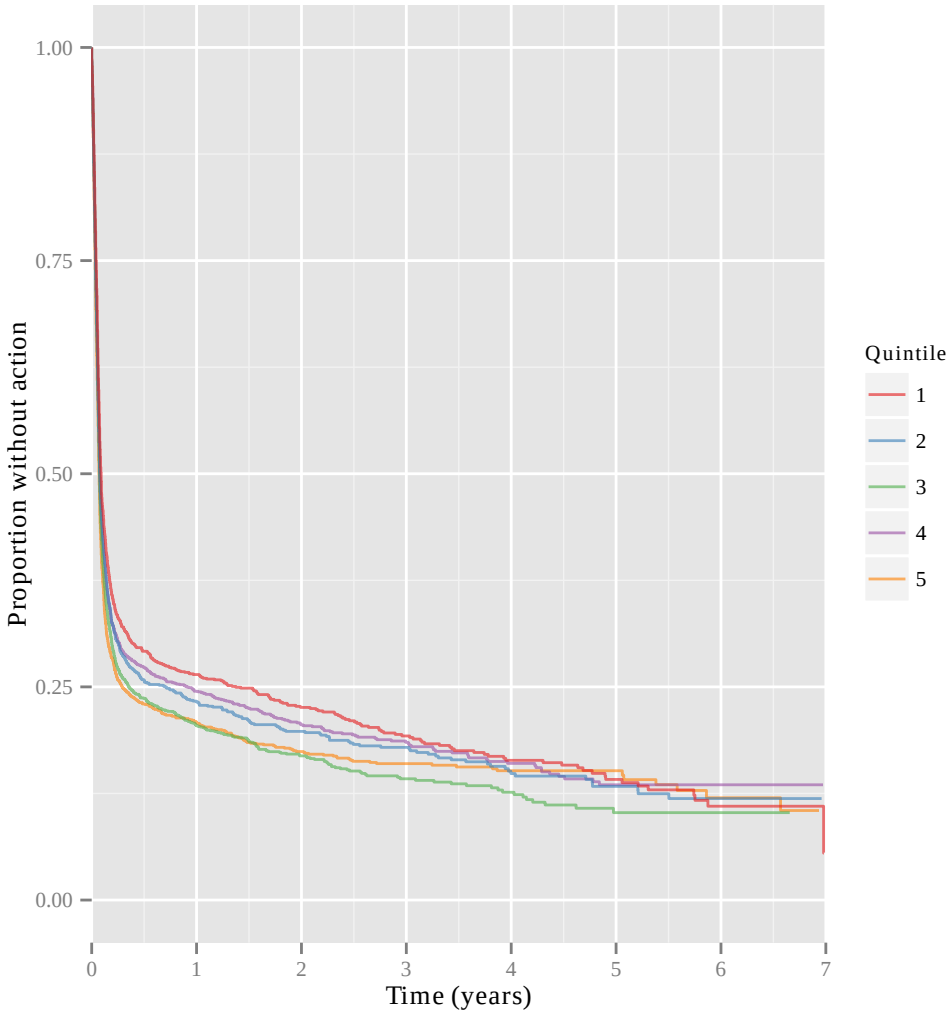
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.74	(0.59; 0.93)
Quintile 3	0.89	(0.72; 1.10)
Quintile 4	0.94	(0.75; 1.17)
Quintile 5	0.79	(0.64; 0.99)
Age 35 to 39	0.51	(0.22; 1.20)
Age 40 to 44	0.61	(0.41; 0.92)
Age 45 to 49	0.73	(0.53; 1.01)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.77	(0.57; 1.05)
Age 60 to 64	0.83	(0.61; 1.12)
Age 65 to 69	0.70	(0.52; 0.94)
Age 70 to 74	0.72	(0.54; 0.97)
Age 75 to 79	0.56	(0.41; 0.75)
Age 80 to 84	0.39	(0.29; 0.53)
Age 85+	0.30	(0.22; 0.41)
Male	1	(Reference)
Female	1.07	(0.93; 1.25)
Non−smoker	1	(Reference)
Smoker	1.10	(0.93; 1.31)
BMI low / norm.	1	(Reference)
Overweight	0.90	(0.74; 1.09)
Obese	0.96	(0.79; 1.17)
No hyp.	1	(Reference)
Hyp. contr.	0.89	(0.76; 1.05)
Hyp. uncontr.	1.09	(0.87; 1.35)
Untreat. hyp.	1.10	(0.84; 1.44)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.66	(1.31; 2.10)
No CVA	1	(Reference)
CVA	0.91	(0.72; 1.17)
No oth. co.	1	(Reference)
Other co.	0.52	(0.44; 0.61)
No diabetes	1	(Reference)
Diabetes	0.77	(0.61; 0.98)

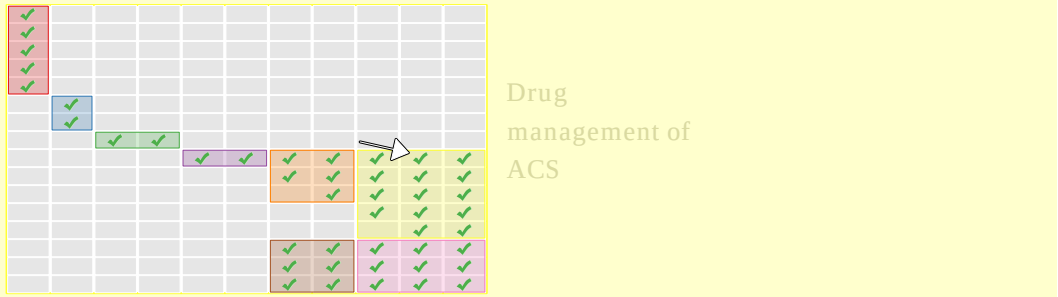
Number of clinical triggers 2112; Number of clinical actions 963. ICC for practice = 0.042. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'statin'. Incident clinical trigger (triggers = 13907; actions = 9207)



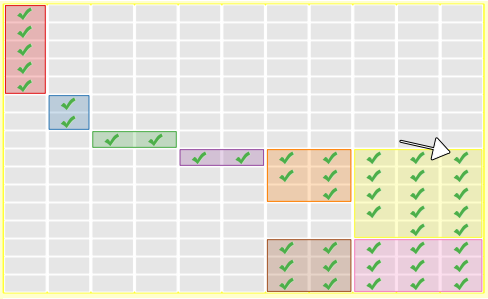


Mixed−effects model for 'unstable angina' and 'statin'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.12	(0.96; 1.32)
Quintile 3	1.18	(1.01; 1.38)
Quintile 4	1.03	(0.88; 1.21)
Quintile 5	1.03	(0.88; 1.20)
Age 35 to 39	0.72	(0.44; 1.18)
Age 40 to 44	0.75	(0.56; 1.01)
Age 45 to 49	1.02	(0.80; 1.30)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.16	(0.94; 1.44)
Age 60 to 64	1.35	(1.09; 1.66)
Age 65 to 69	1.26	(1.01; 1.57)
Age 70 to 74	1.14	(0.92; 1.42)
Age 75 to 79	0.96	(0.77; 1.21)
Age 80 to 84	0.87	(0.70; 1.10)
Age 85+	0.70	(0.55; 0.88)
Male	1	(Reference)
Female	0.81	(0.74; 0.90)
Non−smoker	1	(Reference)
Smoker	1.16	(1.03; 1.30)
BMI low / norm.	1	(Reference)
Overweight	1.20	(1.06; 1.36)
Obese	1.18	(1.03; 1.36)
No hyp.	1	(Reference)
Hyp. contr.	0.91	(0.82; 1.01)
Hyp. uncontr.	1.08	(0.94; 1.25)
Untreat. hyp.	1.13	(0.91; 1.40)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.02	(0.90; 1.16)
No CVA	1	(Reference)
CVA	0.83	(0.70; 0.97)
No oth. co.	1	(Reference)
Other co.	0.71	(0.64; 0.78)
No diabetes	1	(Reference)
Diabetes	0.87	(0.76; 1.00)
Elect. adm.	1	(Reference)
Emer. adm.	1.14	(0.88; 1.46)

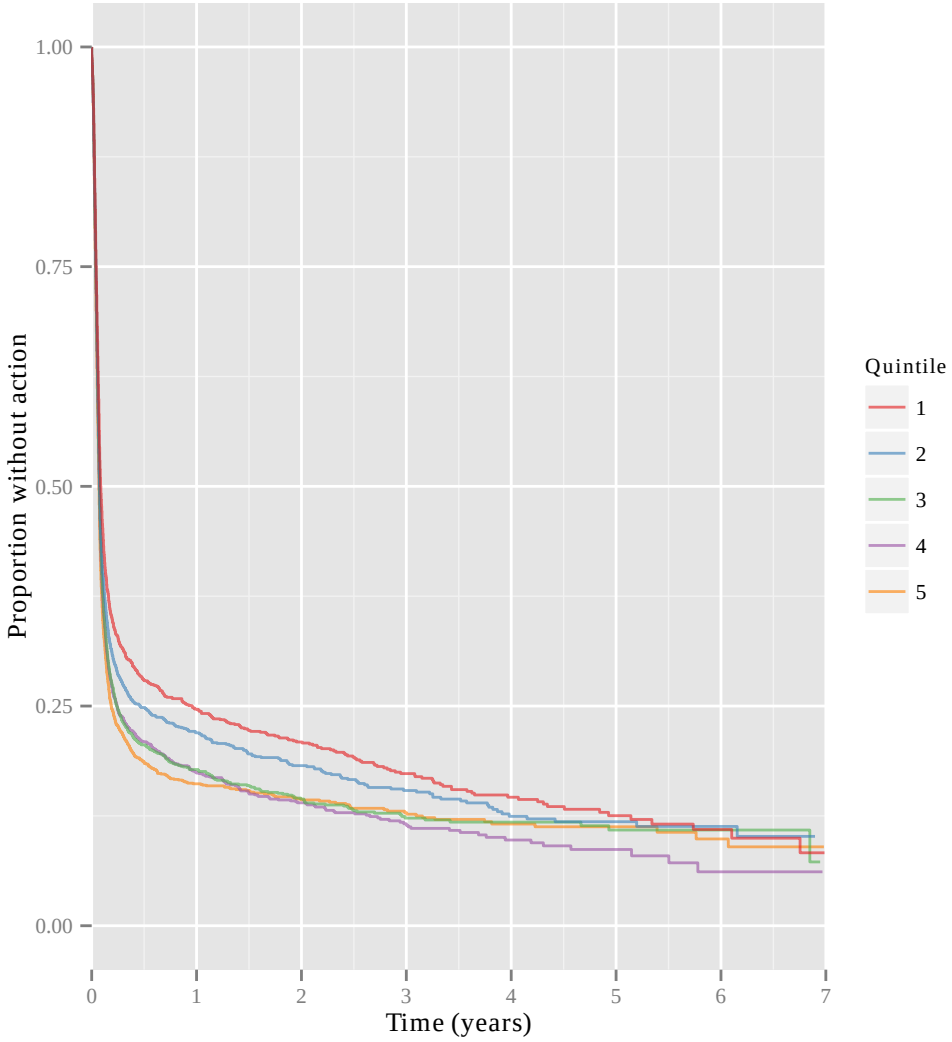
	HR	95% CI
Other adm.	1.48	(1.13; 1.93)
Cardiac cen.	1	(Reference)
Other cen.	0.76	(0.62; 0.94)
Cardiology	1	(Reference)
Med. spec.	0.53	(0.48; 0.59)
Other spec.	0.41	(0.34; 0.50)
Indication 1	1	(Reference)
Indication 2	1.26	(1.12; 1.43)
Indication 3	1.22	(1.04; 1.43)
Indication 4	0.87	(0.66; 1.15)
Indication 5+	0.57	(0.36; 0.91)
Indic. years	1.00	(0.99; 1.01)

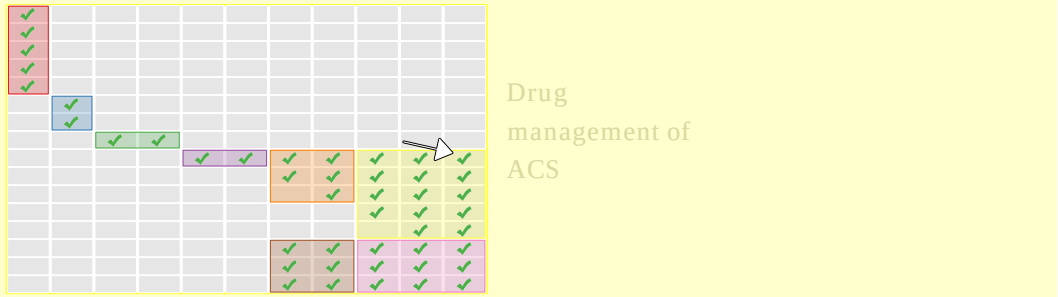
Number of clinical triggers 4462; Number of clinical actions 2178. ICC for practice = 0.079. ICC for hospital = 0.011. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'statin'. Incident clinical trigger (triggers = 20467; actions = 11376)



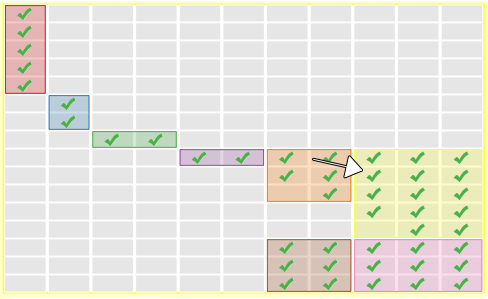


Mixed−effects model for 'MI' and 'statin'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.02	(0.92; 1.13)
Quintile 3	1.00	(0.90; 1.11)
Quintile 4	1.04	(0.94; 1.15)
Quintile 5	0.97	(0.87; 1.08)
Age 35 to 39	1.21	(0.97; 1.51)
Age 40 to 44	1.08	(0.91; 1.28)
Age 45 to 49	1.26	(1.09; 1.46)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.03	(0.91; 1.17)
Age 60 to 64	1.02	(0.90; 1.15)
Age 65 to 69	0.95	(0.84; 1.08)
Age 70 to 74	0.86	(0.76; 0.98)
Age 75 to 79	0.78	(0.68; 0.89)
Age 80 to 84	0.66	(0.58; 0.76)
Age 85+	0.38	(0.33; 0.44)
Male	1	(Reference)
Female	0.93	(0.87; 0.99)
Non−smoker	1	(Reference)
Smoker	1.04	(0.97; 1.11)
BMI low / norm.	1	(Reference)
Overweight	1.15	(1.06; 1.24)
Obese	1.05	(0.96; 1.14)
No hyp.	1	(Reference)
Hyp. contr.	0.97	(0.90; 1.03)
Hyp. uncontr.	1.05	(0.96; 1.16)
Untreat. hyp.	1.03	(0.91; 1.16)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.18	(1.09; 1.27)
No CVA	1	(Reference)
CVA	0.77	(0.68; 0.87)
No oth. co.	1	(Reference)
Other co.	0.68	(0.64; 0.72)
No diabetes	1	(Reference)
Diabetes	0.86	(0.78; 0.94)
Elect. adm.	1	(Reference)
Emer. adm.	1.28	(1.05; 1.56)

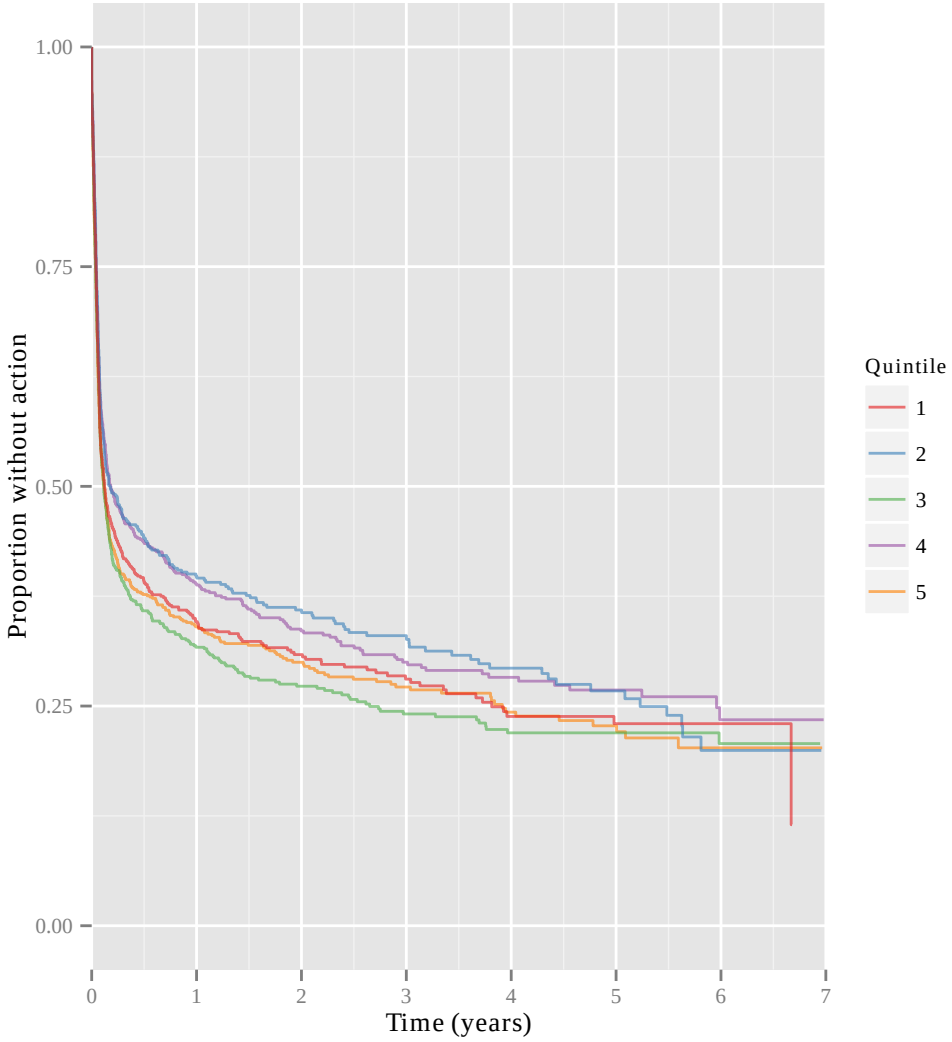
	HR	95% CI
Other adm.	1.44	(1.17; 1.77)
Cardiac cen.	1	(Reference)
Other cen.	0.84	(0.62; 1.14)
Cardiology	1	(Reference)
Med. spec.	0.64	(0.60; 0.69)
Other spec.	0.40	(0.35; 0.46)
Indication 1	1	(Reference)
Indication 2	1.16	(1.08; 1.26)
Indication 3	1.13	(1.02; 1.26)
Indication 4	1.09	(0.90; 1.32)
Indication 5+	0.93	(0.66; 1.32)
Indic. years	1.00	(0.99; 1.00)

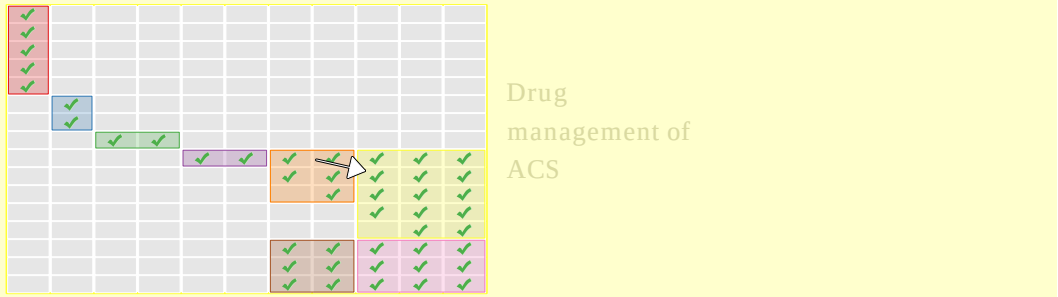
Number of clinical triggers 10442; Number of clinical actions 5372. ICC for practice = 0.095. ICC for hospital = 0.041. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'old ACS' and 'aspirin'. Incident clinical trigger (triggers = 4256; actions = 2691)

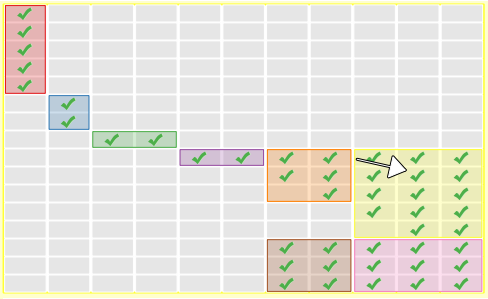




Mixed−effects model for 'old ACS' and 'aspirin'. Incident clinical trigger

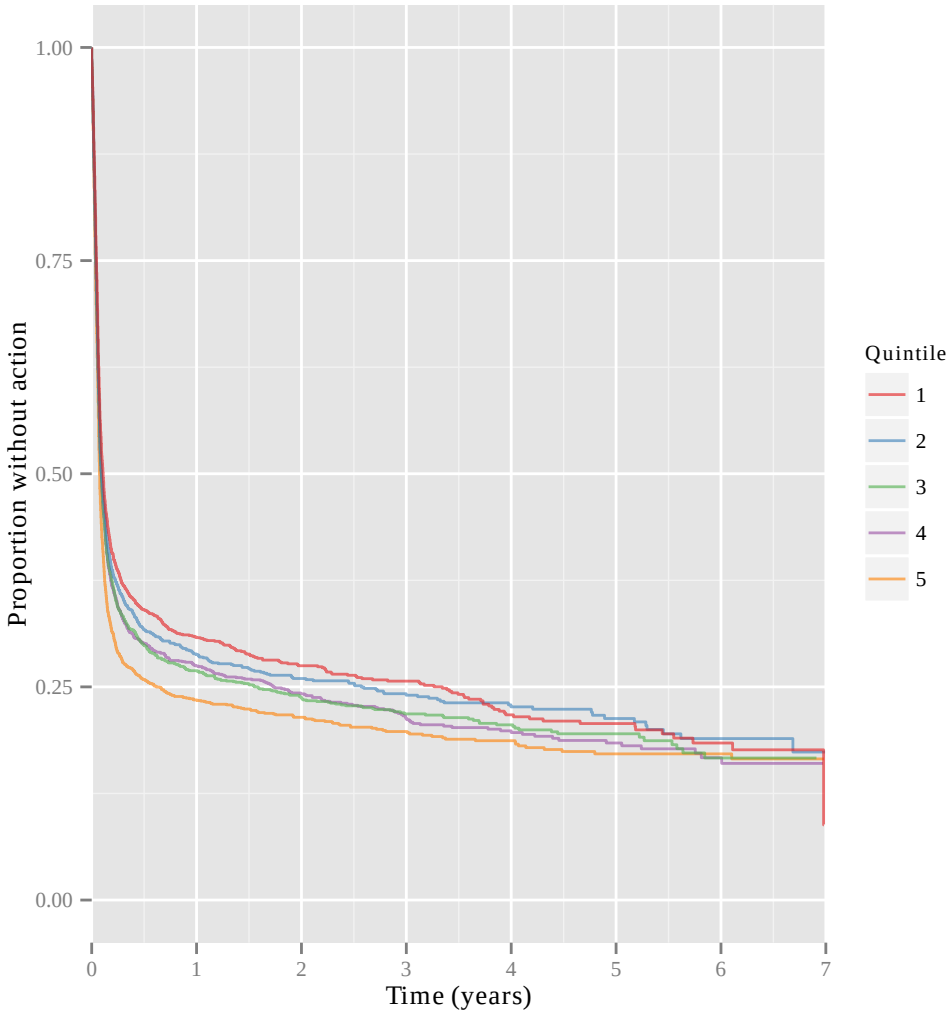
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.75	(0.59; 0.94)
Quintile 3	0.98	(0.79; 1.22)
Quintile 4	0.77	(0.62; 0.96)
Quintile 5	0.81	(0.65; 1.01)
Age 35 to 39	0.85	(0.42; 1.71)
Age 40 to 44	0.68	(0.47; 0.98)
Age 45 to 49	0.65	(0.46; 0.91)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.69	(0.52; 0.92)
Age 60 to 64	0.75	(0.57; 1.00)
Age 65 to 69	0.67	(0.51; 0.89)
Age 70 to 74	0.89	(0.67; 1.17)
Age 75 to 79	0.66	(0.48; 0.89)
Age 80 to 84	0.63	(0.46; 0.85)
Age 85+	0.68	(0.49; 0.94)
Male	1	(Reference)
Female	1.05	(0.89; 1.23)
Non−smoker	1	(Reference)
Smoker	1.29	(1.10; 1.51)
BMI low / norm.	1	(Reference)
Overweight	1.00	(0.83; 1.21)
Obese	1.02	(0.84; 1.25)
No hyp.	1	(Reference)
Hyp. contr.	0.86	(0.73; 1.02)
Hyp. uncontr.	1.08	(0.86; 1.34)
Untreat. hyp.	1.23	(0.94; 1.62)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.39	(1.04; 1.86)
No CVA	1	(Reference)
CVA	0.58	(0.44; 0.77)
No oth. co.	1	(Reference)
Other co.	0.56	(0.48; 0.66)
No diabetes	1	(Reference)
Diabetes	0.95	(0.78; 1.17)

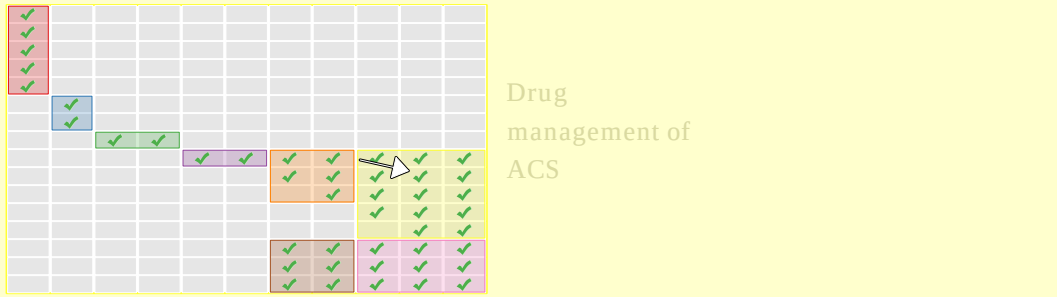
Number of clinical triggers 1794; Number of clinical actions 915. ICC for practice = 0.051. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'aspirin'. Incident clinical trigger (triggers = 13907; actions = 8660)



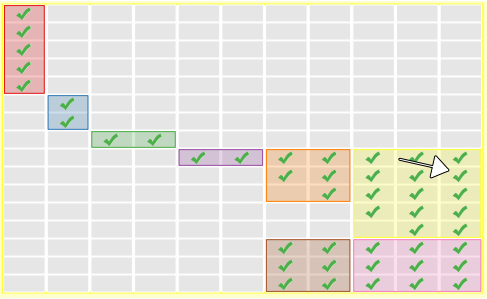


Mixed−effects model for 'unstable angina' and 'aspirin'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.08	(0.91; 1.28)
Quintile 3	1.26	(1.06; 1.48)
Quintile 4	1.15	(0.97; 1.35)
Quintile 5	1.24	(1.05; 1.46)
Age 35 to 39	0.91	(0.57; 1.46)
Age 40 to 44	0.68	(0.51; 0.90)
Age 45 to 49	0.90	(0.71; 1.15)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.03	(0.85; 1.25)
Age 60 to 64	1.18	(0.97; 1.43)
Age 65 to 69	1.03	(0.83; 1.26)
Age 70 to 74	1.01	(0.81; 1.25)
Age 75 to 79	0.81	(0.65; 1.02)
Age 80 to 84	1.03	(0.82; 1.28)
Age 85+	0.90	(0.71; 1.13)
Male	1	(Reference)
Female	0.78	(0.71; 0.86)
Non−smoker	1	(Reference)
Smoker	1.20	(1.07; 1.36)
BMI low / norm.	1	(Reference)
Overweight	0.95	(0.83; 1.09)
Obese	1.05	(0.92; 1.20)
No hyp.	1	(Reference)
Hyp. contr.	1.00	(0.90; 1.12)
Hyp. uncontr.	1.26	(1.09; 1.44)
Untreat. hyp.	1.32	(1.05; 1.64)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.05	(0.85; 1.31)
No CVA	1	(Reference)
CVA	0.78	(0.64; 0.94)
No oth. co.	1	(Reference)
Other co.	0.75	(0.68; 0.83)
No diabetes	1	(Reference)
Diabetes	0.93	(0.82; 1.06)
Elect. adm.	1	(Reference)
Emer. adm.	0.92	(0.72; 1.19)

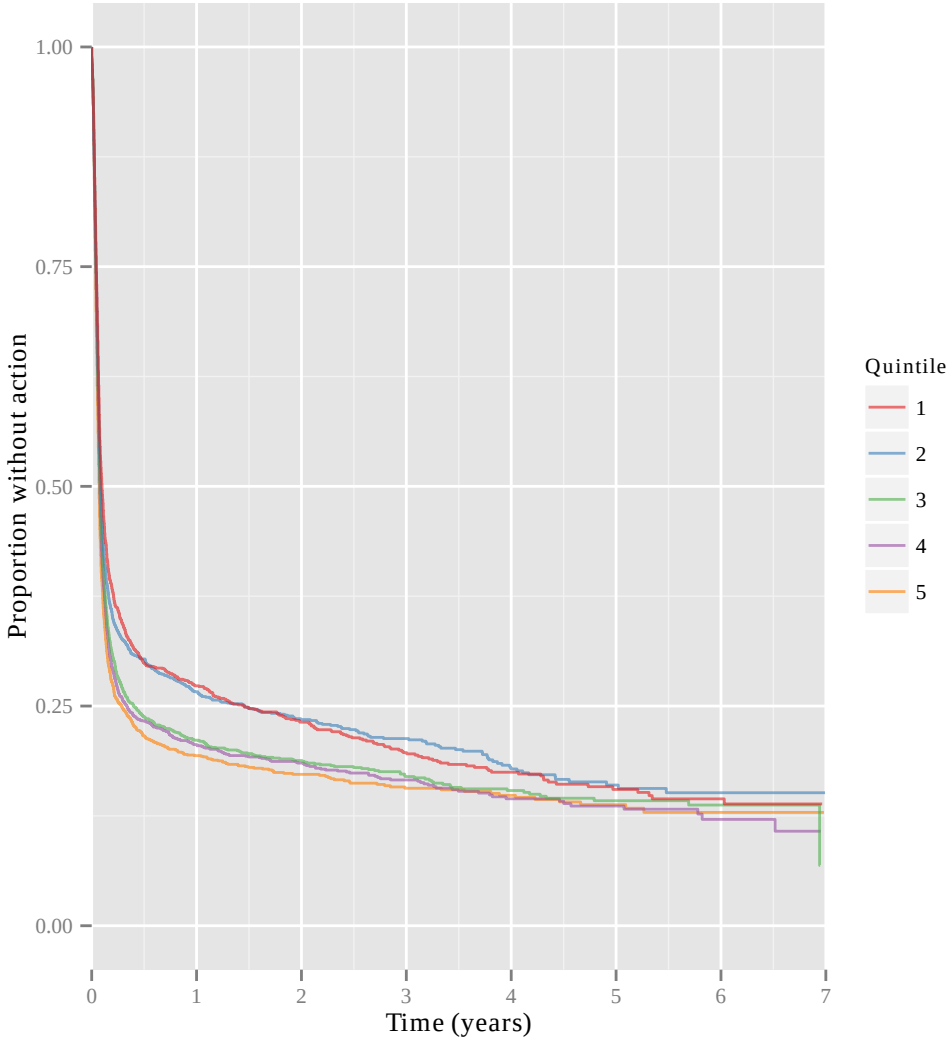
	HR	95% CI
Other adm.	1.68	(1.29; 2.19)
Cardiac cen.	1	(Reference)
Other cen.	0.77	(0.59; 0.99)
Cardiology	1	(Reference)
Med. spec.	0.66	(0.59; 0.74)
Other spec.	0.58	(0.48; 0.71)
Indication 1	1	(Reference)
Indication 2	0.80	(0.71; 0.91)
Indication 3	0.64	(0.51; 0.79)
Indication 4	0.51	(0.35; 0.74)
Indication 5+	0.43	(0.27; 0.68)
Indic. years	0.99	(0.98; 1.00)

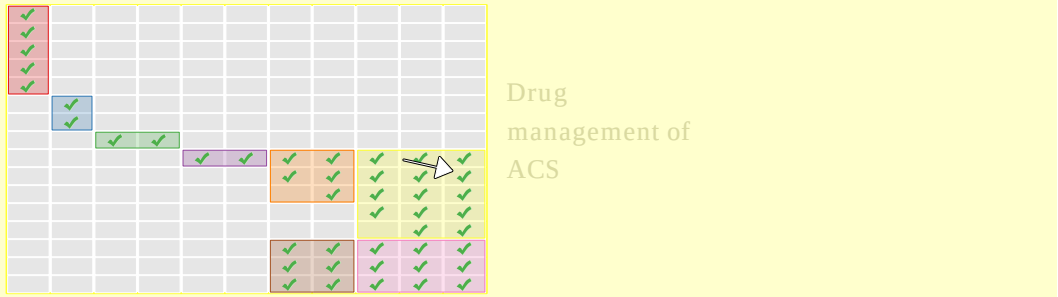
Number of clinical triggers 4172; Number of clinical actions 2041. ICC for practice = 0.084. ICC for hospital = 0.021. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'aspirin'. Incident clinical trigger (triggers = 20467; actions = 11007)



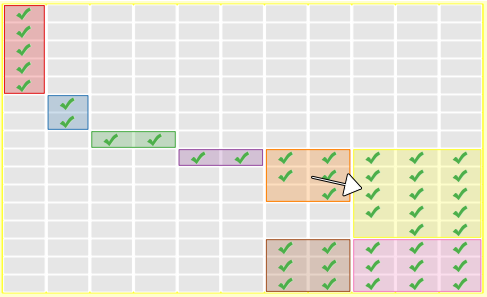


Mixed−effects model for 'MI' and 'aspirin'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.98	(0.88; 1.09)
Quintile 3	1.01	(0.91; 1.12)
Quintile 4	0.98	(0.88; 1.09)
Quintile 5	0.99	(0.89; 1.10)
Age 35 to 39	1.12	(0.90; 1.39)
Age 40 to 44	1.10	(0.93; 1.29)
Age 45 to 49	1.10	(0.95; 1.26)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.00	(0.89; 1.13)
Age 60 to 64	0.98	(0.87; 1.11)
Age 65 to 69	0.98	(0.87; 1.11)
Age 70 to 74	0.83	(0.73; 0.94)
Age 75 to 79	0.78	(0.68; 0.90)
Age 80 to 84	0.68	(0.58; 0.79)
Age 85+	0.61	(0.52; 0.71)
Male	1	(Reference)
Female	0.85	(0.79; 0.90)
Non−smoker	1	(Reference)
Smoker	1.06	(0.98; 1.15)
BMI low / norm.	1	(Reference)
Overweight	1.08	(1.00; 1.16)
Obese	1.03	(0.95; 1.13)
No hyp.	1	(Reference)
Hyp. contr.	0.98	(0.92; 1.05)
Hyp. uncontr.	1.02	(0.93; 1.11)
Untreat. hyp.	1.06	(0.94; 1.20)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.15	(1.00; 1.31)
No CVA	1	(Reference)
CVA	0.56	(0.48; 0.66)
No oth. co.	1	(Reference)
Other co.	0.72	(0.67; 0.77)
No diabetes	1	(Reference)
Diabetes	0.88	(0.80; 0.96)
Elect. adm.	1	(Reference)
Emer. adm.	1.13	(0.92; 1.39)

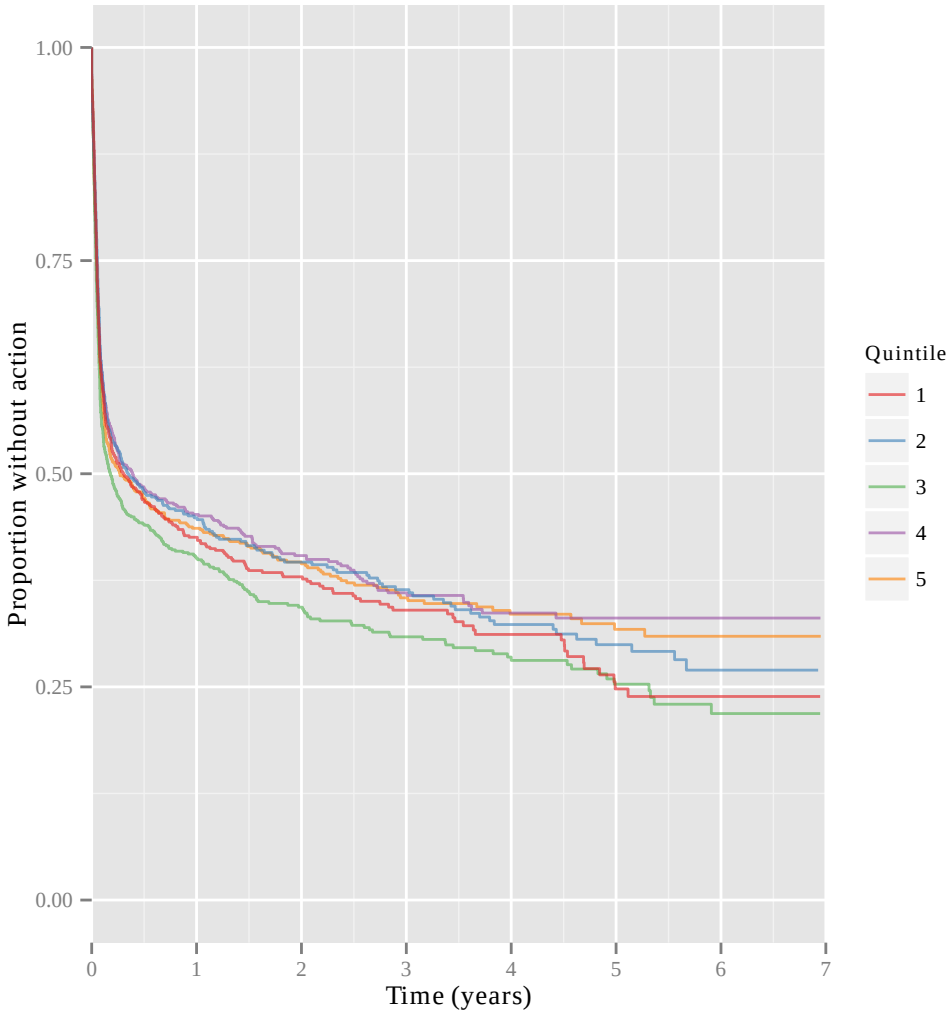
	HR	95% CI
Other adm.	1.35	(1.08; 1.67)
Cardiac cen.	1	(Reference)
Other cen.	0.85	(0.65; 1.12)
Cardiology	1	(Reference)
Med. spec.	0.72	(0.66; 0.77)
Other spec.	0.46	(0.40; 0.52)
Indication 1	1	(Reference)
Indication 2	0.97	(0.89; 1.06)
Indication 3	0.86	(0.73; 1.01)
Indication 4	0.67	(0.48; 0.95)
Indication 5+	0.49	(0.26; 0.92)
Indic. years	0.98	(0.97; 0.99)

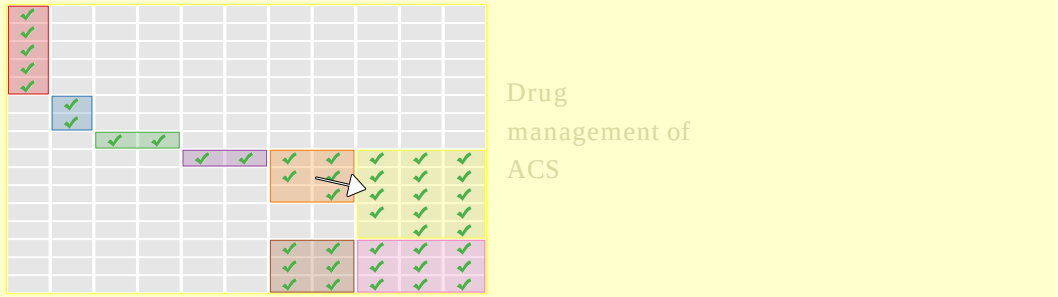
Number of clinical triggers 9577; Number of clinical actions 5098. ICC for practice = 0.107. ICC for hospital = 0.031. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'old ACS' and 'ACE inhibitor'. Incident clinical trigger (triggers = 4256; actions = 2440)

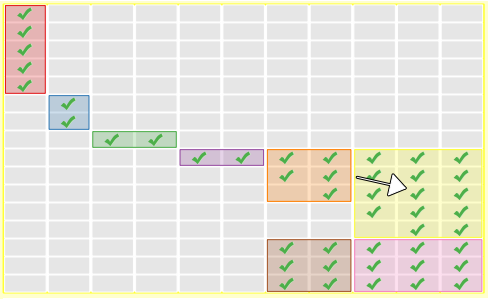




Mixed−effects model for 'old ACS' and 'ACE inhibitor'. Incident clinical trigger

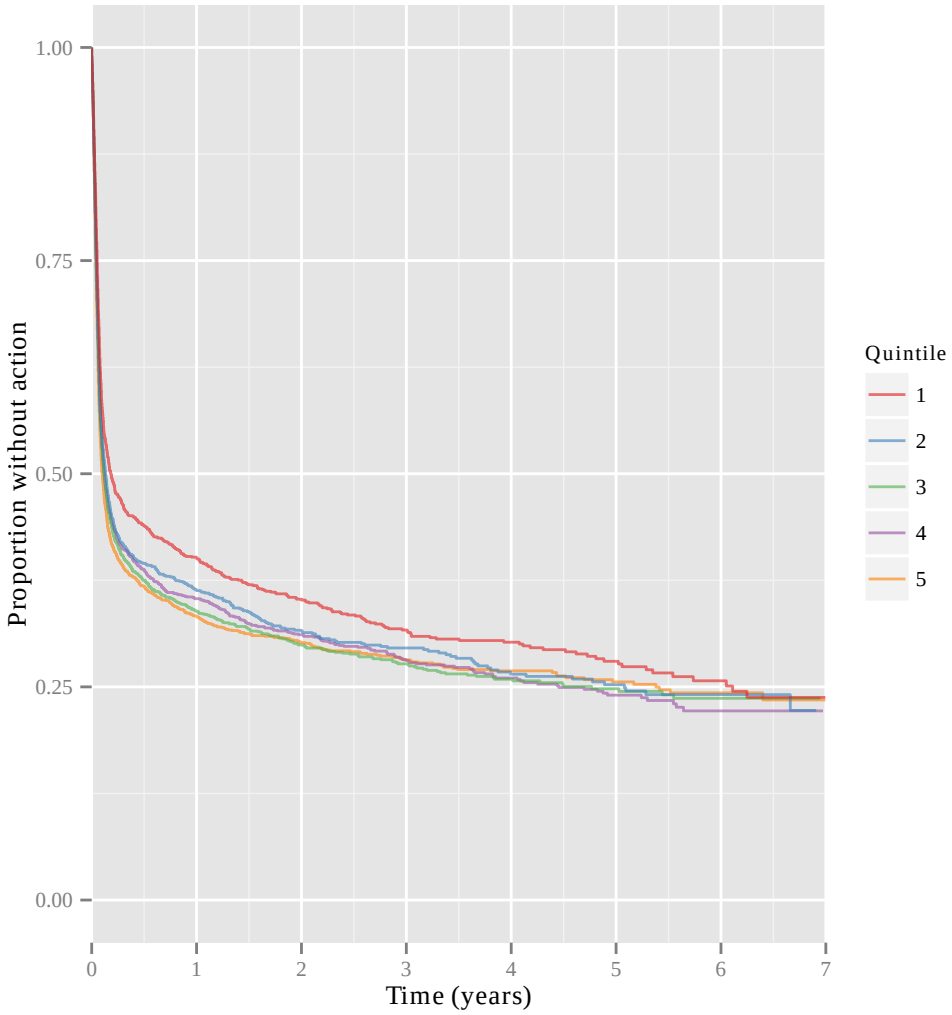
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.86	(0.69; 1.08)
Quintile 3	0.98	(0.79; 1.21)
Quintile 4	0.84	(0.68; 1.05)
Quintile 5	0.80	(0.64; 1.01)
Age 35 to 39	0.82	(0.40; 1.70)
Age 40 to 44	0.72	(0.48; 1.09)
Age 45 to 49	0.96	(0.69; 1.35)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.77	(0.56; 1.06)
Age 60 to 64	0.85	(0.63; 1.13)
Age 65 to 69	0.69	(0.51; 0.93)
Age 70 to 74	0.93	(0.70; 1.23)
Age 75 to 79	0.69	(0.50; 0.95)
Age 80 to 84	0.89	(0.65; 1.22)
Age 85+	0.61	(0.43; 0.87)
Male	1	(Reference)
Female	0.75	(0.64; 0.87)
Non−smoker	1	(Reference)
Smoker	1.19	(1.01; 1.41)
BMI low / norm.	1	(Reference)
Overweight	1.01	(0.85; 1.20)
Obese	1.20	(0.98; 1.46)
No hyp.	1	(Reference)
Hyp. contr.	1.00	(0.85; 1.18)
Hyp. uncontr.	1.50	(1.18; 1.90)
Untreat. hyp.	1.44	(1.12; 1.85)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.36	(0.90; 2.06)
No CVA	1	(Reference)
CVA	0.85	(0.67; 1.07)
No oth. co.	1	(Reference)
Other co.	0.59	(0.50; 0.70)
No diabetes	1	(Reference)
Diabetes	1.02	(0.84; 1.26)

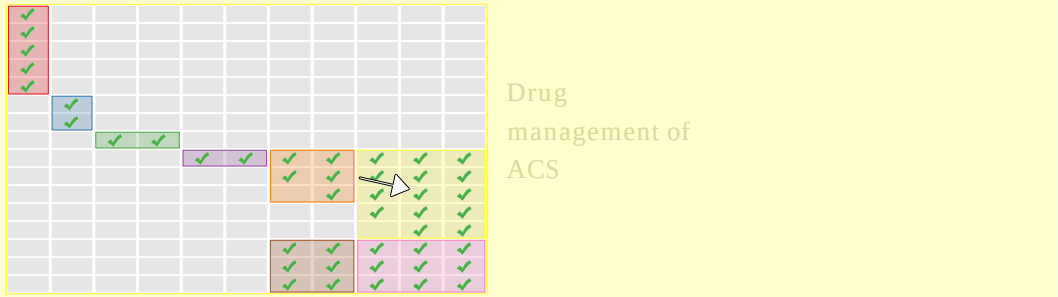
Number of clinical triggers 2215; Number of clinical actions 881. ICC for practice = 0.028. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'ACE inhibitor'. Incident clinical trigger (triggers = 13907; actions = 7859)



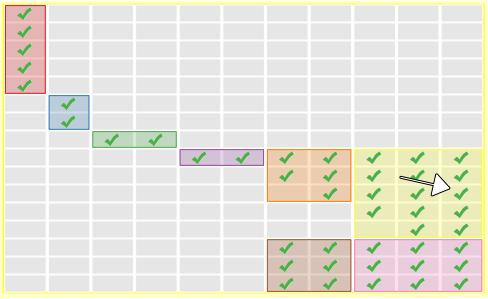


Mixed−effects model for 'unstable angina' and 'ACE inhibitor'.
Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.06	(0.90; 1.25)
Quintile 3	1.21	(1.04; 1.42)
Quintile 4	1.19	(1.01; 1.39)
Quintile 5	1.06	(0.91; 1.25)
Age 35 to 39	0.71	(0.41; 1.23)
Age 40 to 44	0.70	(0.51; 0.97)
Age 45 to 49	1.03	(0.79; 1.33)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.04	(0.84; 1.29)
Age 60 to 64	1.26	(1.02; 1.56)
Age 65 to 69	1.24	(1.00; 1.53)
Age 70 to 74	1.51	(1.21; 1.89)
Age 75 to 79	1.23	(0.98; 1.55)
Age 80 to 84	1.27	(1.00; 1.60)
Age 85+	1.03	(0.80; 1.31)
Male	1	(Reference)
Female	0.80	(0.72; 0.88)
Non−smoker	1	(Reference)
Smoker	1.35	(1.21; 1.51)
BMI low / norm.	1	(Reference)
Overweight	1.05	(0.93; 1.18)
Obese	1.07	(0.93; 1.24)
No hyp.	1	(Reference)
Hyp. contr.	1.20	(1.08; 1.33)
Hyp. uncontr.	1.52	(1.30; 1.78)
Untreat. hyp.	1.26	(1.02; 1.55)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.03	(0.84; 1.27)
No CVA	1	(Reference)
CVA	0.98	(0.84; 1.14)
No oth. co.	1	(Reference)
Other co.	0.76	(0.69; 0.84)
No diabetes	1	(Reference)
Diabetes	1.17	(1.02; 1.34)
Elect. adm.	1	(Reference)
Emer. adm.	1.51	(1.20; 1.88)

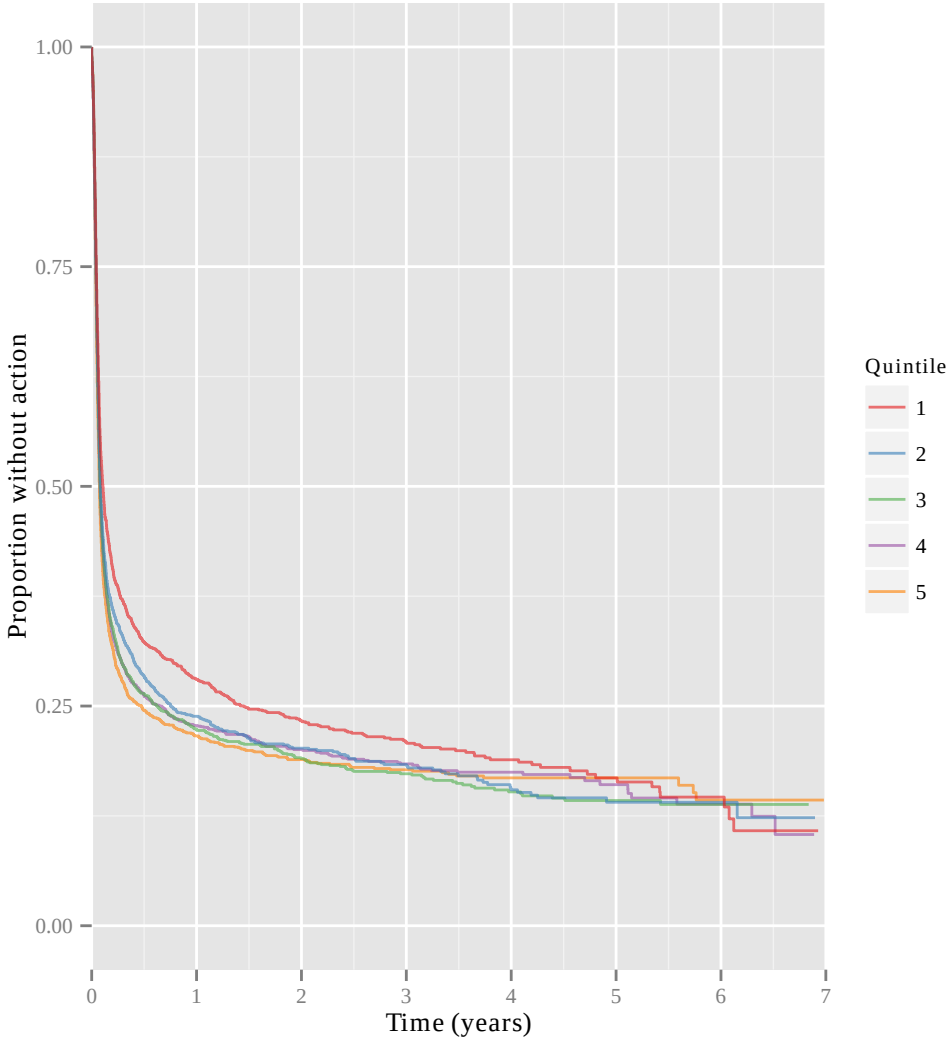
	HR	95% CI
Other adm.	2.27	(1.79; 2.86)
Cardiac cen.	1	(Reference)
Other cen.	0.75	(0.57; 0.97)
Cardiology	1	(Reference)
Med. spec.	0.55	(0.49; 0.62)
Other spec.	0.52	(0.43; 0.62)
Indication 1	1	(Reference)
Indication 2	1.15	(1.01; 1.30)
Indication 3	0.96	(0.75; 1.22)
Indication 4	1.03	(0.70; 1.51)
Indication 5+	0.57	(0.35; 0.92)
Indic. years	0.96	(0.93; 1.00)

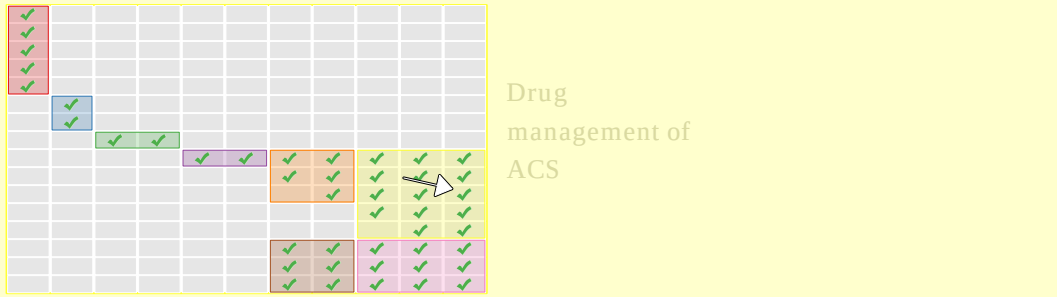
Number of clinical triggers 5287; Number of clinical actions 1967. ICC for practice = 0.039. ICC for hospital = 0.024. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'ACE inhibitor'. Incident clinical trigger (triggers = 20467; actions = 10770)



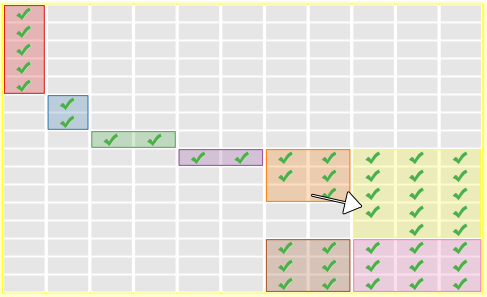


Mixed−effects model for 'MI' and 'ACE inhibitor'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.05	(0.95; 1.16)
Quintile 3	1.01	(0.91; 1.12)
Quintile 4	1.02	(0.92; 1.12)
Quintile 5	1.02	(0.91; 1.13)
Age 35 to 39	0.86	(0.69; 1.07)
Age 40 to 44	1.01	(0.86; 1.19)
Age 45 to 49	1.09	(0.94; 1.25)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.96	(0.85; 1.08)
Age 60 to 64	1.04	(0.92; 1.17)
Age 65 to 69	0.98	(0.86; 1.11)
Age 70 to 74	0.83	(0.73; 0.94)
Age 75 to 79	0.84	(0.74; 0.96)
Age 80 to 84	0.78	(0.69; 0.90)
Age 85+	0.46	(0.40; 0.54)
Male	1	(Reference)
Female	0.89	(0.83; 0.94)
Non−smoker	1	(Reference)
Smoker	1.05	(0.98; 1.12)
BMI low / norm.	1	(Reference)
Overweight	1.22	(1.13; 1.31)
Obese	1.20	(1.10; 1.31)
No hyp.	1	(Reference)
Hyp. contr.	1.02	(0.95; 1.09)
Hyp. uncontr.	1.19	(1.08; 1.32)
Untreat. hyp.	1.12	(1.00; 1.25)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.10	(1.01; 1.20)
No CVA	1	(Reference)
CVA	0.82	(0.73; 0.91)
No oth. co.	1	(Reference)
Other co.	0.73	(0.68; 0.77)
No diabetes	1	(Reference)
Diabetes	1.05	(0.96; 1.15)
Elect. adm.	1	(Reference)
Emer. adm.	1.26	(1.04; 1.53)

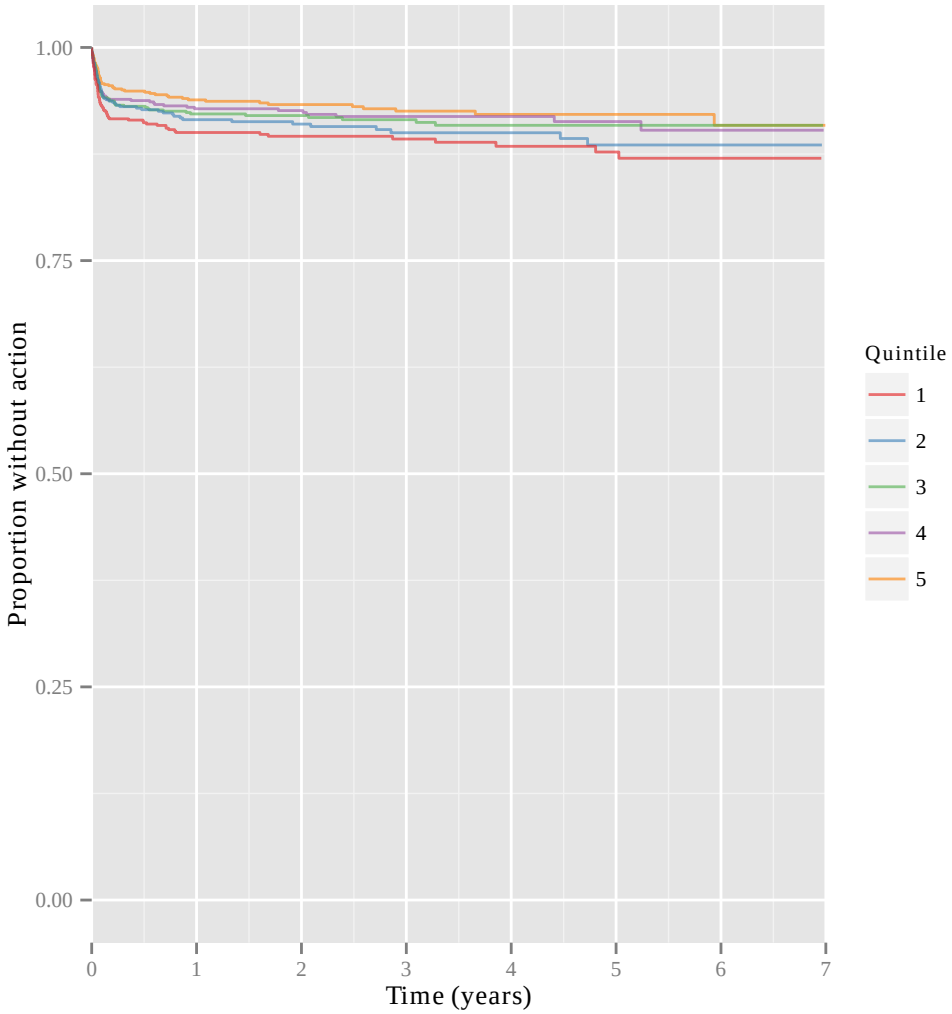
	HR	95% CI
Other adm.	1.45	(1.19; 1.77)
Cardiac cen.	1	(Reference)
Other cen.	1.04	(0.82; 1.32)
Cardiology	1	(Reference)
Med. spec.	0.69	(0.64; 0.74)
Other spec.	0.38	(0.34; 0.44)
Indication 1	1	(Reference)
Indication 2	1.04	(0.95; 1.14)
Indication 3	0.99	(0.84; 1.18)
Indication 4	0.91	(0.61; 1.36)
Indication 5+	0.83	(0.41; 1.70)
Indic. years	0.94	(0.91; 0.96)

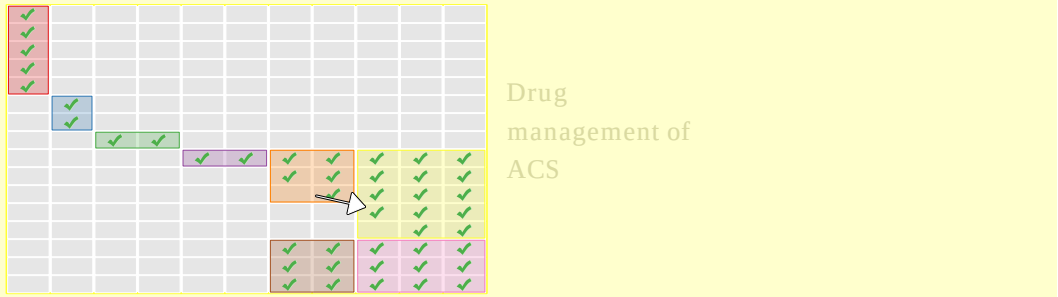
Number of clinical triggers 10595; Number of clinical actions 5270. ICC for practice = 0.048. ICC for hospital = 0.024. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'old ACS' and 'beta−blocker'. Incident clinical trigger (triggers = 4256; actions = 332)

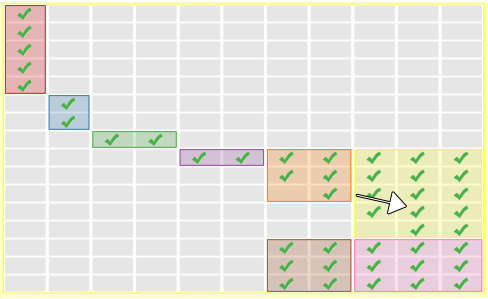




Mixed−effects model for 'old ACS' and 'beta−blocker'. Incident clinical trigger

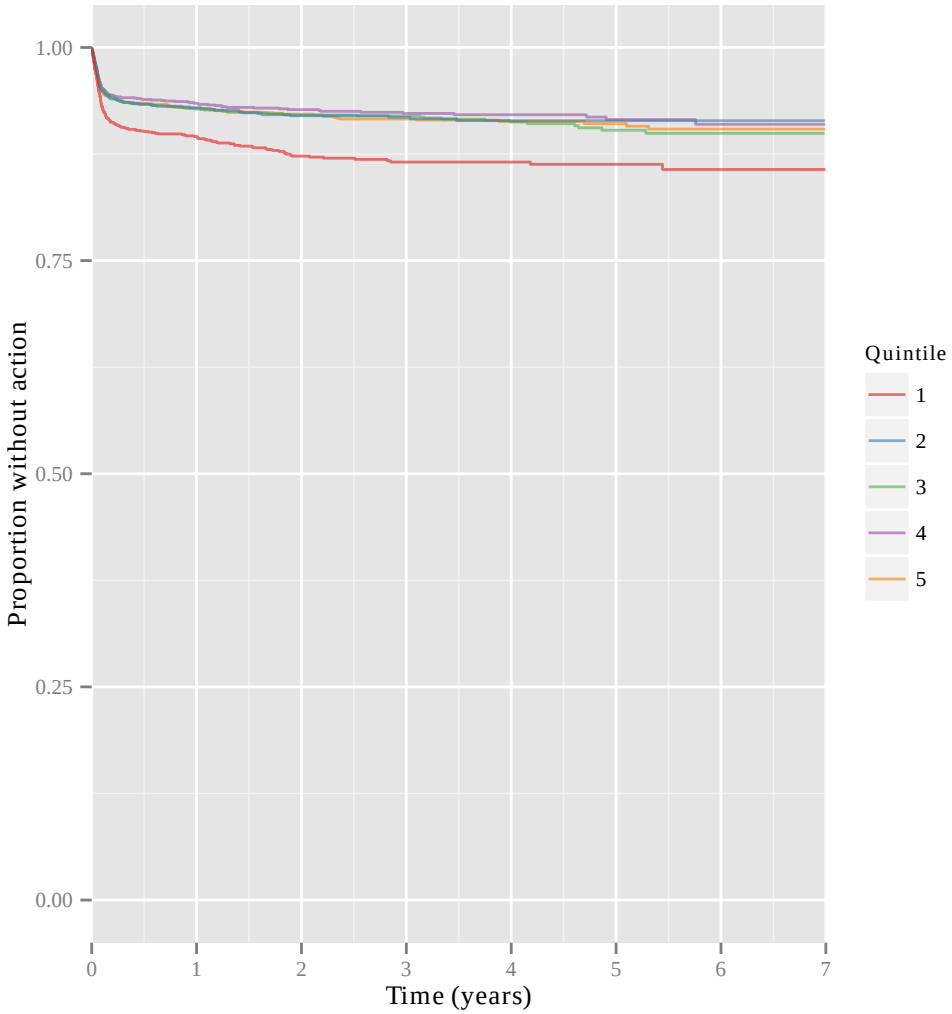
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.86	(0.47; 1.56)
Quintile 3	0.82	(0.46; 1.45)
Quintile 4	1.07	(0.61; 1.86)
Quintile 5	1.00	(0.57; 1.74)
Age 35 to 39	0.00	(0.00; >99)
Age 40 to 44	0.76	(0.31; 1.88)
Age 45 to 49	0.51	(0.20; 1.31)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.76	(0.38; 1.54)
Age 60 to 64	0.66	(0.33; 1.35)
Age 65 to 69	0.57	(0.28; 1.18)
Age 70 to 74	0.83	(0.43; 1.62)
Age 75 to 79	0.59	(0.28; 1.24)
Age 80 to 84	0.48	(0.21; 1.07)
Age 85+	0.10	(0.02; 0.43)
Male	1	(Reference)
Female	1.01	(0.68; 1.51)
Non−smoker	1	(Reference)
Smoker	1.20	(0.79; 1.83)
BMI low / norm.	1	(Reference)
Overweight	1.05	(0.64; 1.74)
Obese	1.09	(0.61; 1.95)
No hyp.	1	(Reference)
Hyp. contr.	1.10	(0.71; 1.69)
Hyp. uncontr.	1.14	(0.64; 2.05)
Untreat. hyp.	1.44	(0.72; 2.88)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.43	(0.77; 2.66)
No CVA	1	(Reference)
CVA	0.31	(0.12; 0.77)
No oth. co.	1	(Reference)
Other co.	0.31	(0.19; 0.51)
No diabetes	1	(Reference)
Diabetes	0.77	(0.47; 1.25)

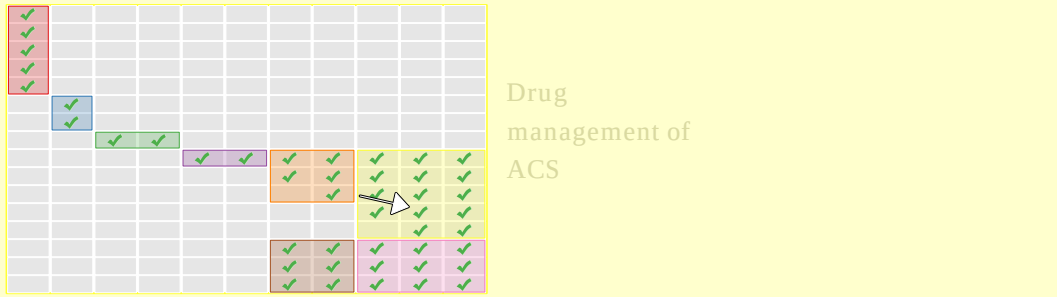
Number of clinical triggers 3538; Number of clinical actions 124. ICC for practice = 0.044. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'beta−blocker'. Incident clinical trigger (triggers = 13907; actions = 968)



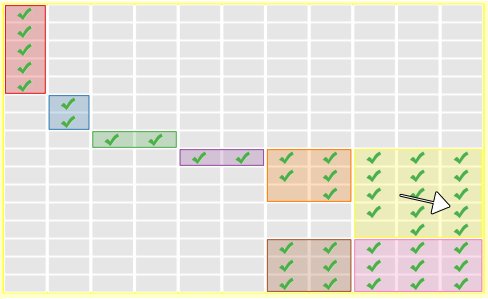


Mixed−effects model for 'unstable angina' and 'beta−blocker'.
Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.60	(0.39; 0.92)
Quintile 3	0.83	(0.57; 1.21)
Quintile 4	0.86	(0.59; 1.26)
Quintile 5	0.91	(0.63; 1.32)
Age 35 to 39	0.85	(0.20; 3.68)
Age 40 to 44	1.80	(0.94; 3.46)
Age 45 to 49	0.73	(0.35; 1.56)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.11	(0.66; 1.86)
Age 60 to 64	0.80	(0.46; 1.36)
Age 65 to 69	0.58	(0.33; 1.02)
Age 70 to 74	0.79	(0.46; 1.36)
Age 75 to 79	0.64	(0.36; 1.12)
Age 80 to 84	0.87	(0.50; 1.51)
Age 85+	0.34	(0.17; 0.66)
Male	1	(Reference)
Female	1.03	(0.80; 1.32)
Non−smoker	1	(Reference)
Smoker	0.79	(0.57; 1.10)
BMI low / norm.	1	(Reference)
Overweight	0.94	(0.67; 1.33)
Obese	0.78	(0.53; 1.15)
No hyp.	1	(Reference)
Hyp. contr.	1.64	(1.21; 2.22)
Hyp. uncontr.	2.38	(1.66; 3.41)
Untreat. hyp.	1.72	(0.94; 3.16)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.12	(0.73; 1.70)
No CVA	1	(Reference)
CVA	0.98	(0.67; 1.44)
No oth. co.	1	(Reference)
Other co.	0.40	(0.30; 0.53)
No diabetes	1	(Reference)
Diabetes	0.75	(0.55; 1.04)
Elect. adm.	1	(Reference)
Emer. adm.	1.53	(0.87; 2.70)

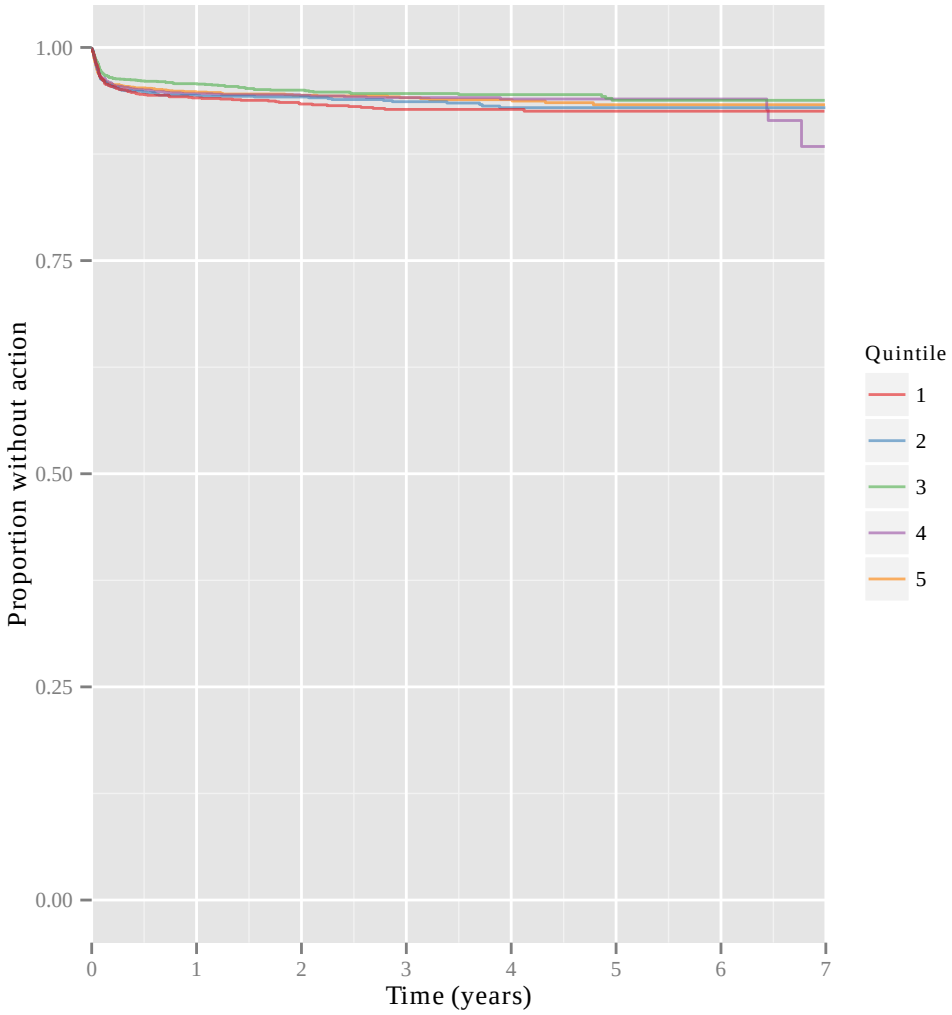
	HR	95% CI
Other adm.	1.66	(0.91; 3.05)
Cardiac cen.	1	(Reference)
Other cen.	0.86	(0.30; 2.47)
Cardiology	1	(Reference)
Med. spec.	1.21	(0.88; 1.67)
Other spec.	1.33	(0.84; 2.11)
Indication 1	1	(Reference)
Indication 2	0.75	(0.53; 1.07)
Indication 3	0.68	(0.36; 1.26)
Indication 4	0.24	(0.06; 1.03)
Indication 5+	0.27	(0.06; 1.19)
Indic. years	0.92	(0.80; 1.08)

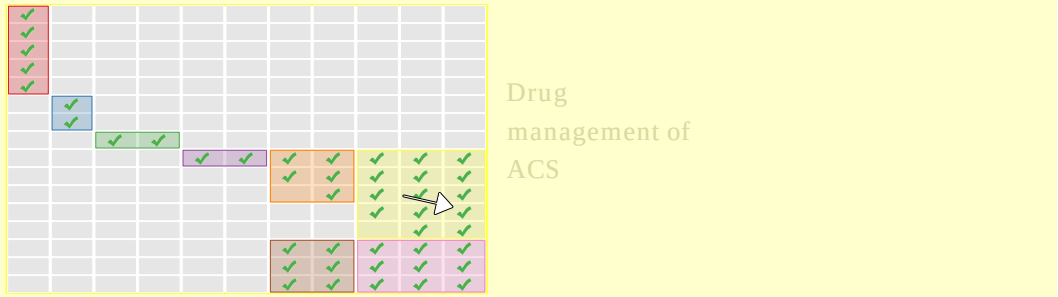
Number of clinical triggers 10405; Number of clinical actions 285. ICC for practice = 0.093. ICC for hospital = 0.292. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'beta−blocker'. Incident clinical trigger (triggers = 20467; actions = 819)



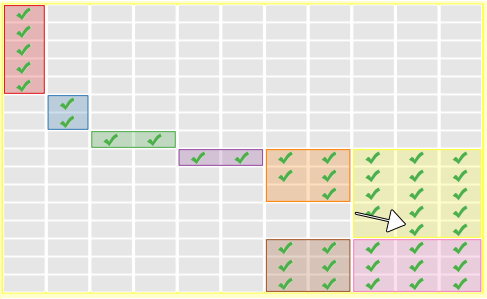


Mixed−effects model for 'MI' and 'beta−blocker'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.93	(0.66; 1.30)
Quintile 3	0.76	(0.54; 1.07)
Quintile 4	0.81	(0.58; 1.13)
Quintile 5	0.83	(0.59; 1.17)
Age 35 to 39	1.06	(0.49; 2.30)
Age 40 to 44	1.70	(1.00; 2.88)
Age 45 to 49	1.18	(0.71; 1.96)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.83	(0.53; 1.31)
Age 60 to 64	0.95	(0.62; 1.47)
Age 65 to 69	0.87	(0.55; 1.35)
Age 70 to 74	0.60	(0.37; 0.97)
Age 75 to 79	0.56	(0.34; 0.92)
Age 80 to 84	0.58	(0.35; 0.96)
Age 85+	0.24	(0.13; 0.44)
Male	1	(Reference)
Female	1.07	(0.84; 1.35)
Non−smoker	1	(Reference)
Smoker	0.77	(0.59; 1.02)
BMI low / norm.	1	(Reference)
Overweight	1.10	(0.85; 1.44)
Obese	0.98	(0.70; 1.36)
No hyp.	1	(Reference)
Hyp. contr.	1.40	(1.09; 1.80)
Hyp. uncontr.	1.56	(1.13; 2.14)
Untreat. hyp.	0.83	(0.48; 1.45)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.55	(1.01; 2.37)
No CVA	1	(Reference)
CVA	0.75	(0.49; 1.15)
No oth. co.	1	(Reference)
Other co.	0.39	(0.30; 0.52)
No diabetes	1	(Reference)
Diabetes	1.00	(0.76; 1.32)
Elect. adm.	1	(Reference)
Emer. adm.	0.54	(0.29; 0.98)

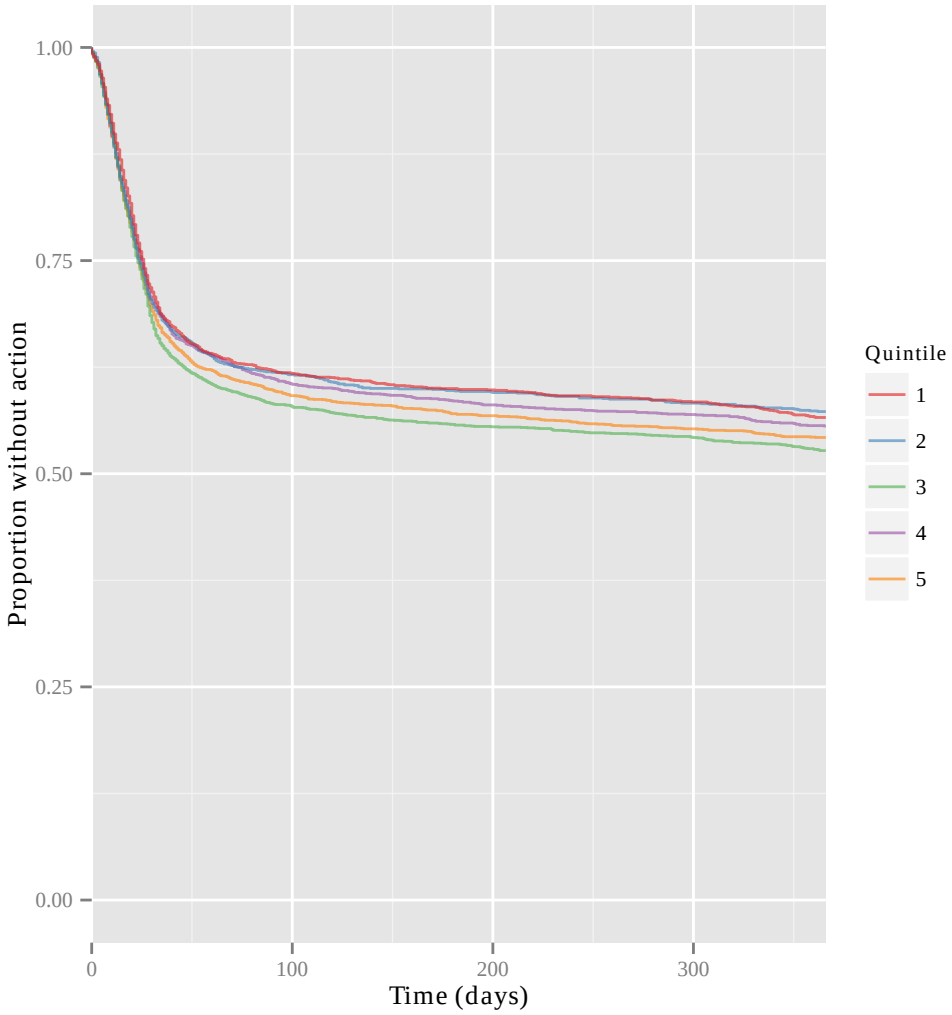
	HR	95% CI
Other adm.	0.48	(0.25; 0.92)
Cardiac cen.	1	(Reference)
Other cen.	0.69	(0.26; 1.84)
Cardiology	1	(Reference)
Med. spec.	1.32	(1.00; 1.75)
Other spec.	0.53	(0.29; 0.95)
Indication 1	1	(Reference)
Indication 2	0.85	(0.60; 1.19)
Indication 3	0.59	(0.29; 1.20)
Indication 4	0.21	(0.03; 1.55)
Indication 5+	0.00	(0.00; >99)
Indic. years	1.00	(0.85; 1.17)

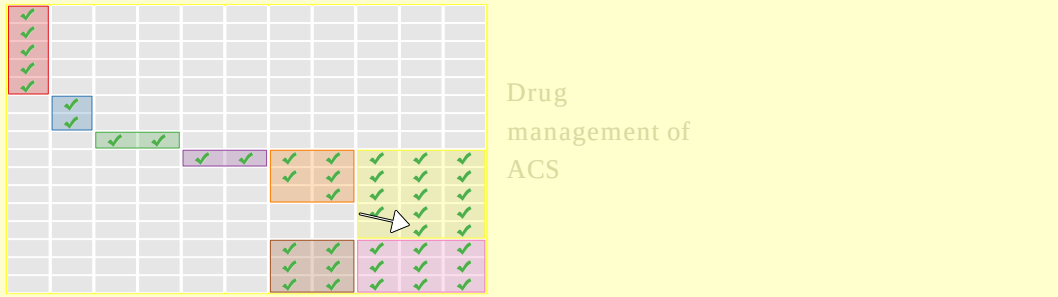
Number of clinical triggers 16639; Number of clinical actions 363. ICC for practice = 0.021. ICC for hospital = 0.305. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'clopidogrel'. Incident clinical trigger (triggers = 13907; actions = 5783)

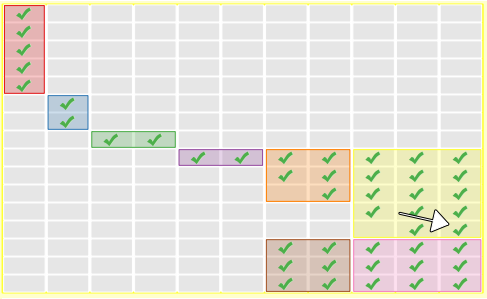




Mixed−effects model for 'unstable angina' and 'clopidogrel'. Incident clinical trigger

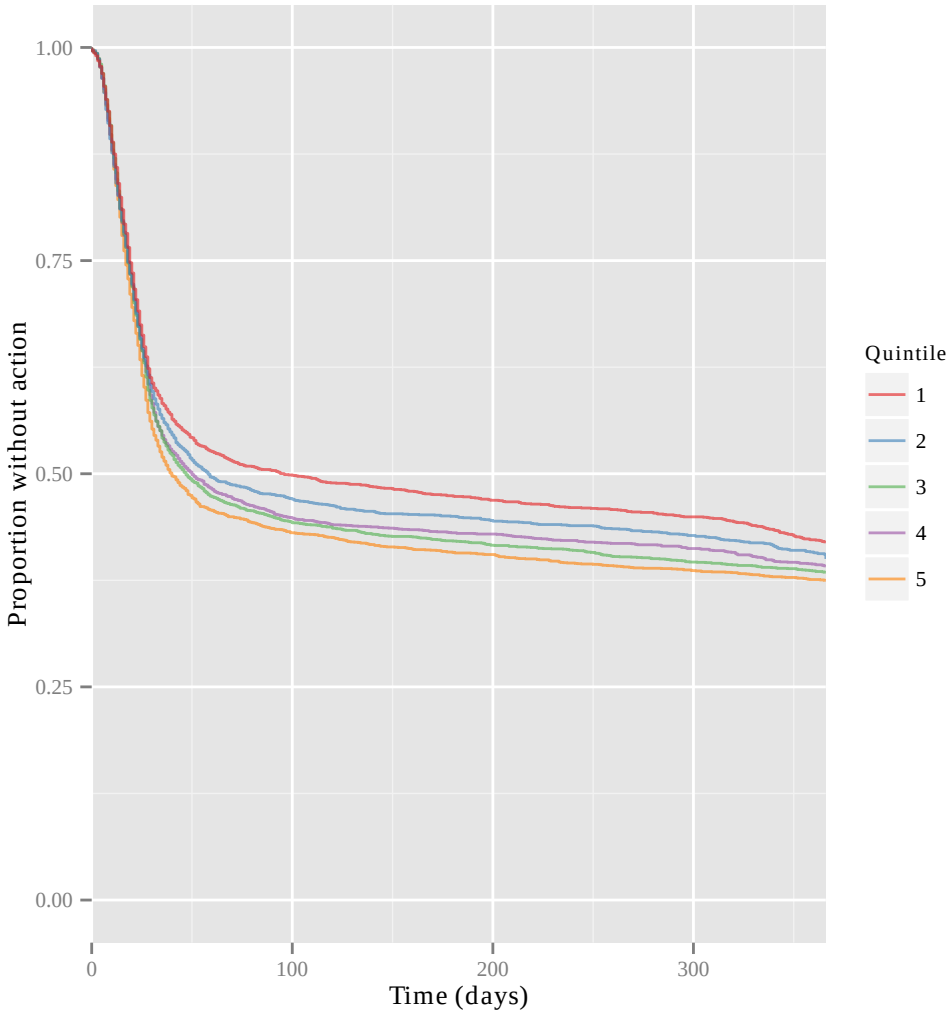
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.99	(0.90; 1.10)
Quintile 3	1.08	(0.98; 1.18)
Quintile 4	1.01	(0.92; 1.11)
Quintile 5	1.02	(0.93; 1.12)
Age 35 to 39	0.88	(0.62; 1.24)
Age 40 to 44	0.83	(0.67; 1.03)
Age 45 to 49	0.98	(0.83; 1.16)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.93	(0.81; 1.06)
Age 60 to 64	0.97	(0.86; 1.10)
Age 65 to 69	0.98	(0.86; 1.11)
Age 70 to 74	0.96	(0.84; 1.09)
Age 75 to 79	0.83	(0.72; 0.94)
Age 80 to 84	0.90	(0.79; 1.03)
Age 85+	0.80	(0.70; 0.92)
Male	1	(Reference)
Female	0.84	(0.79; 0.89)
Non−smoker	1	(Reference)
Smoker	1.15	(1.07; 1.24)
BMI low / norm.	1	(Reference)
Overweight	1.05	(0.97; 1.13)
Obese	1.04	(0.96; 1.12)
No hyp.	1	(Reference)
Hyp. contr.	1.04	(0.97; 1.11)
Hyp. uncontr.	1.02	(0.93; 1.12)
Untreat. hyp.	1.17	(0.99; 1.40)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.18	(1.08; 1.29)
No CVA	1	(Reference)
CVA	1.06	(0.98; 1.13)
No oth. co.	1	(Reference)
Other co.	0.96	(0.91; 1.01)
No diabetes	1	(Reference)
Diabetes	1.07	(1.01; 1.14)
Elect. adm.	1	(Reference)
Emer. adm.	1.03	(0.91; 1.16)
Other adm.	1.36	(1.19; 1.55)
Cardiac cen.	1	(Reference)
Other cen.	0.69	(0.53; 0.91)
Cardiology	1	(Reference)
Med. spec.	0.64	(0.60; 0.68)
Other spec.	0.33	(0.29; 0.38)

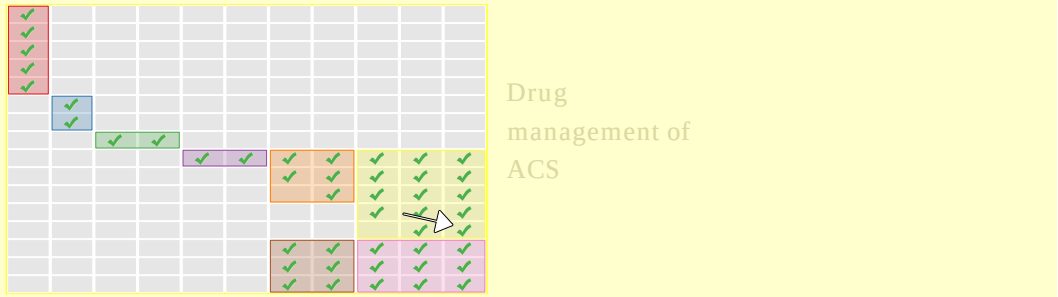
Number of clinical triggers 13907; Number of clinical actions 5783. ICC for practice = 0.04. ICC for hospital = 0.035. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'clopidogrel'. Incident clinical trigger (triggers = 20467; actions = 10132)



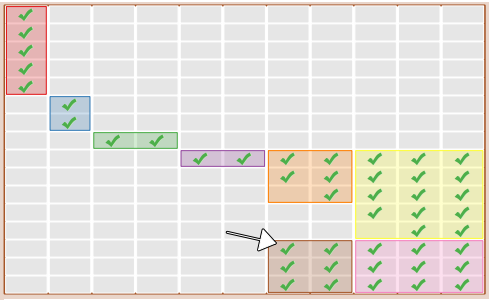


Mixed−effects model for 'MI' and 'clopidogrel'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.04	(0.96; 1.12)
Quintile 3	1.05	(0.97; 1.13)
Quintile 4	1.06	(0.99; 1.15)
Quintile 5	1.03	(0.95; 1.11)
Age 35 to 39	0.93	(0.77; 1.12)
Age 40 to 44	1.00	(0.87; 1.15)
Age 45 to 49	1.03	(0.92; 1.16)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.90	(0.82; 0.99)
Age 60 to 64	0.86	(0.79; 0.95)
Age 65 to 69	0.81	(0.74; 0.89)
Age 70 to 74	0.69	(0.63; 0.76)
Age 75 to 79	0.63	(0.57; 0.69)
Age 80 to 84	0.59	(0.54; 0.65)
Age 85+	0.49	(0.44; 0.54)
Male	1	(Reference)
Female	0.99	(0.94; 1.03)
Non−smoker	1	(Reference)
Smoker	1.03	(0.98; 1.09)
BMI low / norm.	1	(Reference)
Overweight	1.14	(1.08; 1.20)
Obese	1.08	(1.02; 1.15)
No hyp.	1	(Reference)
Hyp. contr.	1.01	(0.96; 1.06)
Hyp. uncontr.	1.06	(1.00; 1.13)
Untreat. hyp.	1.02	(0.92; 1.13)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.03	(0.96; 1.11)
No CVA	1	(Reference)
CVA	0.91	(0.86; 0.97)
No oth. co.	1	(Reference)
Other co.	0.85	(0.81; 0.88)
No diabetes	1	(Reference)
Diabetes	0.97	(0.92; 1.02)
Elect. adm.	1	(Reference)
Emer. adm.	1.13	(0.99; 1.30)

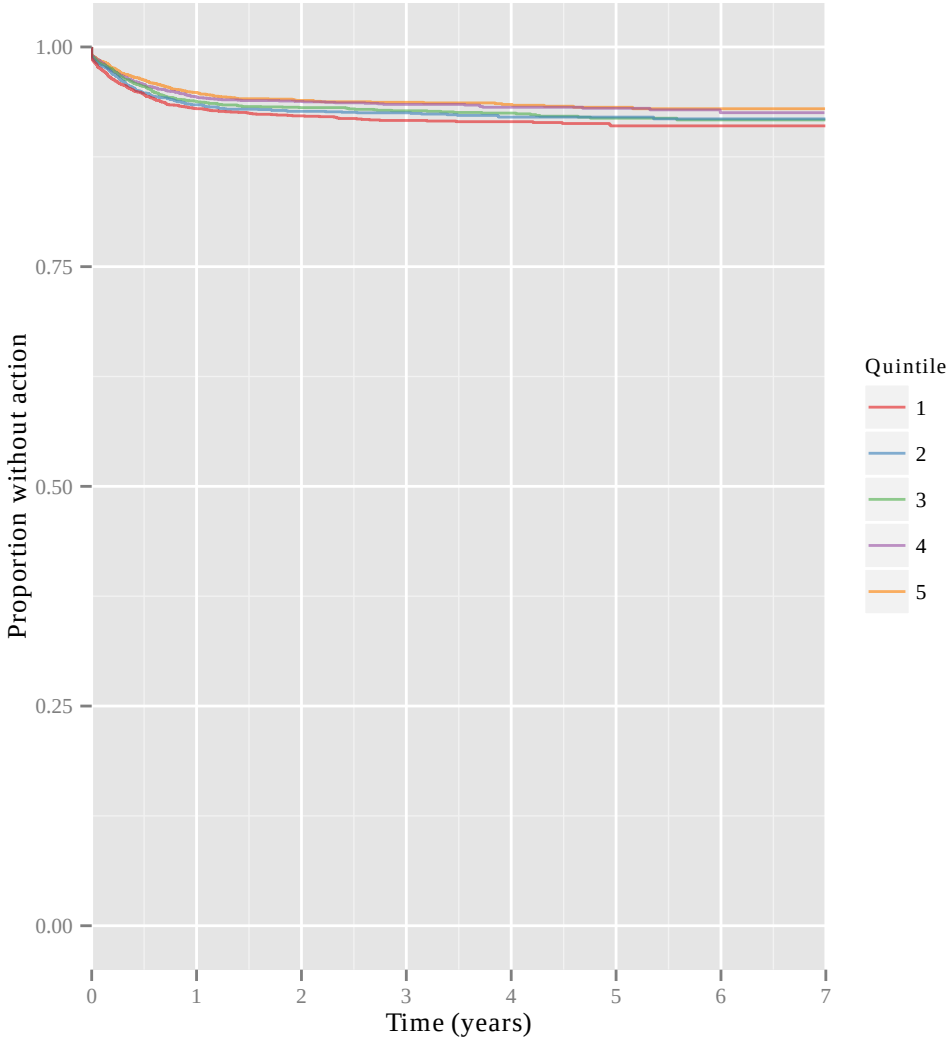
	HR	95% CI
Other adm.	1.24	(1.08; 1.43)
Cardiac cen.	1	(Reference)
Other cen.	0.88	(0.73; 1.06)
Cardiology	1	(Reference)
Med. spec.	0.67	(0.64; 0.70)
Other spec.	0.27	(0.24; 0.31)

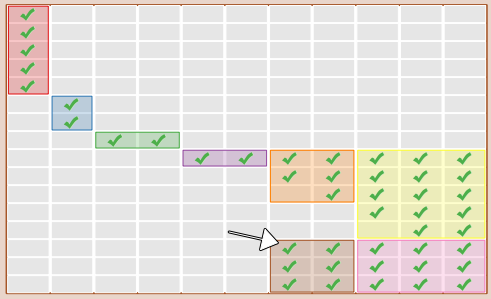
Number of clinical triggers 20467; Number of clinical actions 10132. ICC for practice = 0.05. ICC for hospital = 0.015. Missing values imputed using MICE.



Revascularisation of chronic CHD

Kaplan−Meier plot for 'stable angina' and 'PCI'. Incident clinical trigger (triggers = 18934; actions = 1172)



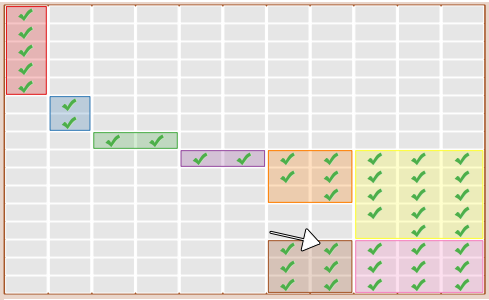


Revascularisation of chronic CHD

Mixed−effects model for 'stable angina' and 'PCI'. Incident clinical trigger

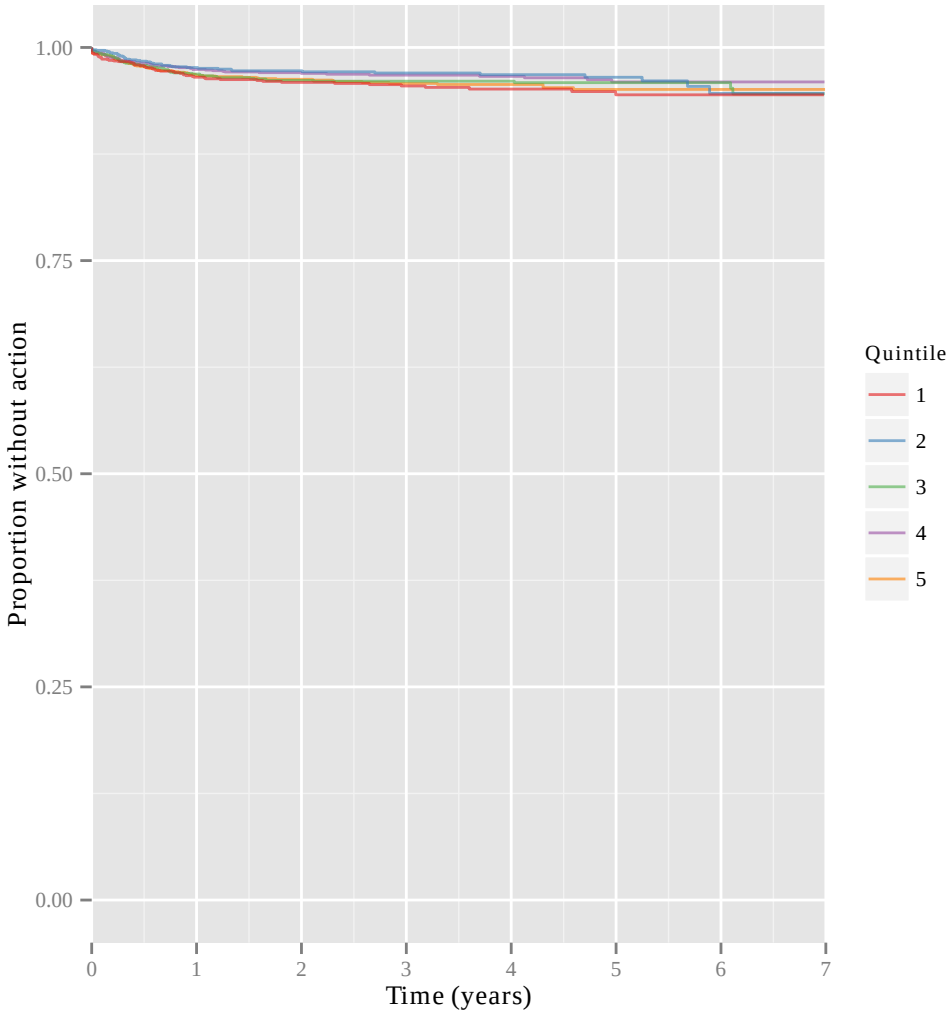
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.97	(0.80; 1.17)
Quintile 3	0.91	(0.75; 1.09)
Quintile 4	0.78	(0.64; 0.96)
Quintile 5	0.72	(0.58; 0.88)
Age 35 to 39	1.07	(0.61; 1.87)
Age 40 to 44	1.27	(0.89; 1.79)
Age 45 to 49	1.22	(0.92; 1.61)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.99	(0.79; 1.26)
Age 60 to 64	1.03	(0.82; 1.29)
Age 65 to 69	0.84	(0.67; 1.07)
Age 70 to 74	0.75	(0.59; 0.96)
Age 75 to 79	0.35	(0.26; 0.47)
Age 80 to 84	0.24	(0.16; 0.35)
Age 85+	0.07	(0.04; 0.15)
Male	1	(Reference)
Female	0.60	(0.53; 0.68)
Non−smoker	1	(Reference)
Smoker	0.97	(0.84; 1.13)
BMI low / norm.	1	(Reference)
Overweight	1.00	(0.85; 1.18)
Obese	0.82	(0.69; 0.96)
No hyp.	1	(Reference)
Hyp. contr.	1.02	(0.88; 1.17)
Hyp. uncontr.	1.26	(1.07; 1.49)
Untreat. hyp.	1.30	(1.04; 1.63)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.75	(1.50; 2.04)
No CVA	1	(Reference)
CVA	0.53	(0.40; 0.70)
No oth. co.	1	(Reference)
Other co.	0.61	(0.52; 0.71)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.00	(0.00; >99)

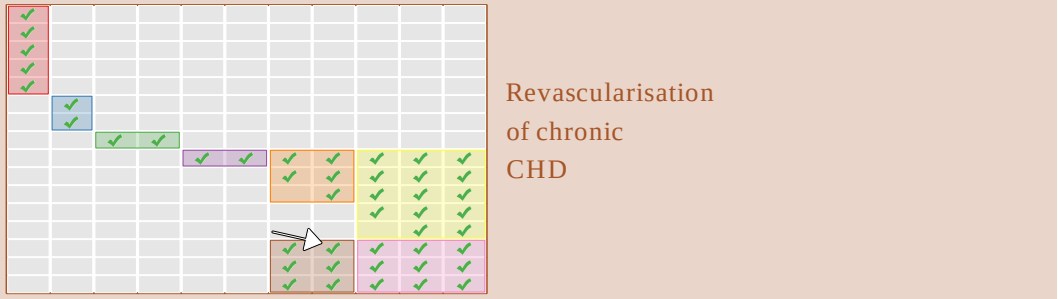
Number of clinical triggers 18934; Number of clinical actions 1172. ICC for practice = 0.084. Missing values imputed using MICE.



Revascularisation of chronic CHD

Kaplan−Meier plot for 'stable angina and diabetes' and 'PCI'. Incident clinical trigger (triggers = 8956; actions = 300)

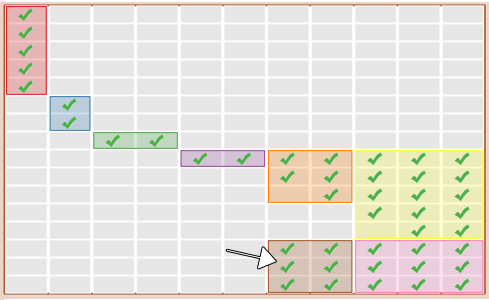




Mixed−effects model for 'stable angina and diabetes' and 'PCI'.
Incident clinical trigger

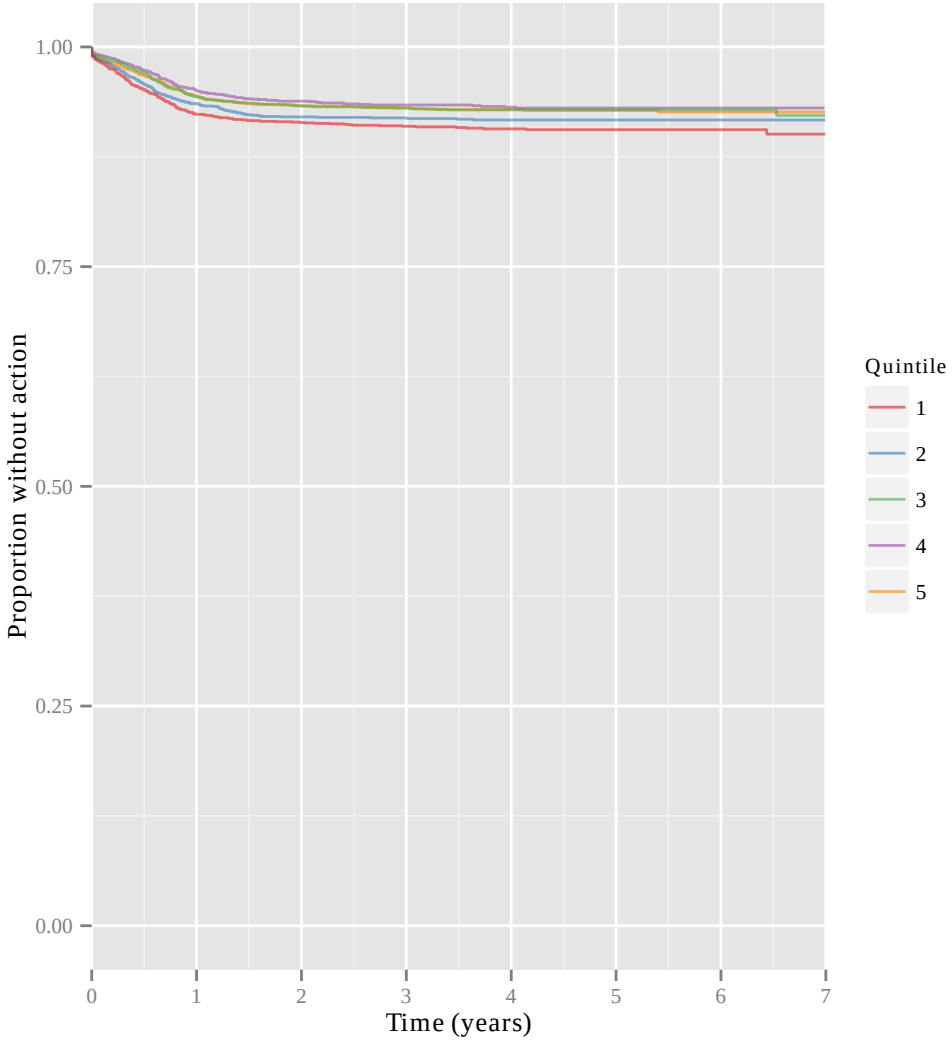
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.71	(0.47; 1.06)
Quintile 3	0.82	(0.57; 1.19)
Quintile 4	0.69	(0.47; 1.01)
Quintile 5	0.84	(0.59; 1.21)
Age 35 to 39	1.12	(0.39; 3.19)
Age 40 to 44	1.35	(0.66; 2.77)
Age 45 to 49	1.29	(0.73; 2.28)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.90	(0.58; 1.42)
Age 60 to 64	0.73	(0.46; 1.14)
Age 65 to 69	0.65	(0.42; 1.03)
Age 70 to 74	0.65	(0.41; 1.02)
Age 75 to 79	0.28	(0.16; 0.50)
Age 80 to 84	0.09	(0.03; 0.25)
Age 85+	0.14	(0.05; 0.40)
Male	1	(Reference)
Female	0.69	(0.53; 0.88)
Non−smoker	1	(Reference)
Smoker	0.87	(0.63; 1.21)
BMI low / norm.	1	(Reference)
Overweight	1.54	(0.99; 2.40)
Obese	1.47	(0.95; 2.27)
No hyp.	1	(Reference)
Hyp. contr.	1.13	(0.83; 1.52)
Hyp. uncontr.	1.14	(0.80; 1.64)
Untreat. hyp.	1.46	(0.80; 2.66)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.97	(0.72; 1.31)
No CVA	1	(Reference)
CVA	0.91	(0.62; 1.33)
No oth. co.	1	(Reference)
Other co.	0.67	(0.51; 0.88)
Indication 1	1	(Reference)
Indication 2	0.40	(0.27; 0.60)
Indic. years	0.95	(0.90; 1.00)
No prev. acti.	1	(Reference)
1+ prev. acti.	1.46	(0.58; 3.68)

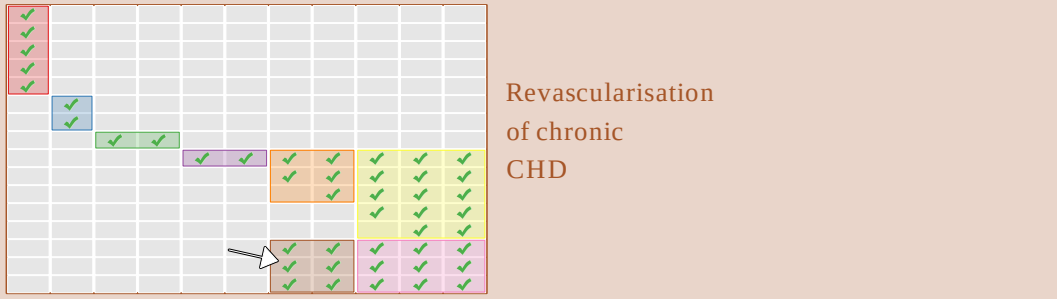
Number of clinical triggers 8956; Number of clinical actions 300. ICC for practice = 0.09. Missing values imputed using MICE.



Revascularisation of chronic CHD

Kaplan−Meier plot for 'stable angina' and 'CABG'. Incident clinical trigger (triggers = 18934; actions = 1150)

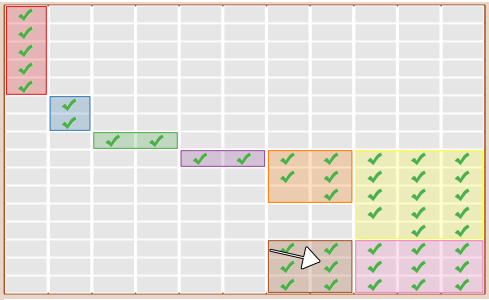




Mixed−effects model for 'stable angina' and 'CABG'. Incident clinical trigger

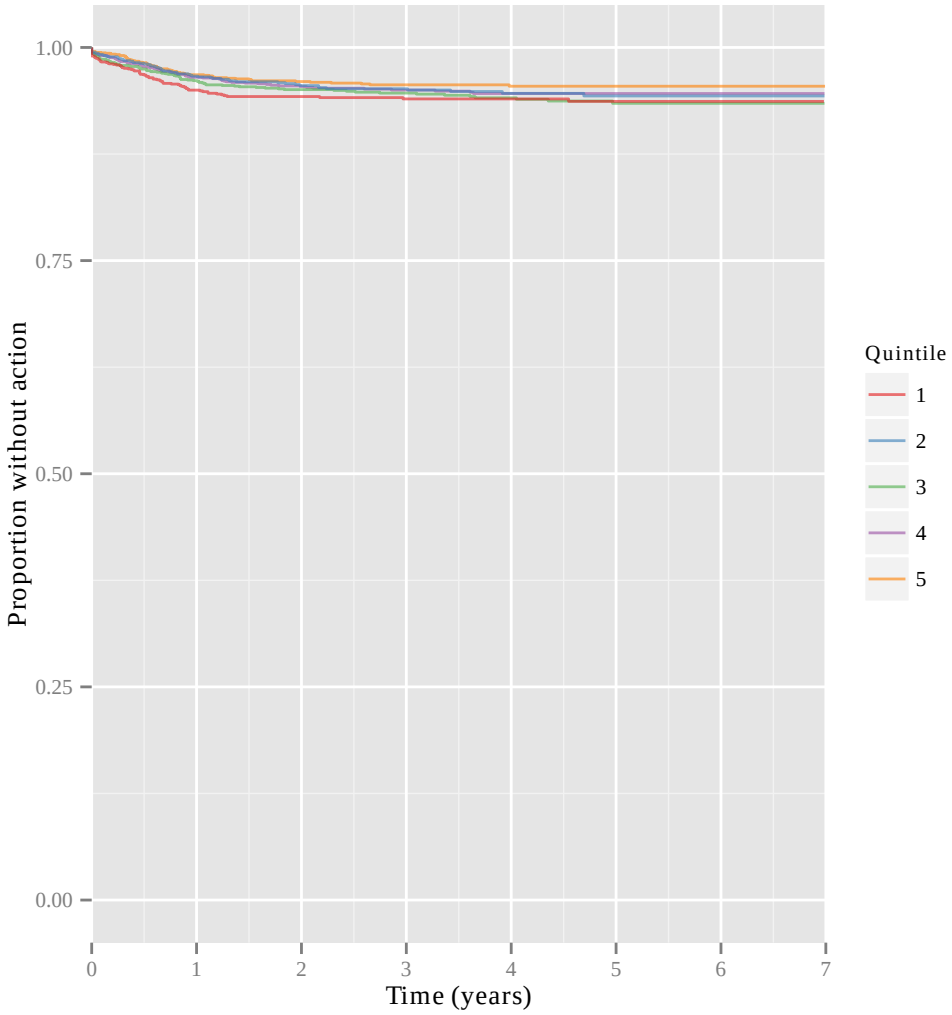
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.93	(0.77; 1.12)
Quintile 3	0.79	(0.66; 0.96)
Quintile 4	0.78	(0.64; 0.96)
Quintile 5	0.87	(0.71; 1.06)
Age 35 to 39	0.64	(0.26; 1.60)
Age 40 to 44	0.36	(0.17; 0.74)
Age 45 to 49	0.93	(0.62; 1.38)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.22	(0.90; 1.64)
Age 60 to 64	1.45	(1.09; 1.94)
Age 65 to 69	1.70	(1.28; 2.25)
Age 70 to 74	1.68	(1.26; 2.24)
Age 75 to 79	1.57	(1.16; 2.11)
Age 80 to 84	0.78	(0.55; 1.11)
Age 85+	0.19	(0.10; 0.36)
Male	1	(Reference)
Female	0.32	(0.28; 0.37)
Non−smoker	1	(Reference)
Smoker	0.88	(0.75; 1.04)
BMI low / norm.	1	(Reference)
Overweight	0.91	(0.77; 1.08)
Obese	0.71	(0.59; 0.85)
No hyp.	1	(Reference)
Hyp. contr.	1.24	(1.08; 1.43)
Hyp. uncontr.	1.31	(1.10; 1.55)
Untreat. hyp.	1.35	(1.07; 1.69)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.49	(1.27; 1.75)
No CVA	1	(Reference)
CVA	0.75	(0.61; 0.93)
No oth. co.	1	(Reference)
Other co.	0.74	(0.64; 0.85)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.00	(0.00; >99)

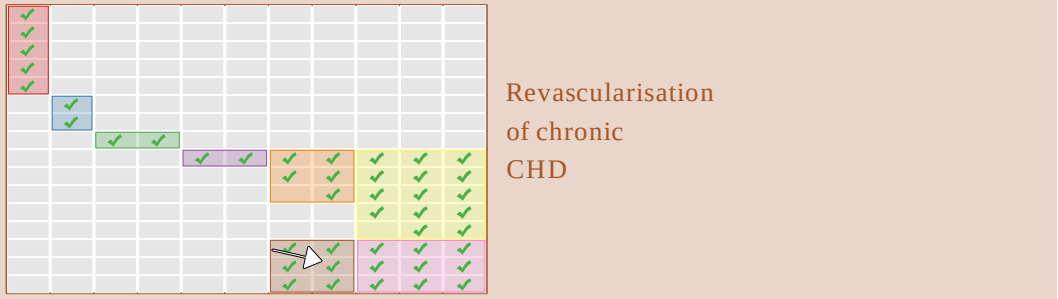
Number of clinical triggers 18934; Number of clinical actions 1150. ICC for practice = 0.072. Missing values imputed using MICE.



Revascularisation of chronic CHD

Kaplan−Meier plot for 'stable angina and diabetes' and 'CABG'. Incident clinical trigger (triggers = 8956; actions = 385)



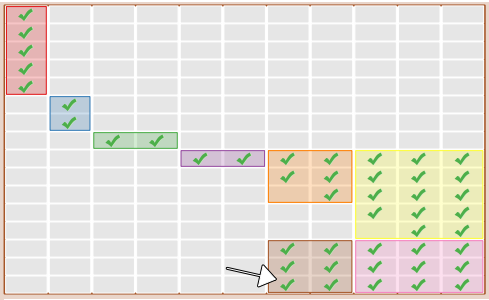


Mixed−effects model for 'stable angina and diabetes' and 'CABG'.
Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.83	(0.59; 1.18)
Quintile 3	0.96	(0.69; 1.34)
Quintile 4	0.91	(0.65; 1.28)
Quintile 5	0.77	(0.54; 1.09)
Age 35 to 39	0.41	(0.05; 3.10)
Age 40 to 44	0.20	(0.03; 1.51)
Age 45 to 49	0.83	(0.36; 1.89)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.57	(0.93; 2.64)
Age 60 to 64	1.51	(0.91; 2.52)
Age 65 to 69	1.54	(0.93; 2.54)
Age 70 to 74	1.55	(0.94; 2.56)
Age 75 to 79	1.40	(0.83; 2.36)
Age 80 to 84	0.63	(0.33; 1.21)
Age 85+	0.21	(0.07; 0.63)
Male	1	(Reference)
Female	0.44	(0.35; 0.56)
Non−smoker	1	(Reference)
Smoker	0.57	(0.40; 0.81)
BMI low / norm.	1	(Reference)
Overweight	0.90	(0.65; 1.26)
Obese	0.79	(0.57; 1.11)
No hyp.	1	(Reference)
Hyp. contr.	1.20	(0.91; 1.57)
Hyp. uncontr.	1.10	(0.79; 1.52)
Untreat. hyp.	0.85	(0.44; 1.65)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.58	(1.22; 2.03)
No CVA	1	(Reference)
CVA	0.87	(0.64; 1.20)
No oth. co.	1	(Reference)
Other co.	0.66	(0.52; 0.83)
Indication 1	1	(Reference)
Indication 2	0.39	(0.27; 0.55)
Indic. years	0.97	(0.93; 1.00)
No prev. acti.	1	(Reference)

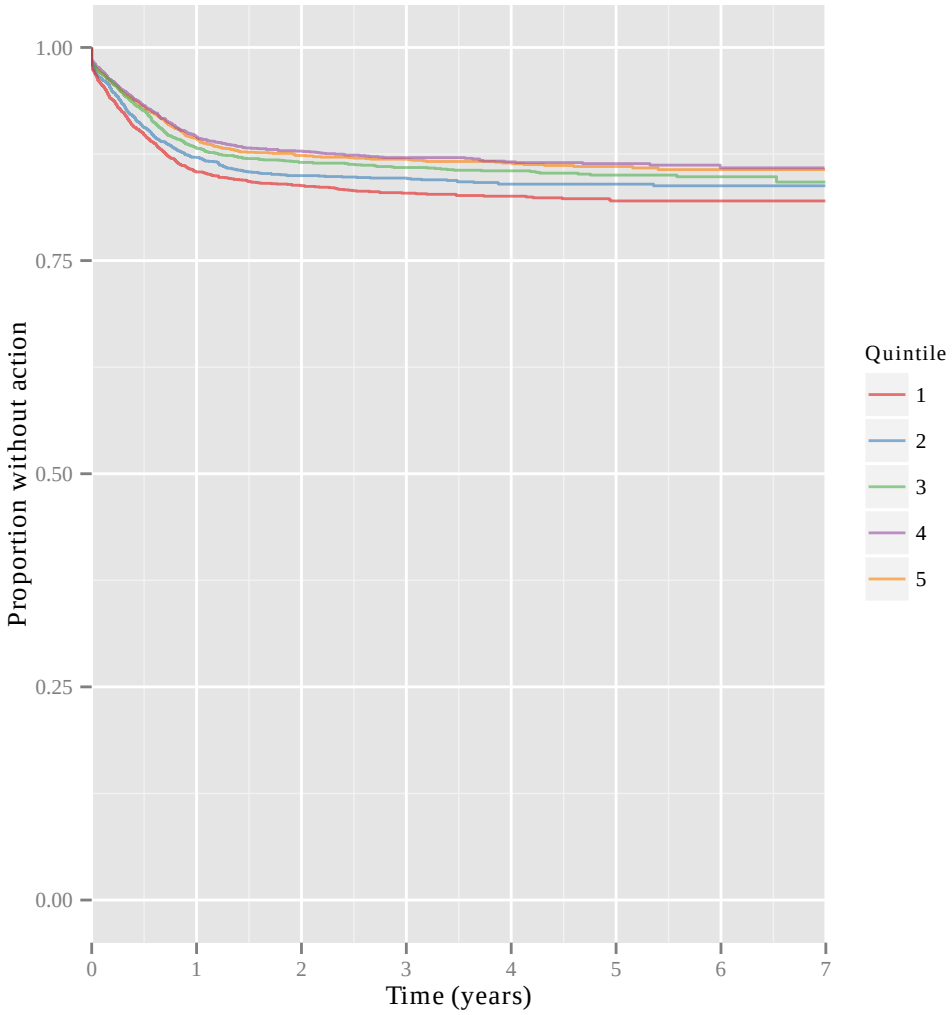
	HR	95% CI
1+ prev. acti.	0.00	(0.00; >99)

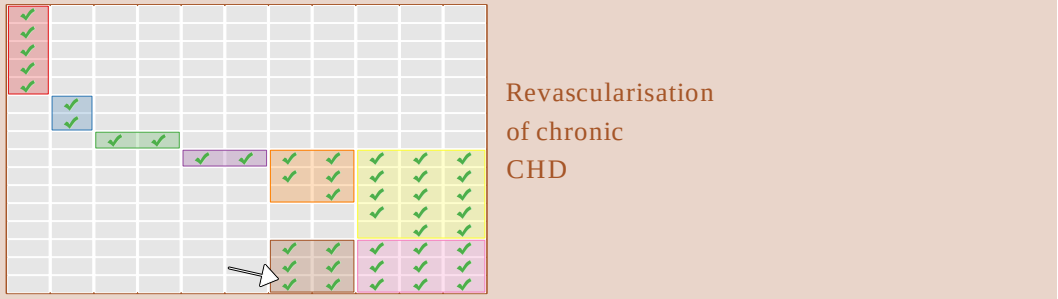
Number of clinical triggers 8956; Number of clinical actions 385. ICC for practice = 0.138. Missing values imputed using MICE.



Revascularisation of chronic CHD

Kaplan−Meier plot for 'stable angina' and 'revascularisation'. Incident clinical trigger (triggers = 18934; actions = 2298)

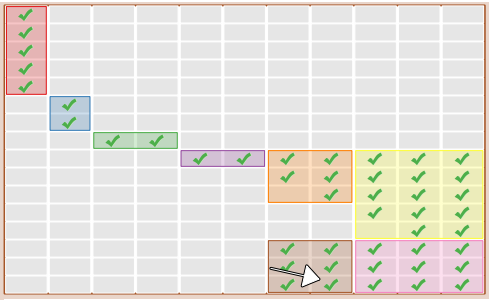




Mixed−effects model for 'stable angina' and 'revascularisation'.
Incident clinical trigger

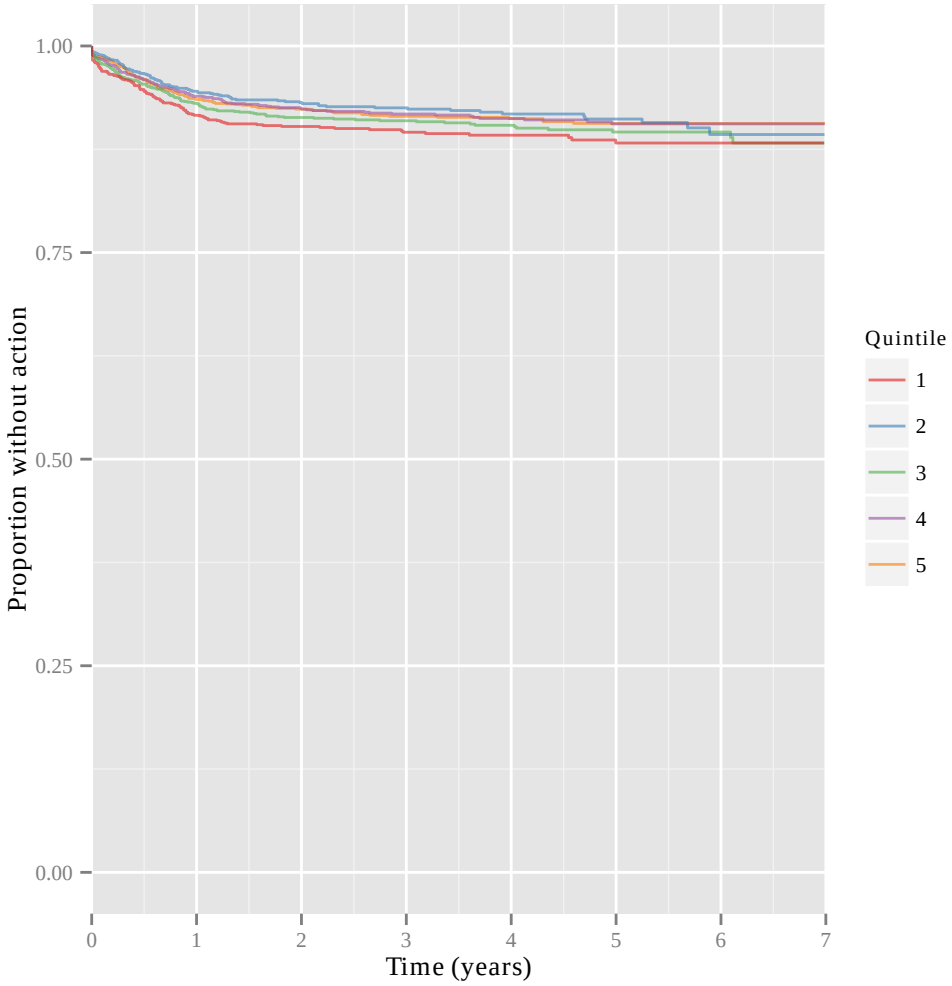
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.96	(0.84; 1.10)
Quintile 3	0.86	(0.75; 0.99)
Quintile 4	0.78	(0.68; 0.90)
Quintile 5	0.79	(0.68; 0.92)
Age 35 to 39	0.90	(0.56; 1.46)
Age 40 to 44	0.91	(0.67; 1.23)
Age 45 to 49	1.12	(0.89; 1.41)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.07	(0.89; 1.29)
Age 60 to 64	1.18	(0.99; 1.41)
Age 65 to 69	1.15	(0.96; 1.38)
Age 70 to 74	1.08	(0.90; 1.30)
Age 75 to 79	0.79	(0.64; 0.96)
Age 80 to 84	0.42	(0.33; 0.55)
Age 85+	0.11	(0.07; 0.18)
Male	1	(Reference)
Female	0.43	(0.39; 0.47)
Non−smoker	1	(Reference)
Smoker	0.93	(0.83; 1.04)
BMI low / norm.	1	(Reference)
Overweight	0.98	(0.88; 1.09)
Obese	0.77	(0.67; 0.89)
No hyp.	1	(Reference)
Hyp. contr.	1.11	(1.01; 1.23)
Hyp. uncontr.	1.29	(1.14; 1.45)
Untreat. hyp.	1.34	(1.14; 1.57)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.57	(1.42; 1.74)
No CVA	1	(Reference)
CVA	0.65	(0.54; 0.77)
No oth. co.	1	(Reference)
Other co.	0.67	(0.60; 0.74)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.00	(0.00; >99)

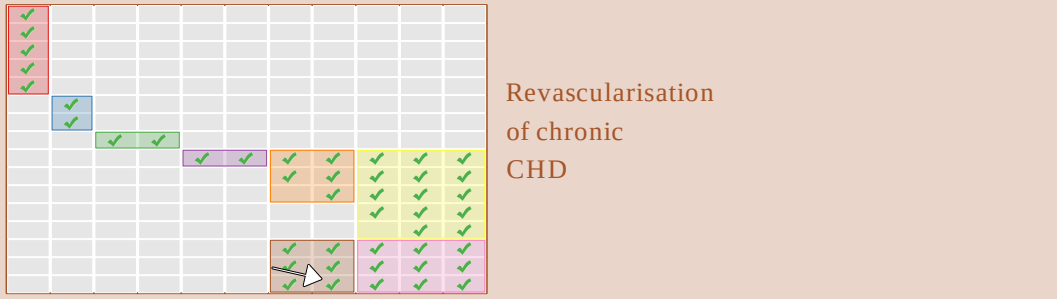
Number of clinical triggers 18934; Number of clinical actions 2298. ICC for practice = 0.074. Missing values imputed using MICE.



Revascularisation of chronic CHD

Kaplan−Meier plot for 'stable angina and diabetes' and 'revascularisation'. Incident clinical trigger (triggers = 8956; actions = 676)

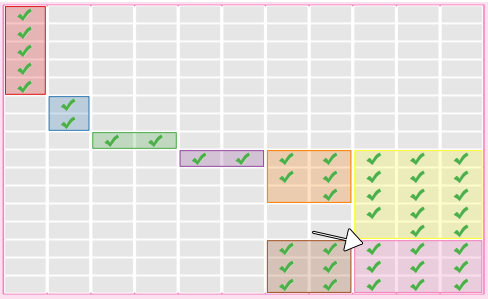




Mixed−effects model for 'stable angina and diabetes' and 'revascularisation'. Incident clinical trigger

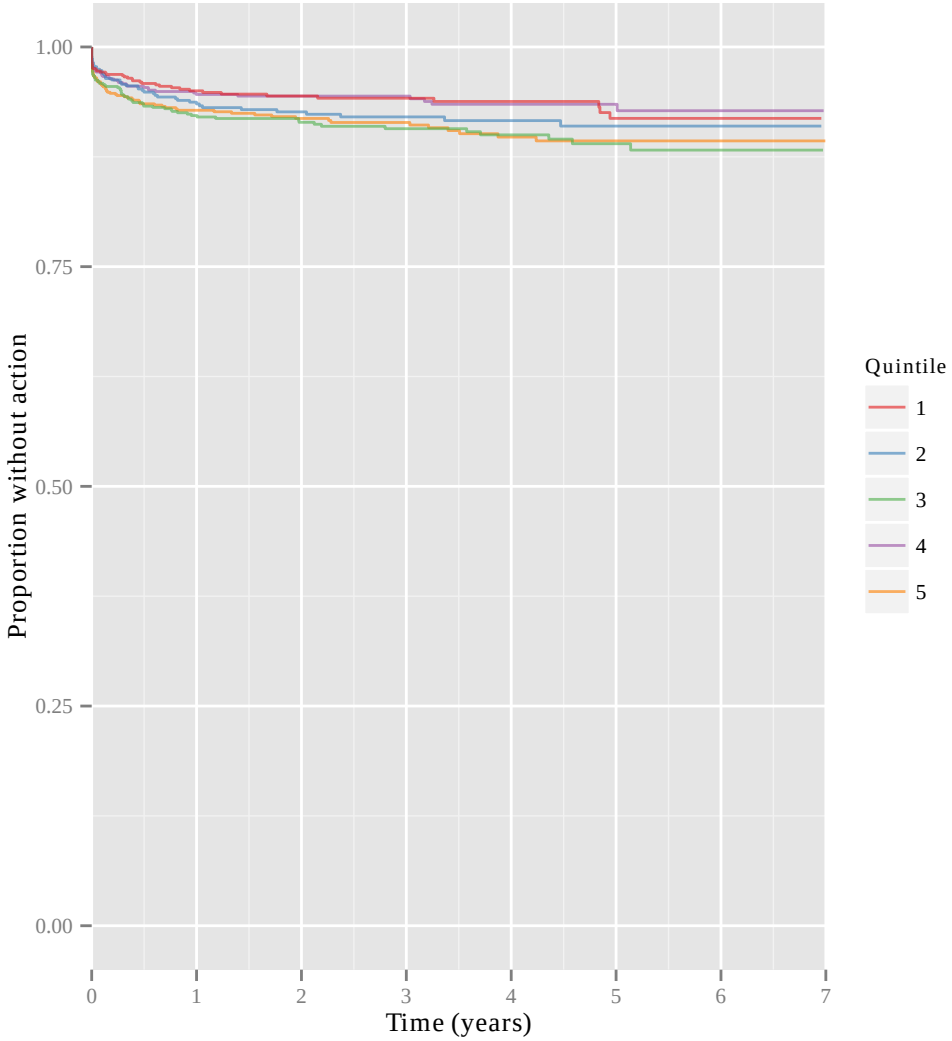
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.75	(0.57; 0.98)
Quintile 3	0.88	(0.68; 1.13)
Quintile 4	0.81	(0.62; 1.04)
Quintile 5	0.79	(0.61; 1.03)
Age 35 to 39	0.83	(0.33; 2.10)
Age 40 to 44	0.87	(0.45; 1.68)
Age 45 to 49	1.12	(0.70; 1.80)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.13	(0.80; 1.58)
Age 60 to 64	1.00	(0.72; 1.40)
Age 65 to 69	0.96	(0.69; 1.33)
Age 70 to 74	0.95	(0.68; 1.33)
Age 75 to 79	0.68	(0.47; 0.97)
Age 80 to 84	0.29	(0.17; 0.48)
Age 85+	0.16	(0.07; 0.34)
Male	1	(Reference)
Female	0.54	(0.45; 0.64)
Non−smoker	1	(Reference)
Smoker	0.70	(0.55; 0.88)
BMI low / norm.	1	(Reference)
Overweight	1.12	(0.86; 1.46)
Obese	1.02	(0.78; 1.32)
No hyp.	1	(Reference)
Hyp. contr.	1.16	(0.95; 1.42)
Hyp. uncontr.	1.10	(0.86; 1.41)
Untreat. hyp.	1.13	(0.72; 1.76)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.30	(1.11; 1.53)
No CVA	1	(Reference)
CVA	0.87	(0.68; 1.11)
No oth. co.	1	(Reference)
Other co.	0.65	(0.54; 0.78)
Indication 1	1	(Reference)
Indication 2	0.39	(0.30; 0.51)
Indic. years	0.96	(0.93; 0.99)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.53	(0.27; 1.04)

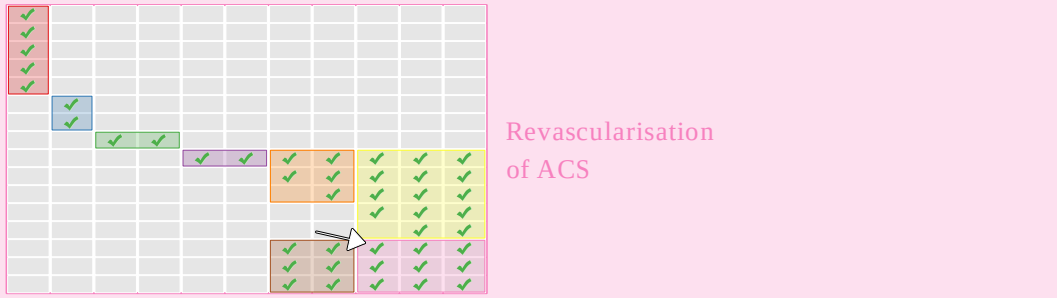
Number of clinical triggers 8956; Number of clinical actions 676. ICC for practice = 0.104. Missing values imputed using MICE.



Revascularisation of ACS

Kaplan−Meier plot for 'old ACS' and 'PCI'. Incident clinical trigger (triggers = 4256; actions = 290)

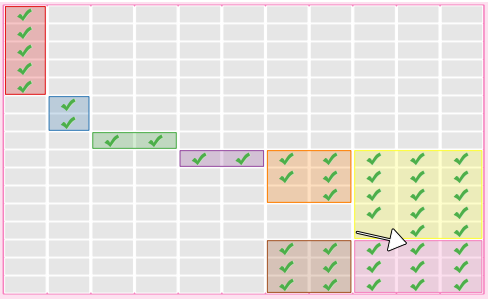




Mixed−effects model for 'old ACS' and 'PCI'. Incident clinical trigger

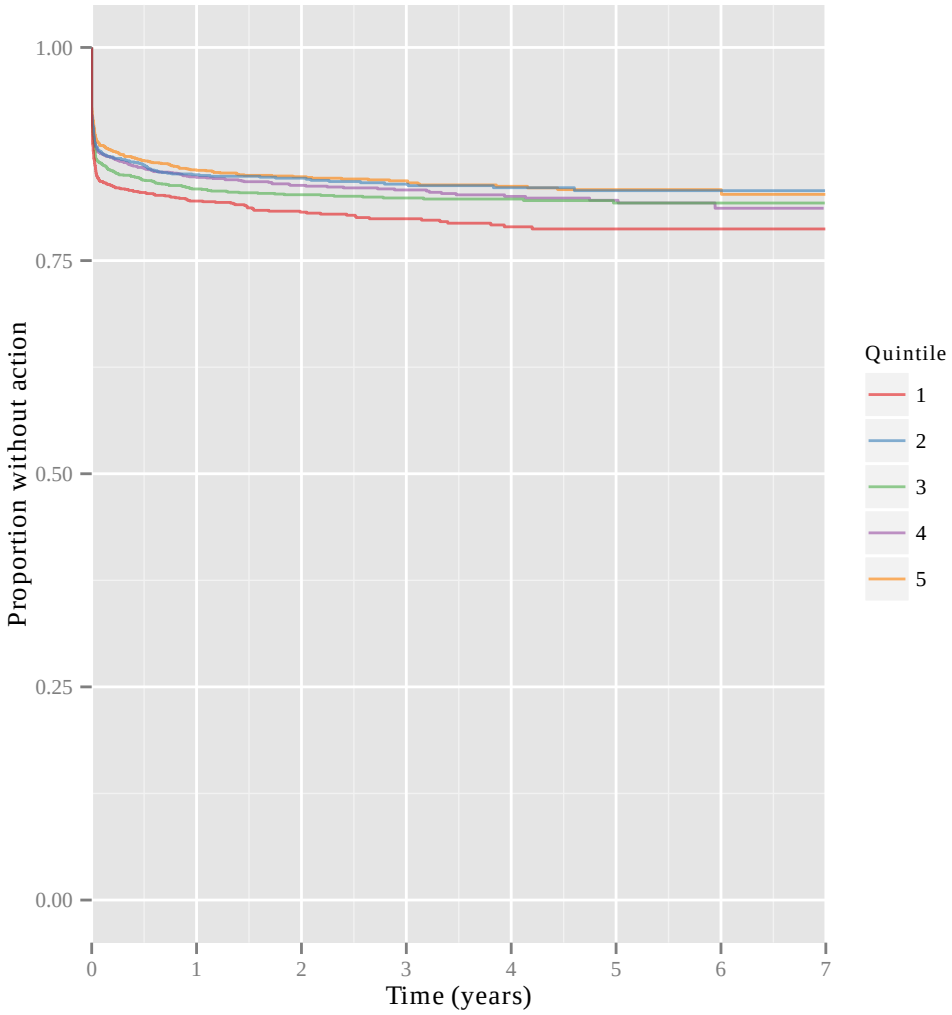
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.21	(0.81; 1.82)
Quintile 3	1.47	(1.02; 2.14)
Quintile 4	0.90	(0.59; 1.36)
Quintile 5	1.33	(0.91; 1.95)
Age 35 to 39	0.68	(0.21; 2.21)
Age 40 to 44	0.83	(0.47; 1.47)
Age 45 to 49	0.71	(0.41; 1.21)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.68	(0.44; 1.06)
Age 60 to 64	0.69	(0.45; 1.06)
Age 65 to 69	0.54	(0.35; 0.85)
Age 70 to 74	0.58	(0.37; 0.89)
Age 75 to 79	0.25	(0.14; 0.44)
Age 80 to 84	0.22	(0.12; 0.41)
Age 85+	0.05	(0.02; 0.17)
Male	1	(Reference)
Female	0.71	(0.54; 0.93)
Non−smoker	1	(Reference)
Smoker	1.30	(0.98; 1.72)
BMI low / norm.	1	(Reference)
Overweight	1.13	(0.81; 1.56)
Obese	1.04	(0.74; 1.45)
No hyp.	1	(Reference)
Hyp. contr.	0.98	(0.74; 1.29)
Hyp. uncontr.	1.27	(0.89; 1.81)
Untreat. hyp.	1.16	(0.69; 1.94)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.50	(1.01; 2.22)
No CVA	1	(Reference)
CVA	0.55	(0.34; 0.89)
No oth. co.	1	(Reference)
Other co.	0.63	(0.48; 0.83)
No diabetes	1	(Reference)
Diabetes	0.76	(0.55; 1.04)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.77	(0.45; 1.30)

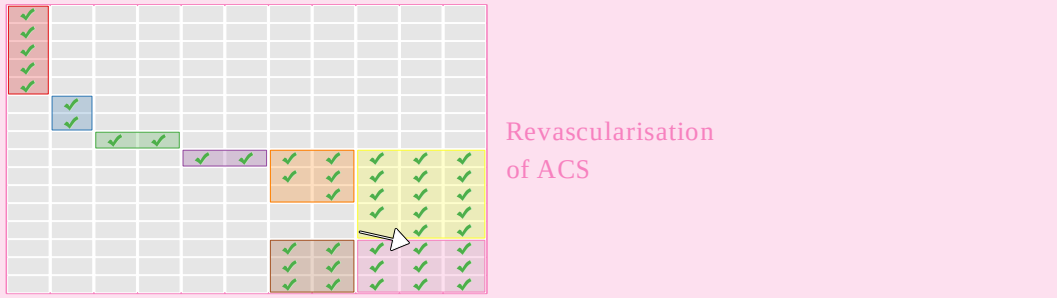
Number of clinical triggers 4256; Number of clinical actions 290. ICC for practice < 0.005. Missing values imputed using MICE.



Revascularisation of ACS

Kaplan−Meier plot for 'unstable angina' and 'PCI'. Incident clinical trigger (triggers = 13907; actions = 2130)



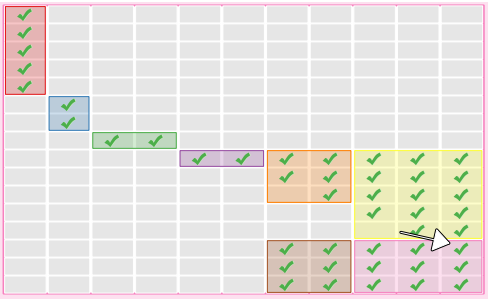


Mixed−effects model for 'unstable angina' and 'PCI'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.83	(0.72; 0.97)
Quintile 3	0.88	(0.76; 1.00)
Quintile 4	0.87	(0.76; 1.00)
Quintile 5	0.76	(0.66; 0.88)
Age 35 to 39	0.81	(0.52; 1.27)
Age 40 to 44	0.53	(0.39; 0.72)
Age 45 to 49	1.00	(0.81; 1.23)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.83	(0.70; 0.99)
Age 60 to 64	0.82	(0.69; 0.97)
Age 65 to 69	0.75	(0.63; 0.89)
Age 70 to 74	0.73	(0.61; 0.87)
Age 75 to 79	0.52	(0.42; 0.63)
Age 80 to 84	0.40	(0.32; 0.50)
Age 85+	0.17	(0.12; 0.24)
Male	1	(Reference)
Female	0.74	(0.67; 0.81)
Non−smoker	1	(Reference)
Smoker	1.16	(1.03; 1.29)
BMI low / norm.	1	(Reference)
Overweight	1.08	(0.96; 1.23)
Obese	0.97	(0.85; 1.11)
No hyp.	1	(Reference)
Hyp. contr.	0.87	(0.78; 0.97)
Hyp. uncontr.	1.03	(0.90; 1.19)
Untreat. hyp.	0.79	(0.59; 1.05)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.37	(1.21; 1.54)
No CVA	1	(Reference)
CVA	0.71	(0.61; 0.82)
No oth. co.	1	(Reference)
Other co.	0.72	(0.66; 0.80)
No diabetes	1	(Reference)
Diabetes	0.85	(0.76; 0.95)
Elect. adm.	1	(Reference)
Emer. adm.	0.94	(0.79; 1.13)

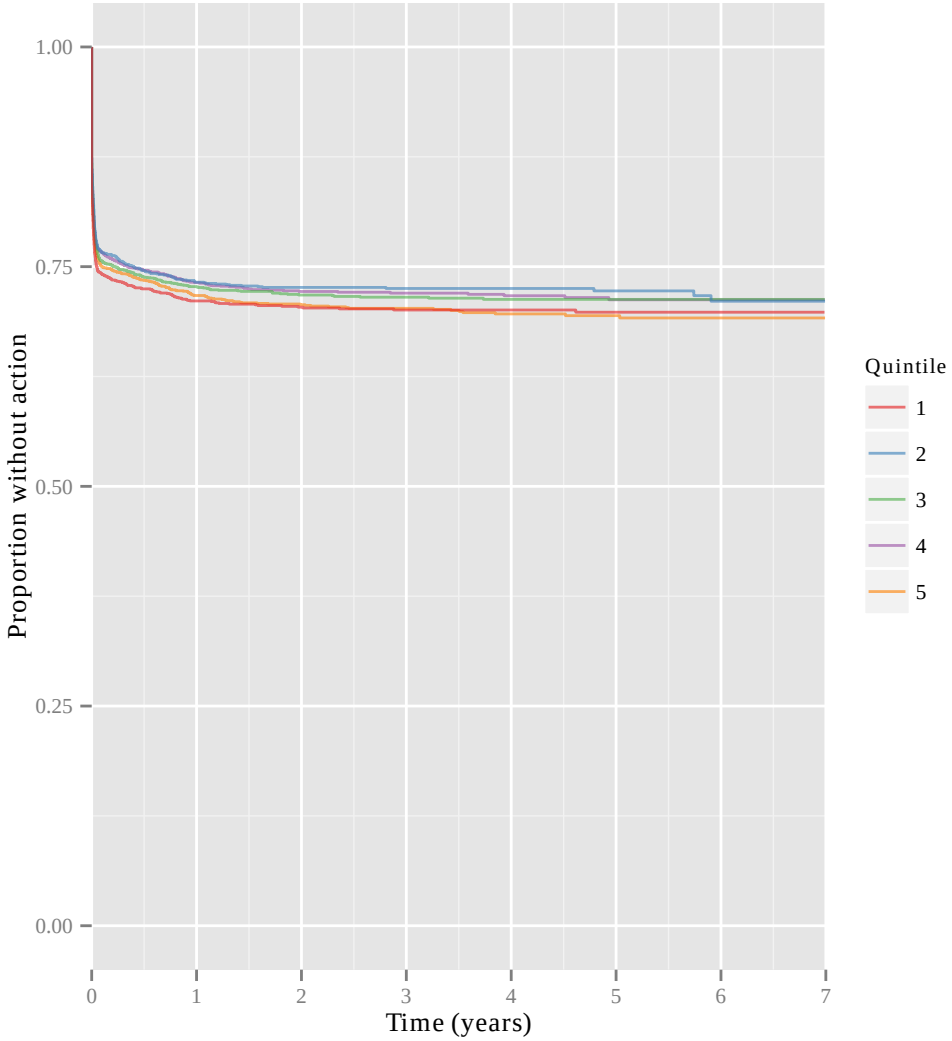
	HR	95% CI
Other adm.	1.81	(1.52; 2.17)
Cardiac cen.	1	(Reference)
Other cen.	0.53	(0.32; 0.86)
Cardiology	1	(Reference)
Med. spec.	0.31	(0.28; 0.35)
Other spec.	0.05	(0.04; 0.08)
Indication 1	1	(Reference)
Indication 2	0.96	(0.86; 1.08)
Indication 3	0.87	(0.75; 1.02)
Indication 4	0.72	(0.58; 0.89)
Indication 5+	0.69	(0.55; 0.86)
Indic. years	1.00	(0.99; 1.01)
No prev. acti.	1	(Reference)
1+ prev. acti.	1.40	(1.22; 1.60)

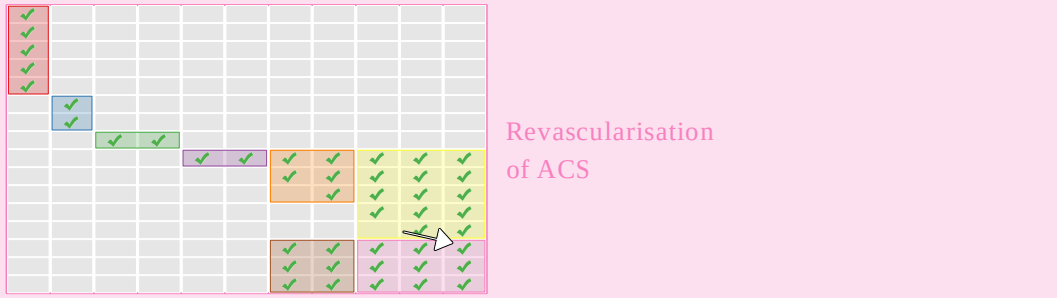
Number of clinical triggers 13907; Number of clinical actions 2130. ICC for practice < 0.005. ICC for hospital = 0.115. Missing values imputed using MICE.



Revascularisation of ACS

Kaplan−Meier plot for 'MI' and 'PCI'. Incident clinical trigger (triggers = 20467; actions = 5118)



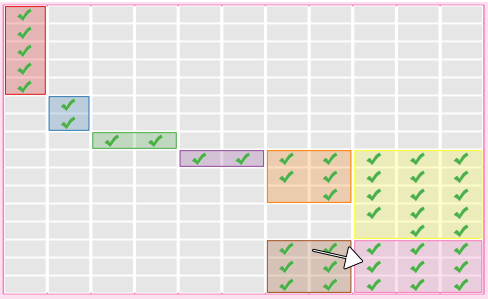


Mixed−effects model for 'MI' and 'PCI'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.89	(0.80; 0.98)
Quintile 3	0.90	(0.82; 0.99)
Quintile 4	0.87	(0.79; 0.95)
Quintile 5	0.83	(0.75; 0.91)
Age 35 to 39	0.77	(0.62; 0.95)
Age 40 to 44	0.90	(0.77; 1.05)
Age 45 to 49	0.90	(0.79; 1.03)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.90	(0.81; 1.01)
Age 60 to 64	0.80	(0.71; 0.89)
Age 65 to 69	0.78	(0.70; 0.87)
Age 70 to 74	0.56	(0.50; 0.63)
Age 75 to 79	0.43	(0.37; 0.48)
Age 80 to 84	0.24	(0.20; 0.28)
Age 85+	0.08	(0.07; 0.10)
Male	1	(Reference)
Female	0.86	(0.80; 0.91)
Non−smoker	1	(Reference)
Smoker	1.15	(1.08; 1.23)
BMI low / norm.	1	(Reference)
Overweight	1.11	(1.01; 1.22)
Obese	1.08	(0.98; 1.18)
No hyp.	1	(Reference)
Hyp. contr.	0.99	(0.92; 1.06)
Hyp. uncontr.	1.04	(0.95; 1.13)
Untreat. hyp.	1.14	(1.00; 1.30)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.18	(1.09; 1.28)
No CVA	1	(Reference)
CVA	0.67	(0.59; 0.75)
No oth. co.	1	(Reference)
Other co.	0.70	(0.65; 0.74)
No diabetes	1	(Reference)
Diabetes	0.82	(0.75; 0.88)
Elect. adm.	1	(Reference)
Emer. adm.	1.67	(1.30; 2.13)

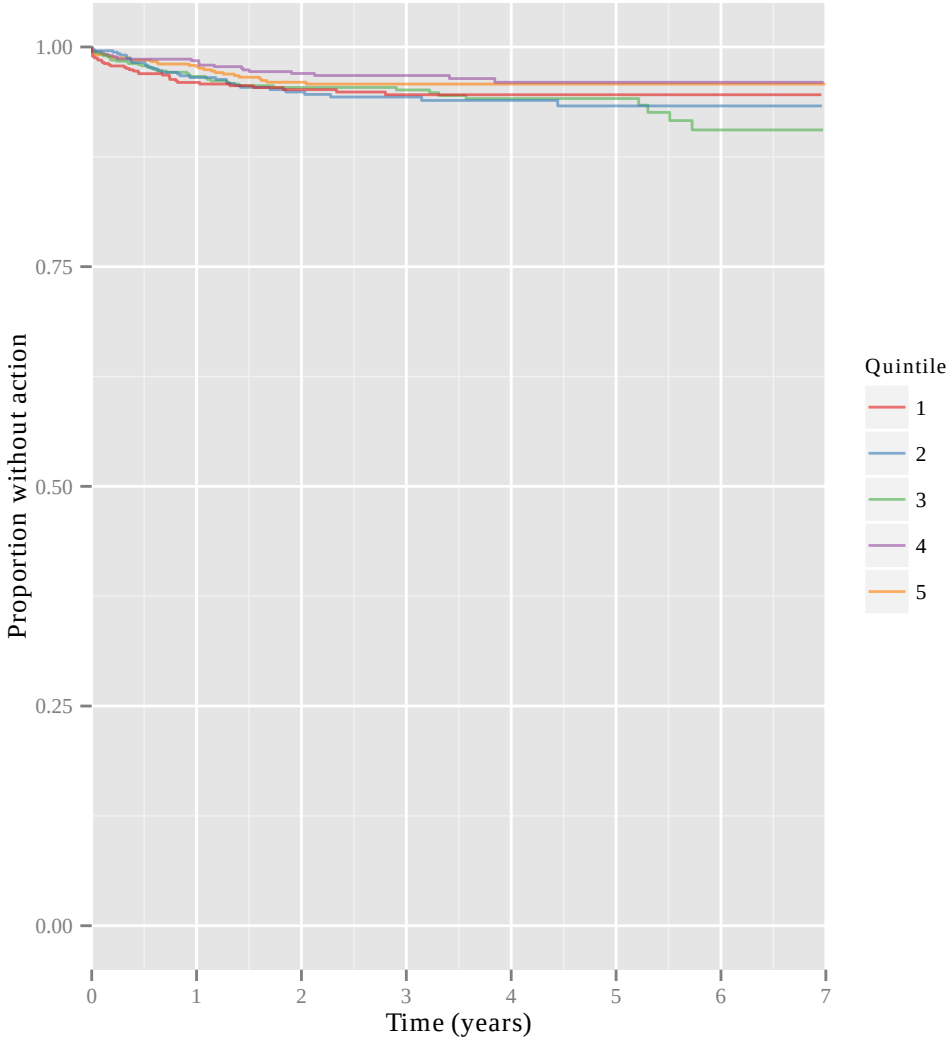
	HR	95% CI
Other adm.	1.97	(1.53; 2.53)
Cardiac cen.	1	(Reference)
Other cen.	0.56	(0.34; 0.92)
Cardiology	1	(Reference)
Med. spec.	0.43	(0.40; 0.46)
Other spec.	0.07	(0.05; 0.09)
Indication 1	1	(Reference)
Indication 2	0.84	(0.77; 0.91)
Indication 3	0.68	(0.60; 0.78)
Indication 4	0.67	(0.55; 0.82)
Indication 5+	0.65	(0.50; 0.84)
Indic. years	1.00	(0.99; 1.01)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.93	(0.81; 1.06)

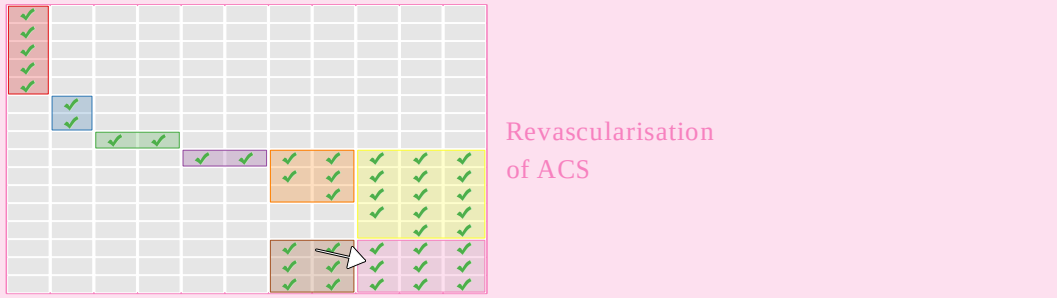
Number of clinical triggers 20467; Number of clinical actions 5118. ICC for practice = 0.013. ICC for hospital = 0.127. Missing values imputed using MICE.



Revascularisation of ACS

Kaplan−Meier plot for 'old ACS' and 'CABG'. Incident clinical trigger (triggers = 4256; actions = 159)

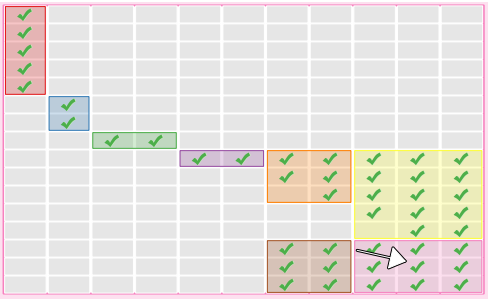




Mixed−effects model for 'old ACS' and 'CABG'. Incident clinical trigger

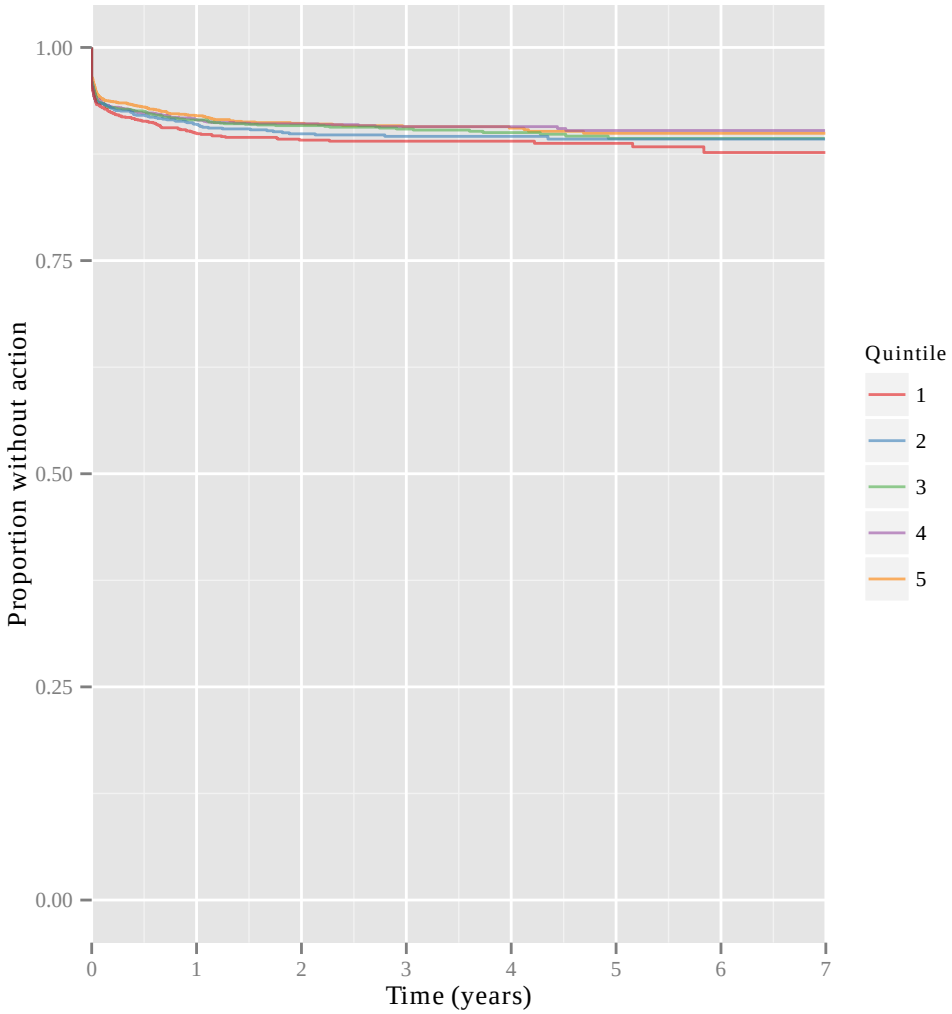
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.01	(0.62; 1.64)
Quintile 3	1.06	(0.67; 1.68)
Quintile 4	0.67	(0.39; 1.14)
Quintile 5	0.78	(0.47; 1.29)
Age 35 to 39	0.00	(0.00; >99)
Age 40 to 44	0.18	(0.02; 1.39)
Age 45 to 49	0.70	(0.24; 1.99)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.03	(0.48; 2.19)
Age 60 to 64	1.42	(0.71; 2.83)
Age 65 to 69	1.39	(0.70; 2.77)
Age 70 to 74	1.64	(0.84; 3.22)
Age 75 to 79	0.82	(0.38; 1.75)
Age 80 to 84	0.47	(0.19; 1.16)
Age 85+	0.00	(0.00; >99)
Male	1	(Reference)
Female	0.48	(0.33; 0.72)
Non−smoker	1	(Reference)
Smoker	0.84	(0.54; 1.30)
BMI low / norm.	1	(Reference)
Overweight	1.23	(0.78; 1.93)
Obese	0.90	(0.55; 1.48)
No hyp.	1	(Reference)
Hyp. contr.	1.15	(0.78; 1.71)
Hyp. uncontr.	1.45	(0.89; 2.34)
Untreat. hyp.	2.02	(1.12; 3.63)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.45	(0.73; 2.90)
No CVA	1	(Reference)
CVA	0.62	(0.35; 1.09)
No oth. co.	1	(Reference)
Other co.	0.61	(0.42; 0.88)
No diabetes	1	(Reference)
Diabetes	1.33	(0.92; 1.92)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.00	(0.00; >99)

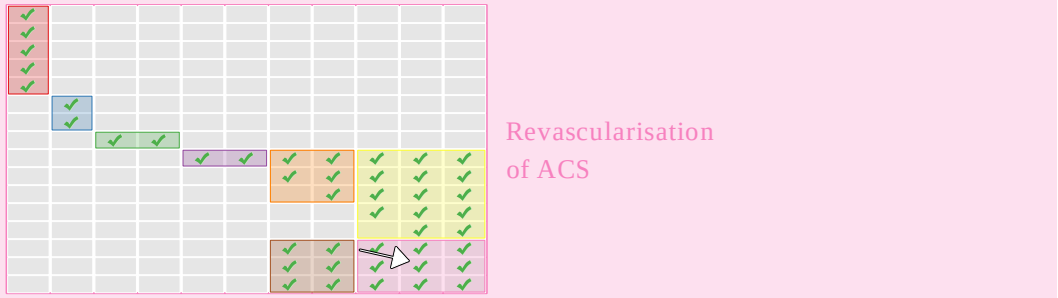
Number of clinical triggers 4256; Number of clinical actions 159. ICC for practice < 0.005. Missing values imputed using MICE.



Revascularisation of ACS

Kaplan−Meier plot for 'unstable angina' and 'CABG'. Incident clinical trigger (triggers = 13907; actions = 1155)



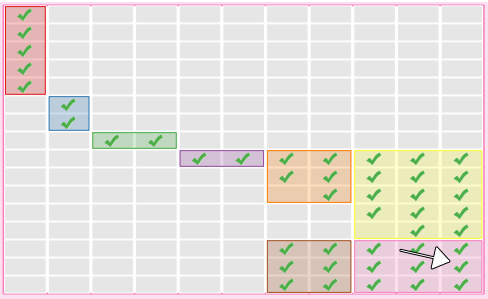


Mixed−effects model for 'unstable angina' and 'CABG'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.02	(0.83; 1.25)
Quintile 3	0.95	(0.78; 1.15)
Quintile 4	1.00	(0.82; 1.22)
Quintile 5	0.97	(0.79; 1.17)
Age 35 to 39	0.52	(0.19; 1.44)
Age 40 to 44	0.54	(0.30; 0.98)
Age 45 to 49	0.48	(0.29; 0.79)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.25	(0.93; 1.68)
Age 60 to 64	1.21	(0.91; 1.61)
Age 65 to 69	1.54	(1.16; 2.04)
Age 70 to 74	1.49	(1.12; 1.97)
Age 75 to 79	1.30	(0.97; 1.74)
Age 80 to 84	0.57	(0.41; 0.81)
Age 85+	0.04	(0.02; 0.09)
Male	1	(Reference)
Female	0.55	(0.48; 0.63)
Non−smoker	1	(Reference)
Smoker	0.77	(0.66; 0.91)
BMI low / norm.	1	(Reference)
Overweight	1.02	(0.85; 1.21)
Obese	0.95	(0.80; 1.14)
No hyp.	1	(Reference)
Hyp. contr.	1.30	(1.11; 1.53)
Hyp. uncontr.	1.63	(1.34; 1.98)
Untreat. hyp.	1.33	(0.93; 1.91)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.47	(1.27; 1.69)
No CVA	1	(Reference)
CVA	0.78	(0.64; 0.94)
No oth. co.	1	(Reference)
Other co.	0.60	(0.52; 0.68)
No diabetes	1	(Reference)
Diabetes	1.20	(1.05; 1.37)
Elect. adm.	1	(Reference)
Emer. adm.	1.15	(0.95; 1.39)

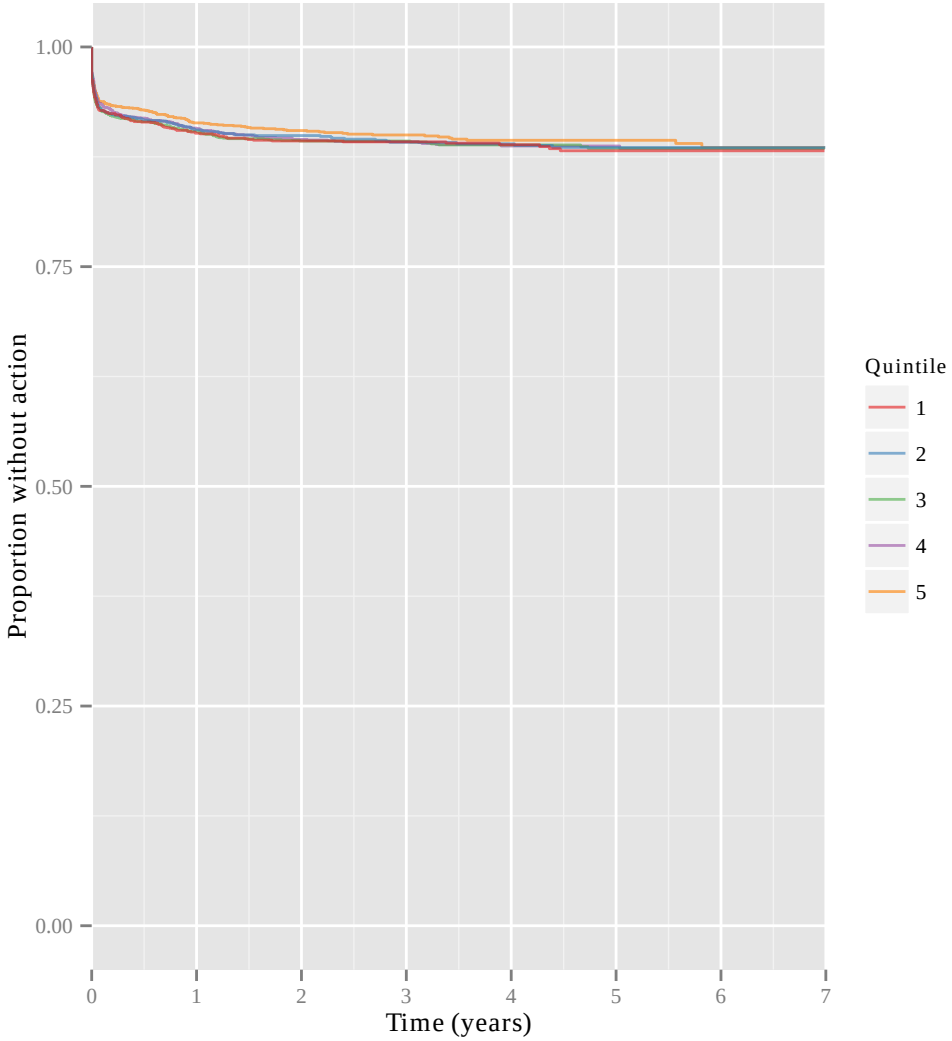
	HR	95% CI
Other adm.	1.63	(1.33; 1.99)
Cardiac cen.	1	(Reference)
Other cen.	0.67	(0.43; 1.04)
Cardiology	1	(Reference)
Med. spec.	0.77	(0.65; 0.92)
Other spec.	8.10	(6.94; 9.47)
Indication 1	1	(Reference)
Indication 2	1.37	(1.17; 1.61)
Indication 3	1.55	(1.27; 1.89)
Indication 4	1.30	(0.99; 1.70)
Indication 5+	0.95	(0.69; 1.29)
Indic. years	0.99	(0.98; 1.00)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.03	(0.01; 0.11)

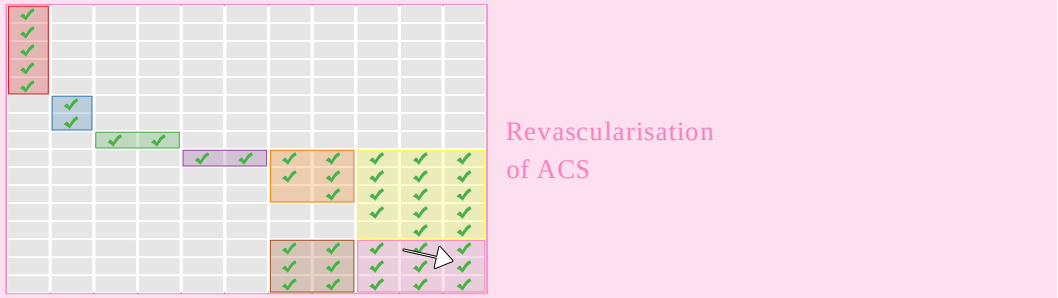
Number of clinical triggers 13907; Number of clinical actions 1155. ICC for practice = 0.031. ICC for hospital = 0.075. Missing values imputed using MICE.



Revascularisation of ACS

Kaplan−Meier plot for 'MI' and 'CABG'. Incident clinical trigger (triggers = 20467; actions = 1645)



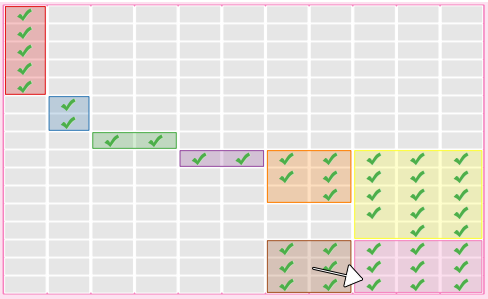


Mixed−effects model for 'MI' and 'CABG'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.98	(0.82; 1.16)
Quintile 3	0.94	(0.80; 1.11)
Quintile 4	0.95	(0.80; 1.13)
Quintile 5	0.89	(0.74; 1.06)
Age 35 to 39	0.33	(0.14; 0.75)
Age 40 to 44	0.70	(0.45; 1.08)
Age 45 to 49	0.80	(0.57; 1.13)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.31	(1.03; 1.67)
Age 60 to 64	1.57	(1.25; 1.97)
Age 65 to 69	1.61	(1.29; 2.03)
Age 70 to 74	1.61	(1.28; 2.02)
Age 75 to 79	1.06	(0.84; 1.36)
Age 80 to 84	0.49	(0.37; 0.65)
Age 85+	0.06	(0.03; 0.10)
Male	1	(Reference)
Female	0.57	(0.50; 0.64)
Non−smoker	1	(Reference)
Smoker	0.85	(0.75; 0.96)
BMI low / norm.	1	(Reference)
Overweight	1.09	(0.95; 1.24)
Obese	1.17	(1.01; 1.35)
No hyp.	1	(Reference)
Hyp. contr.	1.12	(0.98; 1.27)
Hyp. uncontr.	1.31	(1.13; 1.52)
Untreat. hyp.	1.12	(0.87; 1.43)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.09	(0.96; 1.25)
No CVA	1	(Reference)
CVA	0.76	(0.64; 0.90)
No oth. co.	1	(Reference)
Other co.	0.59	(0.53; 0.66)
No diabetes	1	(Reference)
Diabetes	1.22	(1.08; 1.37)
Elect. adm.	1	(Reference)
Emer. adm.	2.89	(2.14; 3.89)

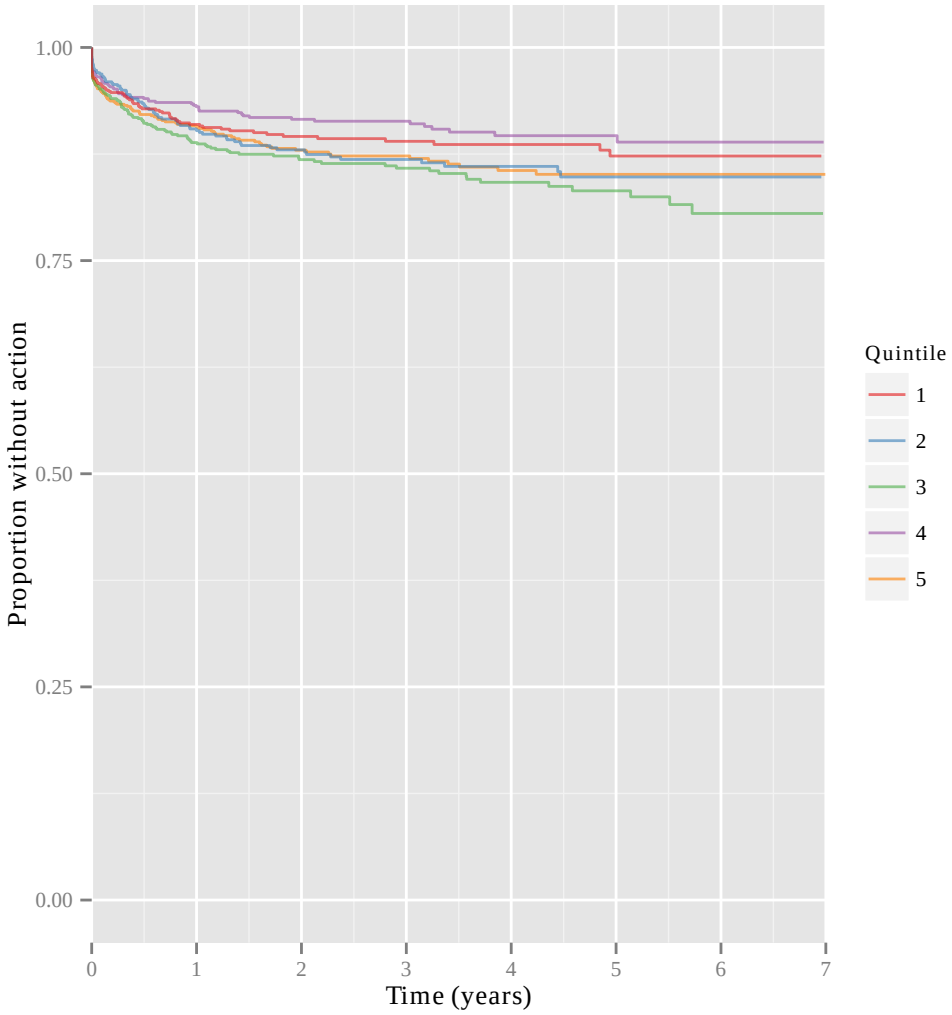
	HR	95% CI
Other adm.	3.35	(2.45; 4.59)
Cardiac cen.	1	(Reference)
Other cen.	0.67	(0.46; 0.98)
Cardiology	1	(Reference)
Med. spec.	0.98	(0.86; 1.13)
Other spec.	8.78	(7.64; 10.09)
Indication 1	1	(Reference)
Indication 2	1.28	(1.13; 1.46)
Indication 3	1.36	(1.13; 1.62)
Indication 4	1.37	(1.04; 1.82)
Indication 5+	1.09	(0.76; 1.55)
Indic. years	1.01	(1.00; 1.02)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.04	(0.01; 0.15)

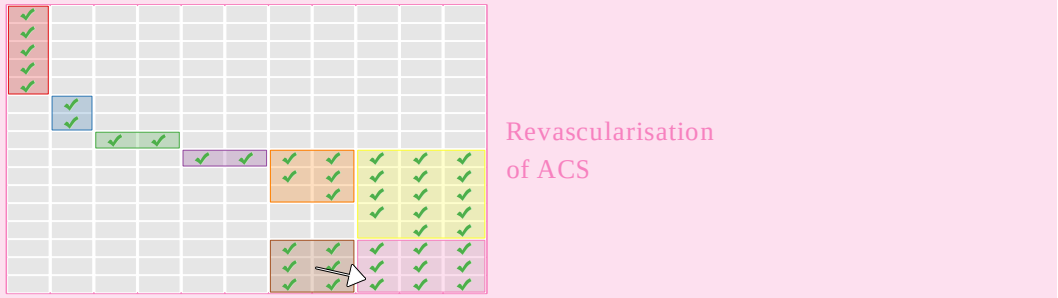
Number of clinical triggers 20467; Number of clinical actions 1645. ICC for practice = 0.05. ICC for hospital = 0.06. Missing values imputed using MICE.



Revascularisation of ACS

Kaplan−Meier plot for 'old ACS' and 'revascularisation'. Incident clinical trigger (triggers = 4256; actions = 441)

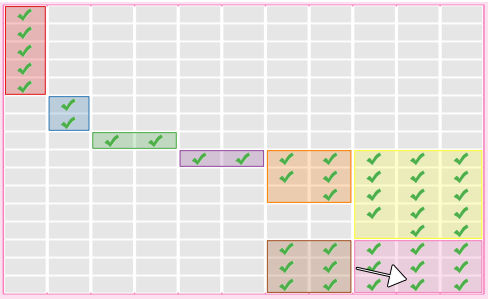




Mixed−effects model for 'old ACS' and 'revascularisation'. Incident clinical trigger

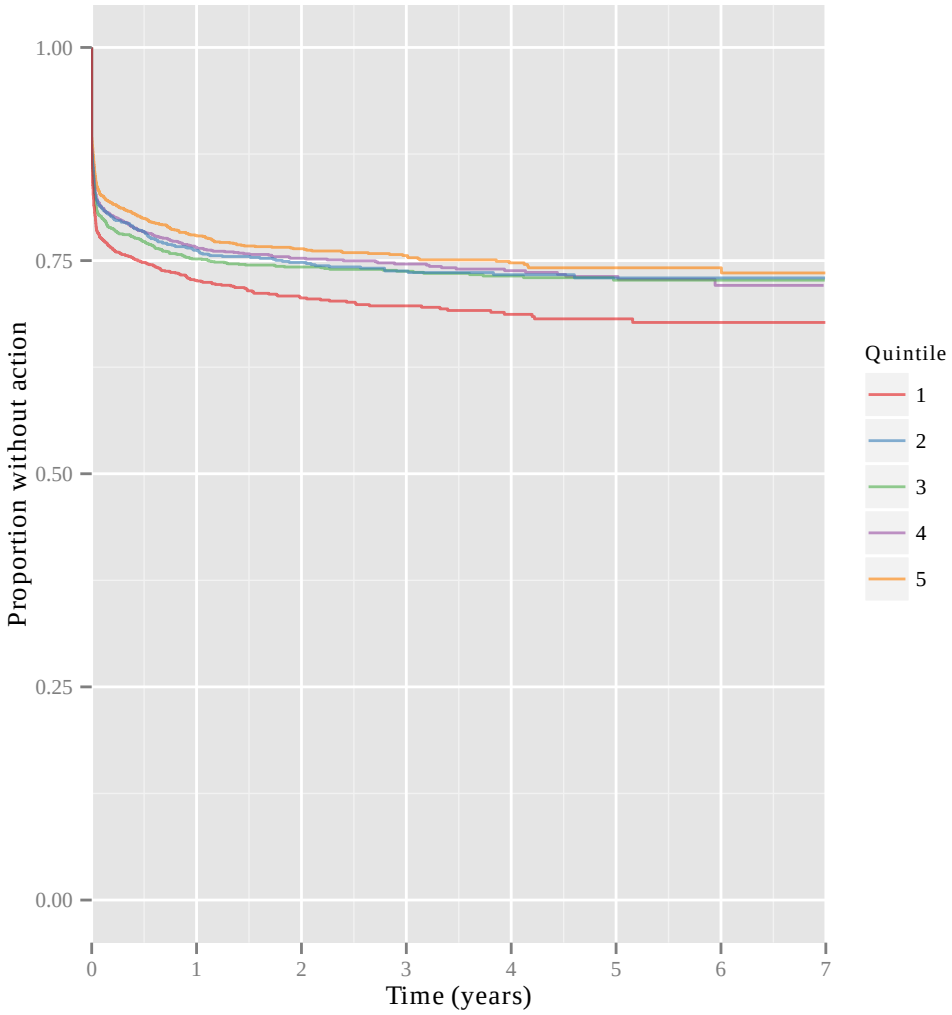
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.09	(0.79; 1.49)
Quintile 3	1.30	(0.97; 1.74)
Quintile 4	0.77	(0.55; 1.07)
Quintile 5	1.10	(0.81; 1.49)
Age 35 to 39	0.55	(0.17; 1.79)
Age 40 to 44	0.70	(0.41; 1.21)
Age 45 to 49	0.70	(0.43; 1.14)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.76	(0.52; 1.12)
Age 60 to 64	0.87	(0.61; 1.24)
Age 65 to 69	0.72	(0.50; 1.05)
Age 70 to 74	0.79	(0.55; 1.13)
Age 75 to 79	0.34	(0.22; 0.53)
Age 80 to 84	0.25	(0.15; 0.42)
Age 85+	0.04	(0.01; 0.12)
Male	1	(Reference)
Female	0.62	(0.49; 0.77)
Non−smoker	1	(Reference)
Smoker	1.12	(0.87; 1.43)
BMI low / norm.	1	(Reference)
Overweight	1.15	(0.86; 1.53)
Obese	0.98	(0.74; 1.31)
No hyp.	1	(Reference)
Hyp. contr.	1.06	(0.85; 1.34)
Hyp. uncontr.	1.28	(0.96; 1.71)
Untreat. hyp.	1.34	(0.90; 1.99)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.47	(1.07; 2.02)
No CVA	1	(Reference)
CVA	0.55	(0.38; 0.79)
No oth. co.	1	(Reference)
Other co.	0.62	(0.50; 0.78)
No diabetes	1	(Reference)
Diabetes	0.89	(0.70; 1.14)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.44	(0.28; 0.70)

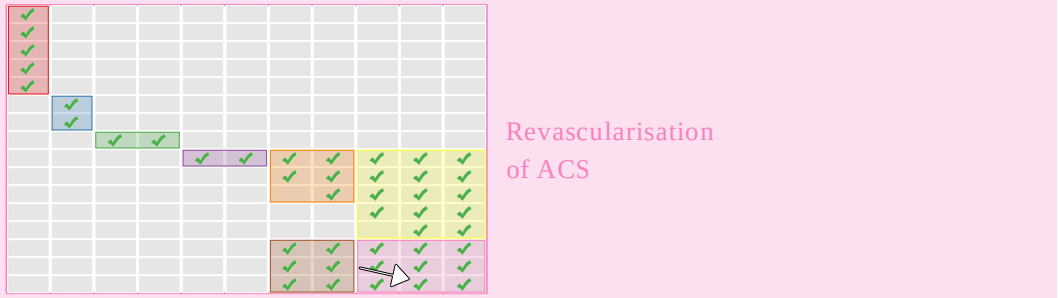
Number of clinical triggers 4256; Number of clinical actions 441. ICC for practice < 0.005. Missing values imputed using MICE.



Revascularisation of ACS

Kaplan−Meier plot for 'unstable angina' and 'revascularisation'. Incident clinical trigger (triggers = 13907; actions = 3230)



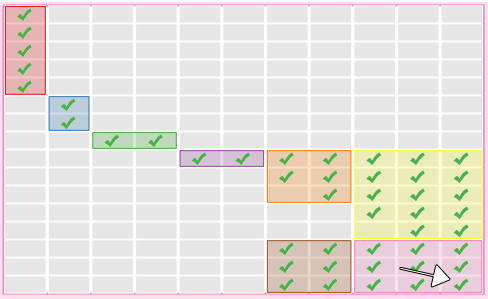


Mixed−effects model for 'unstable angina' and 'revascularisation'. Incident clinical trigger

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.90	(0.80; 1.02)
Quintile 3	0.92	(0.82; 1.04)
Quintile 4	0.92	(0.82; 1.04)
Quintile 5	0.83	(0.74; 0.94)
Age 35 to 39	0.70	(0.47; 1.06)
Age 40 to 44	0.53	(0.40; 0.70)
Age 45 to 49	0.89	(0.73; 1.08)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.93	(0.80; 1.08)
Age 60 to 64	0.90	(0.77; 1.04)
Age 65 to 69	0.93	(0.80; 1.08)
Age 70 to 74	0.88	(0.76; 1.02)
Age 75 to 79	0.69	(0.59; 0.81)
Age 80 to 84	0.41	(0.34; 0.49)
Age 85+	0.11	(0.08; 0.15)
Male	1	(Reference)
Female	0.64	(0.59; 0.70)
Non−smoker	1	(Reference)
Smoker	1.01	(0.92; 1.11)
BMI low / norm.	1	(Reference)
Overweight	1.09	(0.99; 1.21)
Obese	0.96	(0.85; 1.08)
No hyp.	1	(Reference)
Hyp. contr.	0.98	(0.90; 1.07)
Hyp. uncontr.	1.23	(1.10; 1.38)
Untreat. hyp.	0.93	(0.74; 1.16)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.41	(1.25; 1.60)
No CVA	1	(Reference)
CVA	0.70	(0.62; 0.79)
No oth. co.	1	(Reference)
Other co.	0.66	(0.61; 0.71)
No diabetes	1	(Reference)
Diabetes	0.96	(0.88; 1.04)
Elect. adm.	1	(Reference)
Emer. adm.	1.01	(0.89; 1.15)

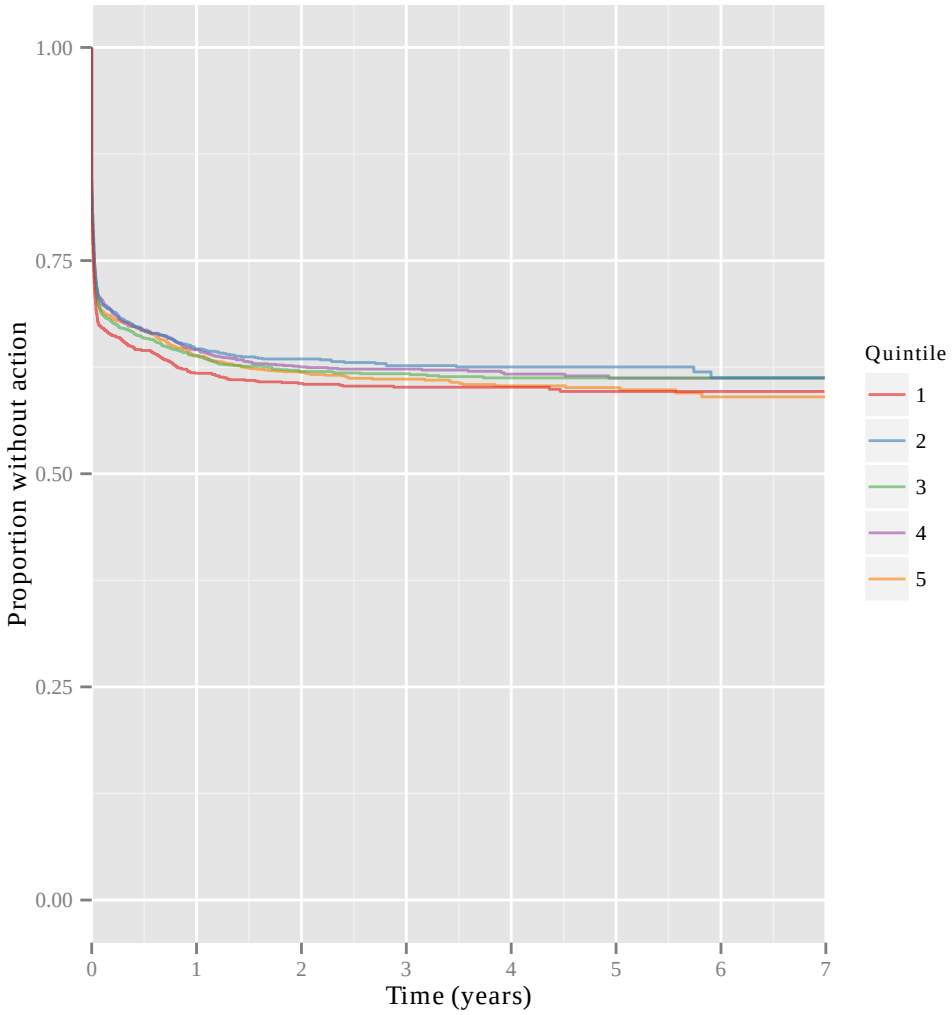
	HR	95% CI
Other adm.	1.88	(1.64; 2.15)
Cardiac cen.	1	(Reference)
Other cen.	0.49	(0.31; 0.77)
Cardiology	1	(Reference)
Med. spec.	0.36	(0.33; 0.40)
Other spec.	1.17	(1.04; 1.31)
Indication 1	1	(Reference)
Indication 2	1.14	(1.04; 1.25)
Indication 3	1.19	(1.06; 1.35)
Indication 4	1.02	(0.86; 1.21)
Indication 5+	0.86	(0.71; 1.03)
Indic. years	0.99	(0.99; 1.00)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.73	(0.65; 0.82)

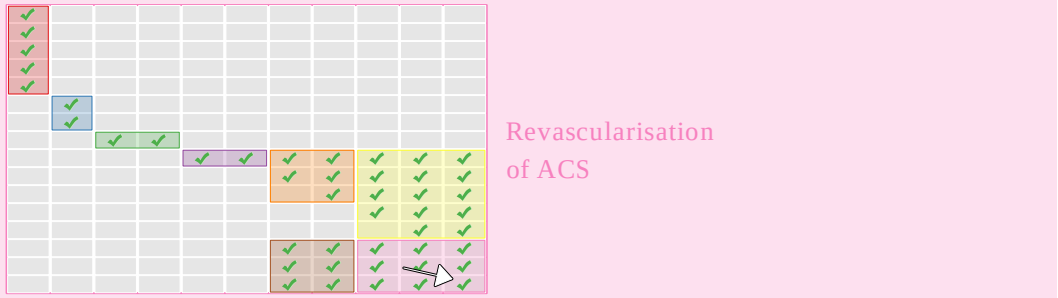
Number of clinical triggers 13907; Number of clinical actions 3230. ICC for practice = 0.01. ICC for hospital = 0.104. Missing values imputed using MICE.



Revascularisation of ACS

Kaplan−Meier plot for 'MI' and 'revascularisation'. Incident clinical trigger (triggers = 20467; actions = 6649)





Mixed−effects model for 'MI' and 'revascularisation'. Incident clinical trigger

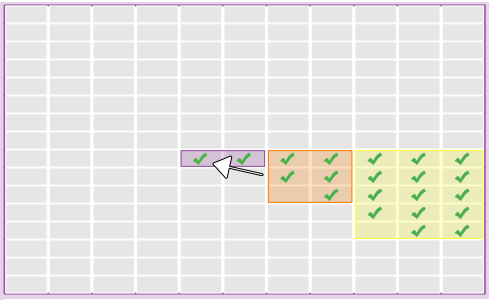
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.89	(0.82; 0.97)
Quintile 3	0.90	(0.83; 0.97)
Quintile 4	0.87	(0.80; 0.95)
Quintile 5	0.83	(0.77; 0.91)
Age 35 to 39	0.68	(0.55; 0.83)
Age 40 to 44	0.87	(0.75; 1.01)
Age 45 to 49	0.89	(0.78; 1.00)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.97	(0.87; 1.07)
Age 60 to 64	0.89	(0.81; 0.98)
Age 65 to 69	0.89	(0.80; 0.98)
Age 70 to 74	0.69	(0.62; 0.76)
Age 75 to 79	0.49	(0.44; 0.55)
Age 80 to 84	0.25	(0.22; 0.28)
Age 85+	0.07	(0.05; 0.08)
Male	1	(Reference)
Female	0.74	(0.70; 0.78)
Non−smoker	1	(Reference)
Smoker	1.10	(1.04; 1.16)
BMI low / norm.	1	(Reference)
Overweight	1.13	(1.06; 1.21)
Obese	1.10	(1.02; 1.19)
No hyp.	1	(Reference)
Hyp. contr.	1.04	(0.97; 1.10)
Hyp. uncontr.	1.12	(1.04; 1.21)
Untreat. hyp.	1.12	(1.00; 1.26)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.17	(1.10; 1.24)
No CVA	1	(Reference)
CVA	0.67	(0.61; 0.74)
No oth. co.	1	(Reference)
Other co.	0.65	(0.61; 0.69)
No diabetes	1	(Reference)
Diabetes	0.90	(0.84; 0.96)
Elect. adm.	1	(Reference)
Emer. adm.	2.14	(1.76; 2.60)

	HR	95% CI
Other adm.	2.73	(2.24; 3.34)
Cardiac cen.	1	(Reference)
Other cen.	0.51	(0.30; 0.87)
Cardiology	1	(Reference)
Med. spec.	0.47	(0.44; 0.50)
Other spec.	0.95	(0.85; 1.06)
Indication 1	1	(Reference)
Indication 2	0.99	(0.92; 1.06)
Indication 3	0.92	(0.83; 1.03)
Indication 4	0.94	(0.80; 1.12)
Indication 5+	0.92	(0.75; 1.14)
Indic. years	1.00	(0.99; 1.01)
No prev. acti.	1	(Reference)
1+ prev. acti.	0.55	(0.49; 0.62)

Number of clinical triggers 20467; Number of clinical actions 6649. ICC for practice = 0.007. ICC for hospital = 0.142. Missing values imputed using MICE.

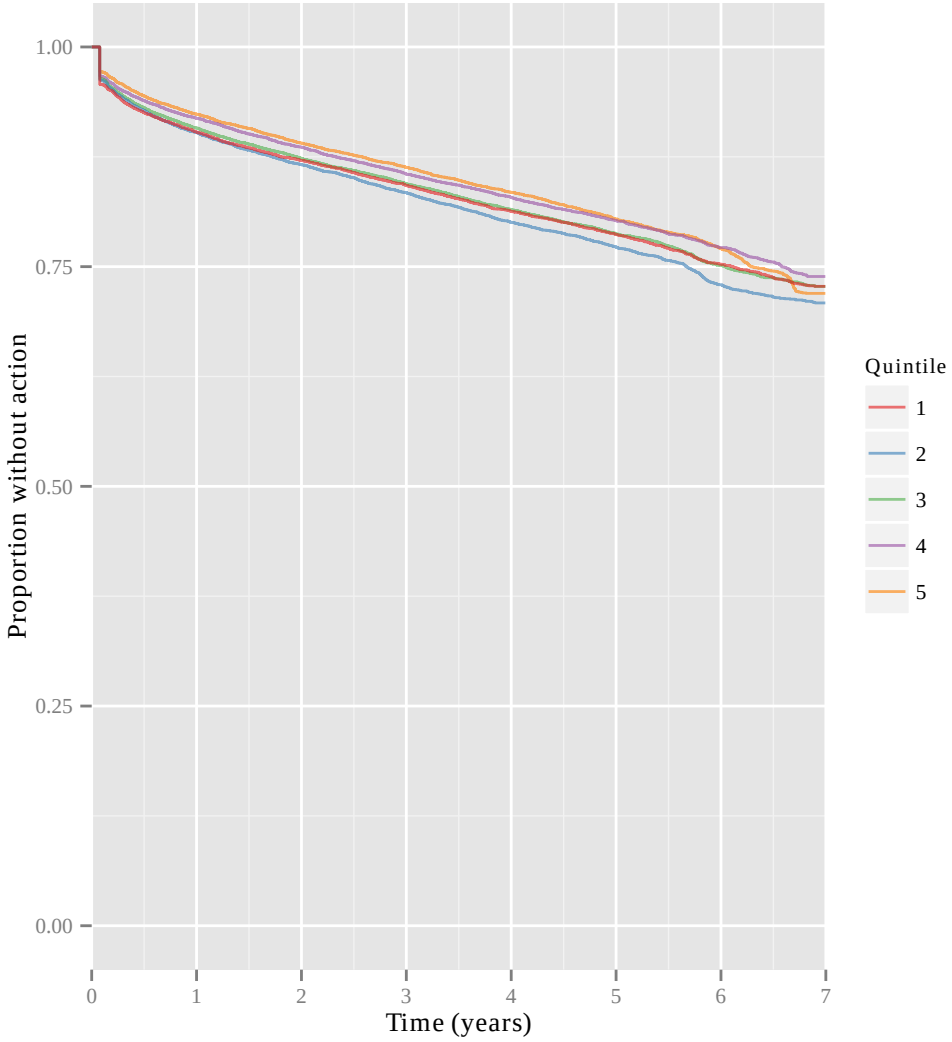
D.2 DRUG-CESSATION ANALYSIS

The analysis presented in subsequent pages related to drug cessation was performed using the same conceptual underpinnings as that for our main analysis. As before I present Kaplan-Meier plots and the summary of results from 'fully-adjusted models'. It is important to note when considering these that the HRs operate in a different direction, because the phenomenon under investigation here is the time to the prescriptions for a drug ceasing to be issued: it is assumed that this happening more quickly in the most deprived quintile compared to the least would constitute evidence of inequity.



High risk statin management

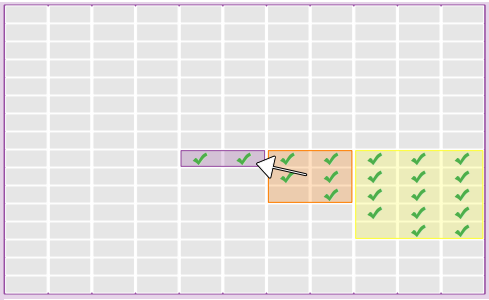
Kaplan−Meier plot for 'risk assessed high' and 'statin'. Drug cessation (triggers = 33228; actions = 5378)



Mixed−effects model for 'risk assessed high' and 'statin'. Drug cessation

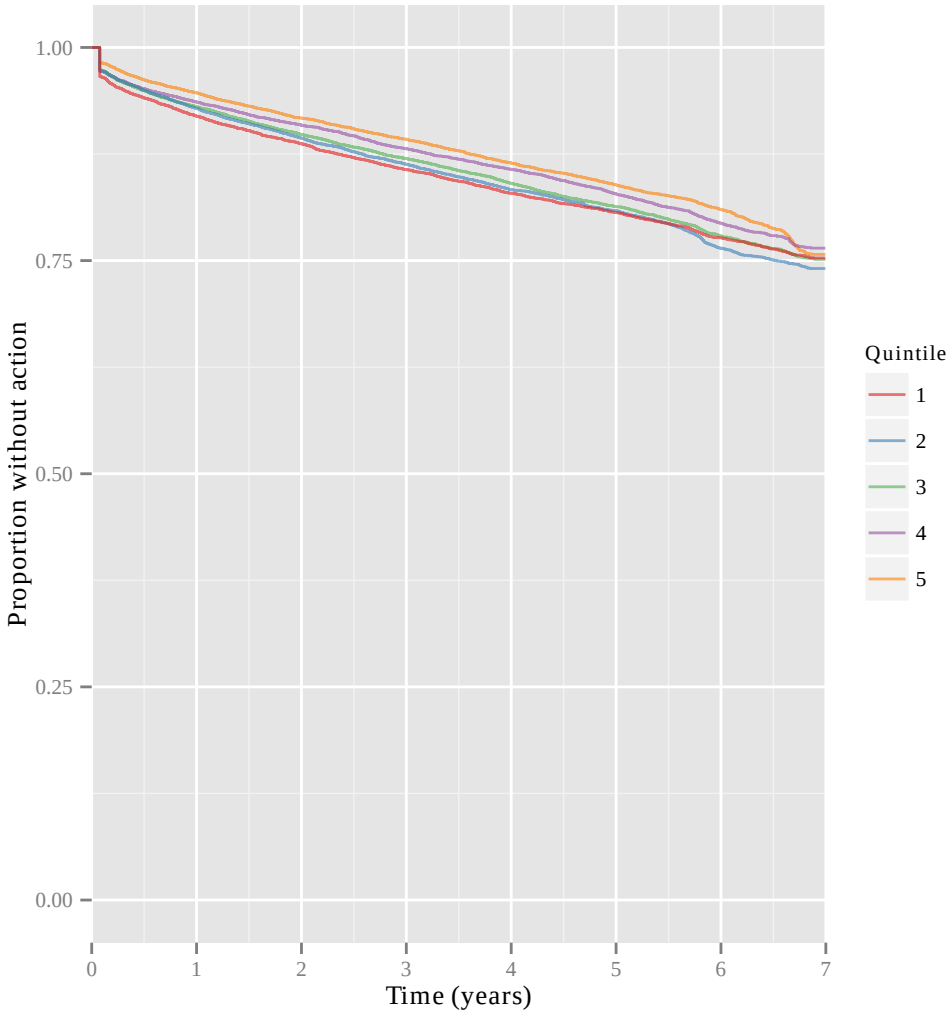
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.00	(0.91; 1.10)
Quintile 3	1.00	(0.91; 1.10)
Quintile 4	0.96	(0.87; 1.06)
Quintile 5	0.95	(0.86; 1.05)
Age 35 to 39	0.64	(0.26; 1.55)
Age 40 to 44	0.91	(0.68; 1.21)
Age 45 to 49	0.92	(0.78; 1.08)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.92	(0.82; 1.03)
Age 60 to 64	1.00	(0.90; 1.12)
Age 65 to 69	0.97	(0.87; 1.09)
Age 70 to 74	1.29	(1.14; 1.45)
Age 75 to 79	1.43	(1.25; 1.63)
Age 80 to 84	1.99	(1.70; 2.33)
Age 85+	3.26	(2.71; 3.93)
Male	1	(Reference)
Female	1.03	(0.97; 1.10)
Non−smoker	1	(Reference)
Smoker	1.13	(1.05; 1.21)
BMI low / norm.	1	(Reference)
Overweight	0.94	(0.88; 1.01)
Obese	0.92	(0.85; 0.99)
No hyp.	1	(Reference)
Hyp. contr.	0.77	(0.71; 0.82)
Hyp. uncontr.	0.82	(0.77; 0.89)
Untreat. hyp.	0.94	(0.85; 1.03)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.07	(1.00; 1.14)
No oth. co.	1	(Reference)
Other co.	1.29	(1.19; 1.40)

Number of clinical triggers 33228; Number of clinical actions 5378. ICC for practice = 0.115. Missing values imputed using MICE.



High risk statin management

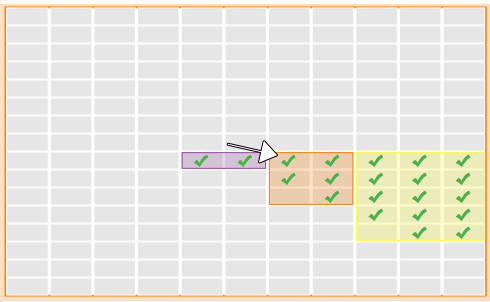
Kaplan−Meier plot for 'high−risk diagnosis' and 'statin'. Drug cessation (triggers = 29208; actions = 4041)



Mixed−effects model for 'high−risk diagnosis' and 'statin'. Drug cessation

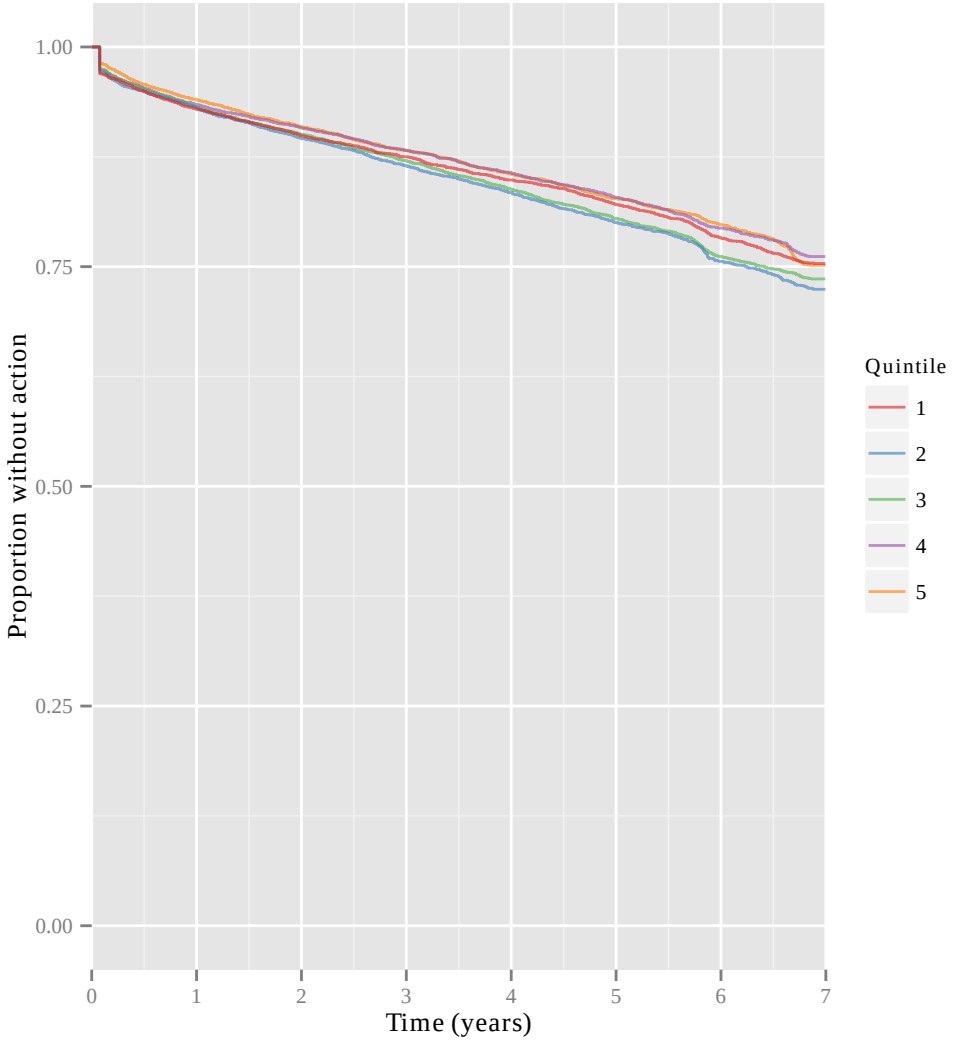
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.89	(0.80; 1.00)
Quintile 3	0.91	(0.82; 1.02)
Quintile 4	0.85	(0.76; 0.96)
Quintile 5	0.78	(0.70; 0.88)
Age 35 to 39	1.44	(1.13; 1.82)
Age 40 to 44	1.30	(1.06; 1.58)
Age 45 to 49	1.08	(0.90; 1.29)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.06	(0.91; 1.24)
Age 60 to 64	1.09	(0.94; 1.26)
Age 65 to 69	1.18	(1.02; 1.37)
Age 70 to 74	1.34	(1.15; 1.55)
Age 75 to 79	1.81	(1.56; 2.10)
Age 80 to 84	2.36	(2.02; 2.76)
Age 85+	3.51	(2.97; 4.14)
Male	1	(Reference)
Female	1.01	(0.95; 1.08)
Non−smoker	1	(Reference)
Smoker	1.10	(1.01; 1.19)
BMI low / norm.	1	(Reference)
Overweight	0.86	(0.78; 0.95)
Obese	0.84	(0.76; 0.92)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.94	(0.83; 1.06)
No oth. co.	1	(Reference)
Other co.	1.36	(1.27; 1.46)

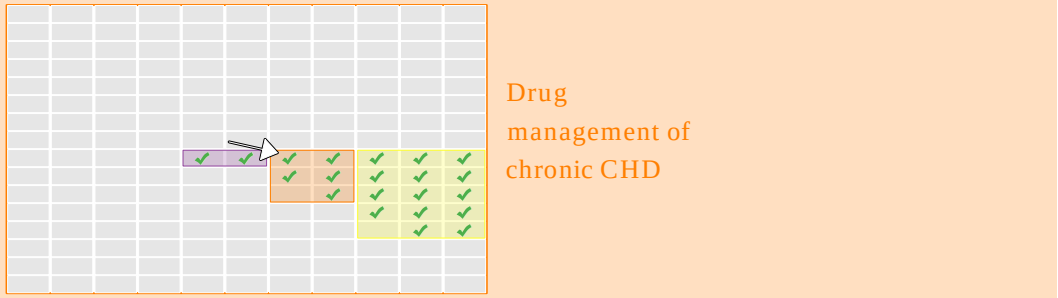
Number of clinical triggers 29208; Number of clinical actions 4041. ICC for practice = 0.133. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina' and 'statin'. Drug cessation (triggers = 11231; actions = 1711)

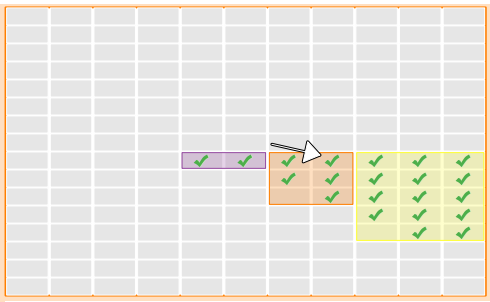




Mixed−effects model for 'stable angina' and 'statin'. Drug cessation

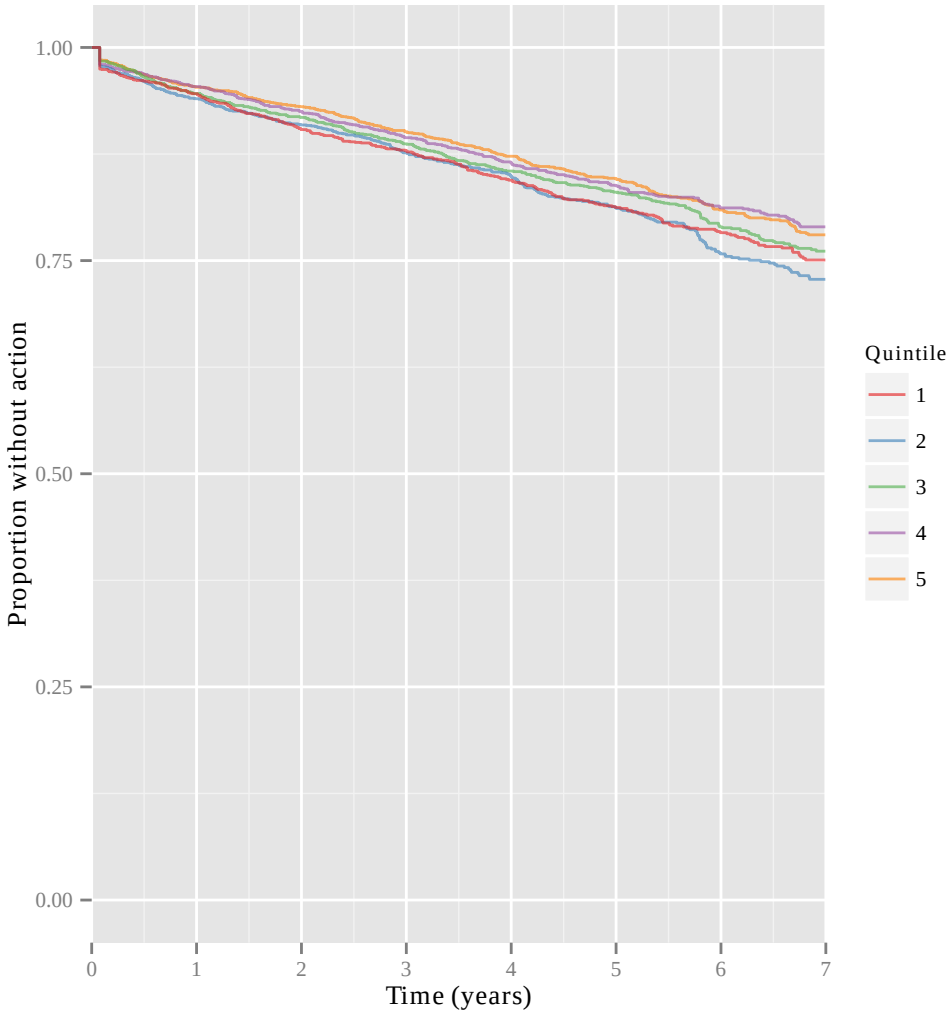
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.17	(1.00; 1.37)
Quintile 3	1.20	(1.02; 1.42)
Quintile 4	1.00	(0.84; 1.19)
Quintile 5	1.06	(0.88; 1.26)
Age 35 to 39	2.84	(1.49; 5.40)
Age 40 to 44	1.51	(0.99; 2.30)
Age 45 to 49	1.43	(1.02; 2.01)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.21	(0.92; 1.59)
Age 60 to 64	1.36	(1.05; 1.78)
Age 65 to 69	1.42	(1.10; 1.85)
Age 70 to 74	1.58	(1.22; 2.06)
Age 75 to 79	2.09	(1.60; 2.73)
Age 80 to 84	2.42	(1.83; 3.20)
Age 85+	3.83	(2.85; 5.16)
Male	1	(Reference)
Female	1.20	(1.08; 1.33)
Non−smoker	1	(Reference)
Smoker	0.98	(0.85; 1.13)
BMI low / norm.	1	(Reference)
Overweight	0.88	(0.77; 1.01)
Obese	0.87	(0.76; 0.99)
No hyp.	1	(Reference)
Hyp. contr.	0.84	(0.75; 0.94)
Hyp. uncontr.	0.82	(0.71; 0.95)
Untreat. hyp.	0.93	(0.74; 1.17)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.99	(0.83; 1.17)
No CVA	1	(Reference)
CVA	0.79	(0.69; 0.92)
No oth. co.	1	(Reference)
Other co.	1.42	(1.28; 1.58)

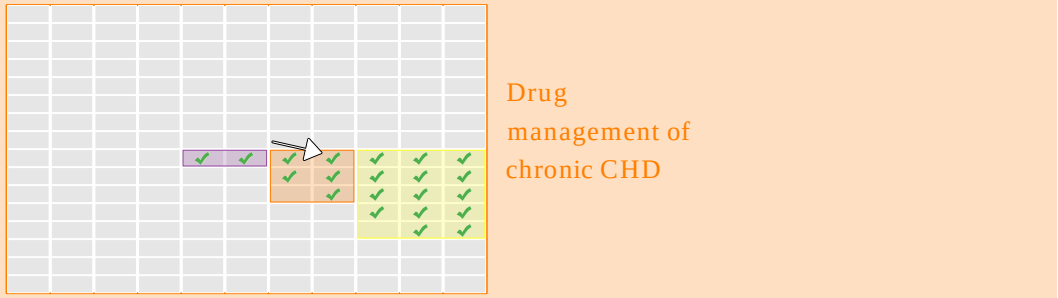
Number of clinical triggers 11231; Number of clinical actions 1711. ICC for practice = 0.125. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina and diabetes' and 'statin'. Drug cessation (triggers = 6588; actions = 782)



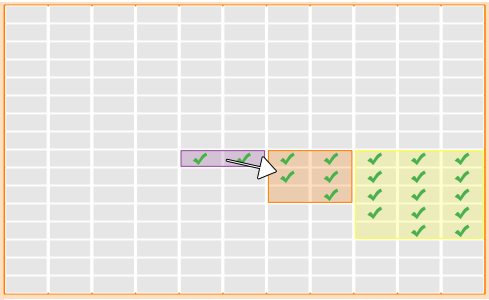


Mixed−effects model for 'stable angina and diabetes' and 'statin'.

Drug cessation

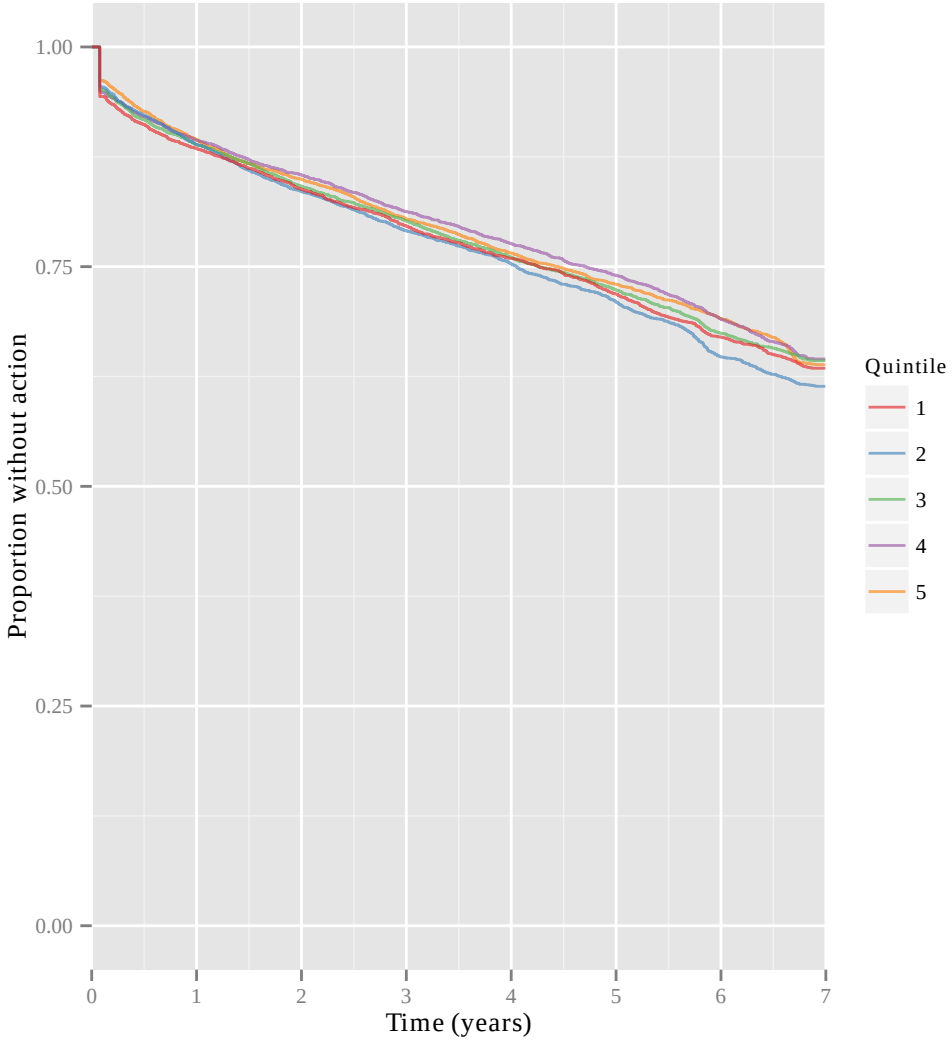
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.99	(0.77; 1.27)
Quintile 3	0.85	(0.66; 1.10)
Quintile 4	0.99	(0.77; 1.27)
Quintile 5	0.84	(0.65; 1.09)
Age 35 to 39	1.60	(0.56; 4.64)
Age 40 to 44	0.89	(0.36; 2.16)
Age 45 to 49	0.51	(0.22; 1.16)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.99	(0.62; 1.57)
Age 60 to 64	1.08	(0.70; 1.69)
Age 65 to 69	1.48	(0.97; 2.25)
Age 70 to 74	1.65	(1.09; 2.52)
Age 75 to 79	2.33	(1.53; 3.54)
Age 80 to 84	2.91	(1.88; 4.49)
Age 85+	5.83	(3.71; 9.14)
Male	1	(Reference)
Female	1.07	(0.92; 1.24)
Non−smoker	1	(Reference)
Smoker	1.07	(0.86; 1.33)
BMI low / norm.	1	(Reference)
Overweight	0.79	(0.64; 0.98)
Obese	0.85	(0.69; 1.04)
No hyp.	1	(Reference)
Hyp. contr.	0.90	(0.75; 1.08)
Hyp. uncontr.	0.80	(0.63; 1.01)
Untreat. hyp.	0.97	(0.62; 1.51)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.09	(0.91; 1.30)
No CVA	1	(Reference)
CVA	1.08	(0.90; 1.30)
No oth. co.	1	(Reference)
Other co.	1.54	(1.33; 1.79)

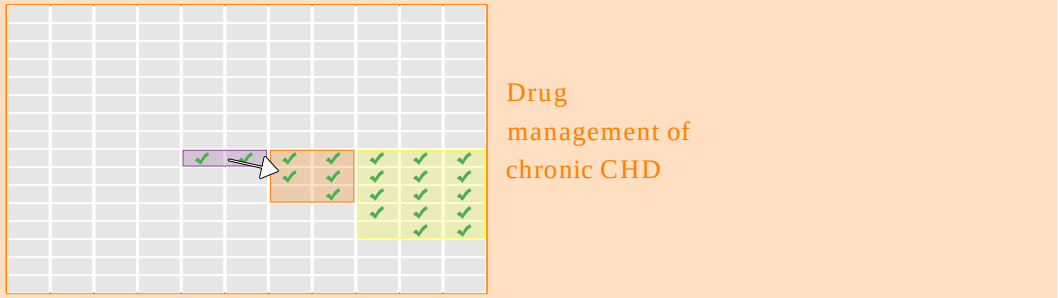
Number of clinical triggers 6588; Number of clinical actions 782. ICC for practice = 0.172. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina' and 'aspirin'. Drug cessation (triggers = 10704; actions = 2590)

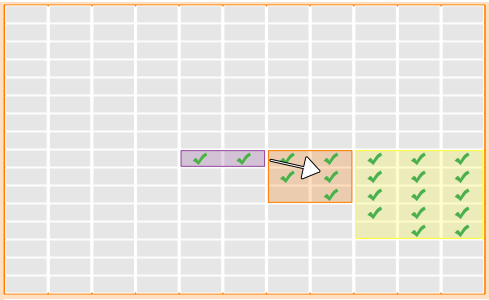




Mixed−effects model for 'stable angina' and 'aspirin'. Drug cessation

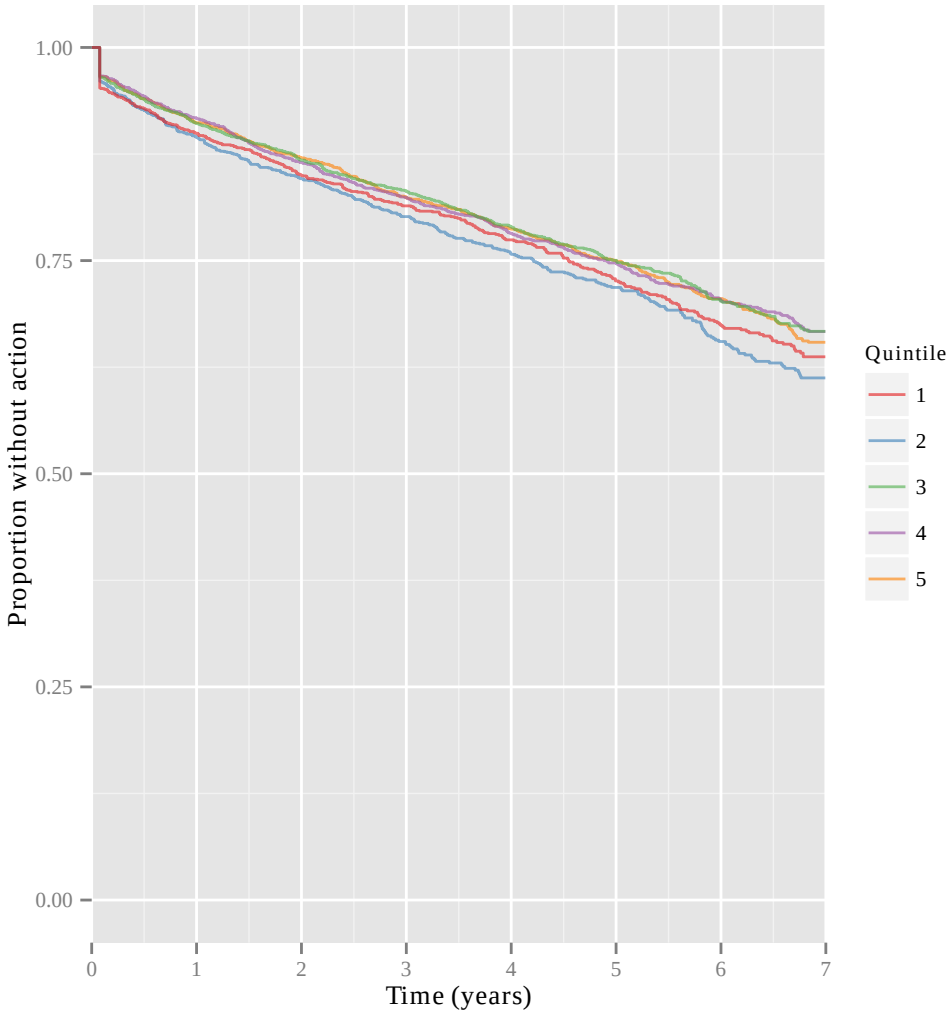
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.03	(0.90; 1.18)
Quintile 3	1.04	(0.91; 1.19)
Quintile 4	0.93	(0.81; 1.07)
Quintile 5	1.01	(0.88; 1.17)
Age 35 to 39	1.42	(0.81; 2.48)
Age 40 to 44	1.46	(1.08; 1.98)
Age 45 to 49	1.03	(0.79; 1.36)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.10	(0.89; 1.35)
Age 60 to 64	0.96	(0.79; 1.18)
Age 65 to 69	0.99	(0.81; 1.21)
Age 70 to 74	1.09	(0.89; 1.33)
Age 75 to 79	1.26	(1.02; 1.54)
Age 80 to 84	1.47	(1.19; 1.81)
Age 85+	1.41	(1.13; 1.75)
Male	1	(Reference)
Female	1.19	(1.09; 1.29)
Non−smoker	1	(Reference)
Smoker	0.91	(0.81; 1.02)
BMI low / norm.	1	(Reference)
Overweight	0.84	(0.75; 0.93)
Obese	0.91	(0.81; 1.02)
No hyp.	1	(Reference)
Hyp. contr.	0.91	(0.83; 0.99)
Hyp. uncontr.	0.77	(0.68; 0.87)
Untreat. hyp.	0.83	(0.69; 1.01)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.89	(0.79; 0.99)
No CVA	1	(Reference)
CVA	0.85	(0.75; 0.96)
No oth. co.	1	(Reference)
Other co.	1.42	(1.31; 1.55)

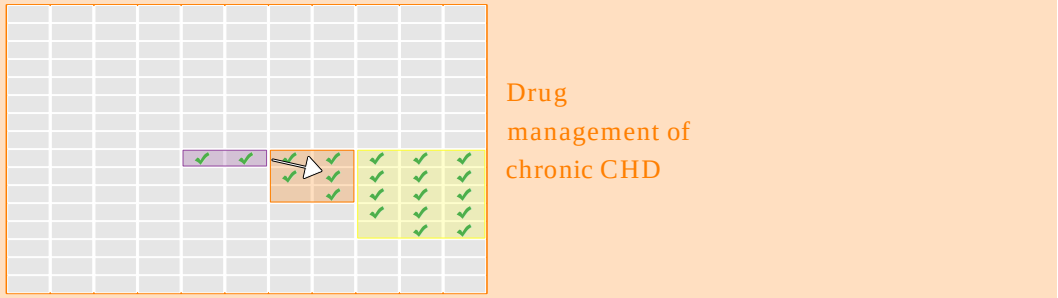
Number of clinical triggers 10704; Number of clinical actions 2590. ICC for practice = 0.1. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina and diabetes' and 'aspirin'. Drug cessation (triggers = 5472; actions = 1056)

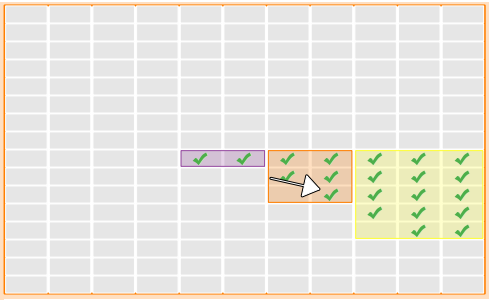




Mixed−effects model for 'stable angina and diabetes' and 'aspirin'.
Drug cessation

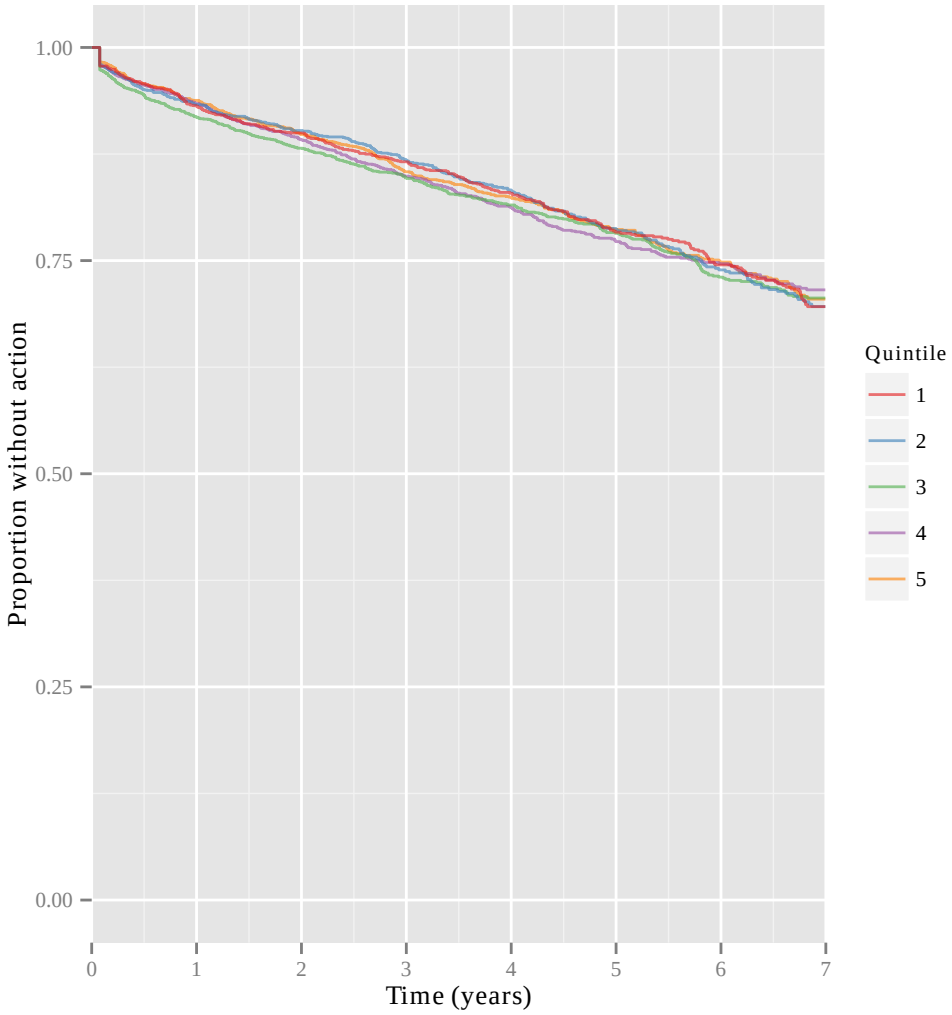
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.97	(0.78; 1.20)
Quintile 3	0.75	(0.60; 0.94)
Quintile 4	0.86	(0.70; 1.07)
Quintile 5	0.86	(0.69; 1.08)
Age 35 to 39	2.16	(0.94; 4.94)
Age 40 to 44	0.99	(0.47; 2.08)
Age 45 to 49	1.01	(0.57; 1.79)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.10	(0.73; 1.66)
Age 60 to 64	1.33	(0.91; 1.96)
Age 65 to 69	1.58	(1.09; 2.29)
Age 70 to 74	1.60	(1.10; 2.32)
Age 75 to 79	2.12	(1.46; 3.08)
Age 80 to 84	2.36	(1.60; 3.48)
Age 85+	3.25	(2.17; 4.86)
Male	1	(Reference)
Female	1.12	(0.99; 1.28)
Non−smoker	1	(Reference)
Smoker	1.05	(0.88; 1.26)
BMI low / norm.	1	(Reference)
Overweight	0.88	(0.74; 1.06)
Obese	0.91	(0.76; 1.09)
No hyp.	1	(Reference)
Hyp. contr.	0.98	(0.84; 1.15)
Hyp. uncontr.	0.89	(0.72; 1.09)
Untreat. hyp.	0.99	(0.67; 1.47)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.98	(0.81; 1.19)
No CVA	1	(Reference)
CVA	0.97	(0.82; 1.15)
No oth. co.	1	(Reference)
Other co.	1.66	(1.46; 1.89)

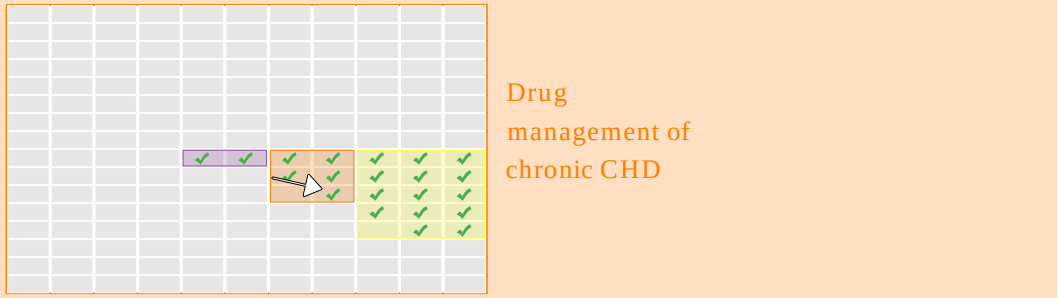
Number of clinical triggers 5472; Number of clinical actions 1056. ICC for practice = 0.138. Missing values imputed using MICE.



Drug management of chronic CHD

Kaplan−Meier plot for 'stable angina and diabetes' and 'ACE inhibitor'. Drug cessation (triggers = 5620; actions = 827)

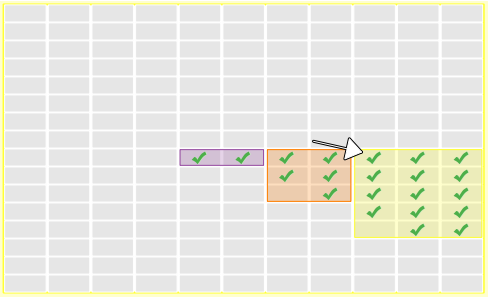




Mixed−effects model for 'stable angina and diabetes' and 'ACE inhibitor'. Drug cessation

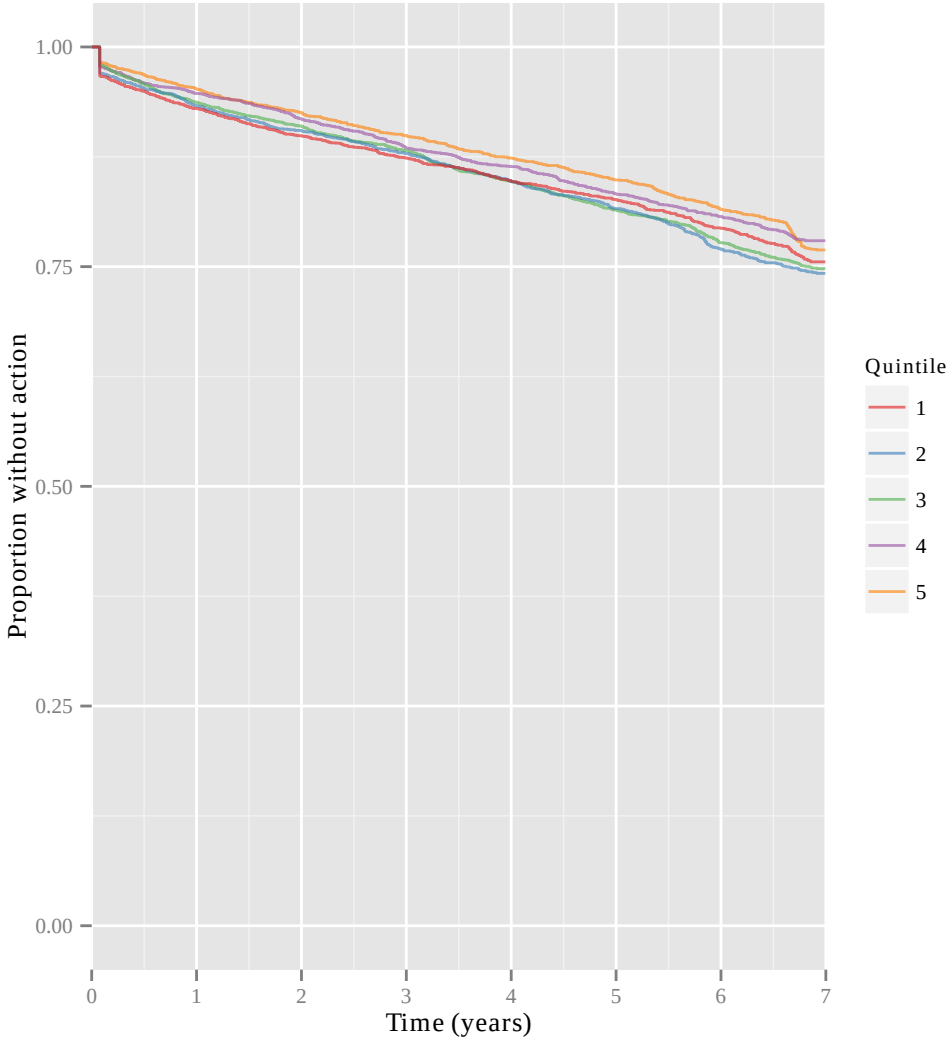
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.91	(0.70; 1.19)
Quintile 3	1.15	(0.89; 1.48)
Quintile 4	1.17	(0.91; 1.51)
Quintile 5	1.10	(0.85; 1.41)
Age 35 to 39	0.84	(0.25; 2.81)
Age 40 to 44	0.53	(0.16; 1.76)
Age 45 to 49	0.77	(0.38; 1.56)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.85	(0.54; 1.35)
Age 60 to 64	0.95	(0.61; 1.46)
Age 65 to 69	1.47	(0.97; 2.22)
Age 70 to 74	1.27	(0.84; 1.92)
Age 75 to 79	1.89	(1.25; 2.85)
Age 80 to 84	3.16	(2.07; 4.82)
Age 85+	3.34	(2.14; 5.22)
Male	1	(Reference)
Female	1.01	(0.88; 1.17)
Non−smoker	1	(Reference)
Smoker	1.29	(1.05; 1.59)
BMI low / norm.	1	(Reference)
Overweight	0.70	(0.57; 0.86)
Obese	0.71	(0.58; 0.88)
No hyp.	1	(Reference)
Hyp. contr.	0.63	(0.52; 0.77)
Hyp. uncontr.	0.51	(0.40; 0.64)
Untreat. hyp.	0.85	(0.52; 1.37)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.93	(0.80; 1.09)
No CVA	1	(Reference)
CVA	1.20	(1.01; 1.43)
No oth. co.	1	(Reference)
Other co.	1.67	(1.45; 1.92)

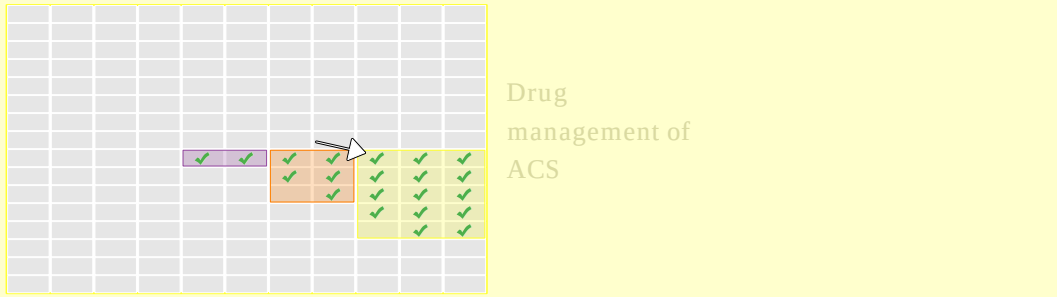
Number of clinical triggers 5620; Number of clinical actions 827. ICC for practice = 0.177. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'old ACS' and 'statin'. Drug cessation (triggers = 2764; actions = 422)

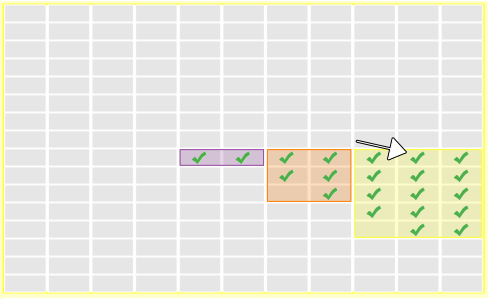




Mixed−effects model for 'old ACS' and 'statin'. Drug cessation

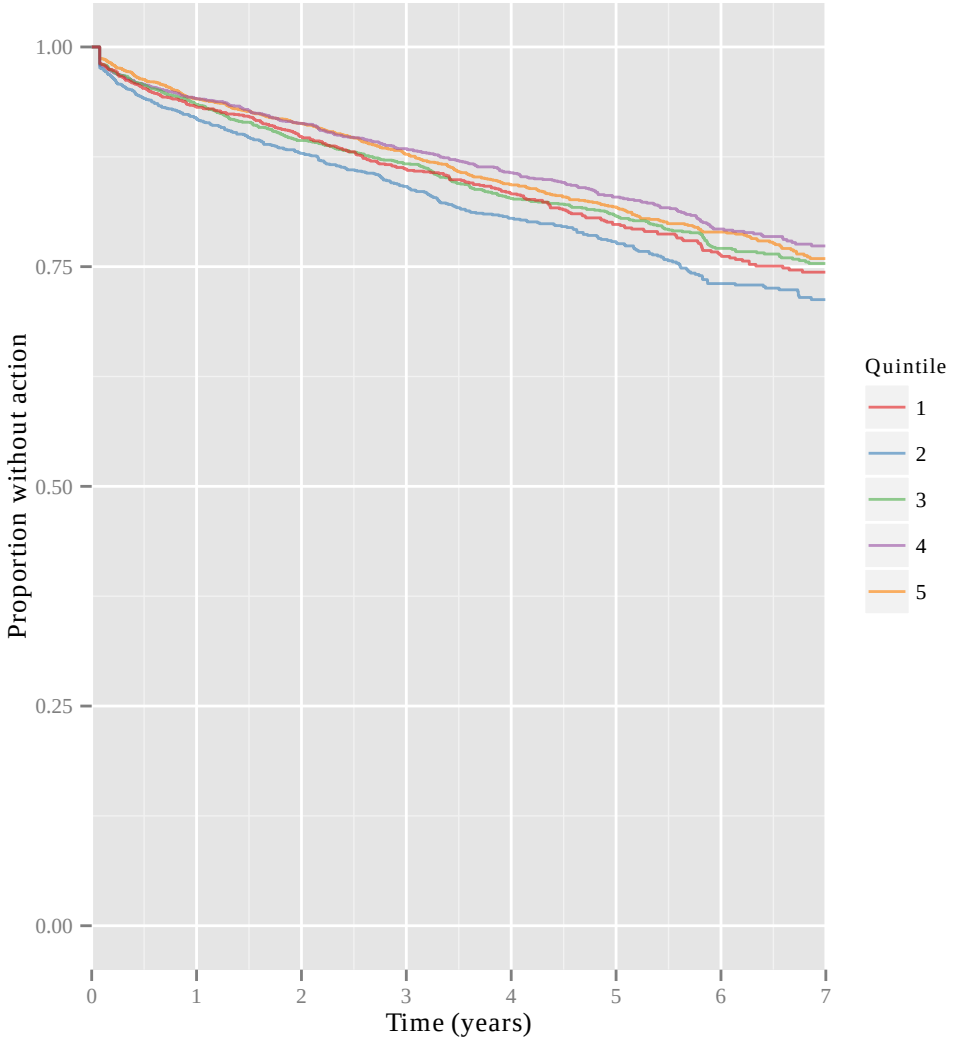
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.97	(0.69; 1.36)
Quintile 3	0.87	(0.62; 1.21)
Quintile 4	0.86	(0.61; 1.20)
Quintile 5	0.70	(0.49; 0.98)
Age 35 to 39	2.87	(0.82; 10.06)
Age 40 to 44	0.96	(0.39; 2.35)
Age 45 to 49	0.98	(0.43; 2.23)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.56	(0.28; 1.12)
Age 60 to 64	0.94	(0.52; 1.72)
Age 65 to 69	1.51	(0.87; 2.61)
Age 70 to 74	1.51	(0.87; 2.62)
Age 75 to 79	2.11	(1.22; 3.66)
Age 80 to 84	3.18	(1.83; 5.54)
Age 85+	7.18	(4.05; 12.72)
Male	1	(Reference)
Female	0.90	(0.73; 1.11)
Non−smoker	1	(Reference)
Smoker	1.30	(0.99; 1.71)
BMI low / norm.	1	(Reference)
Overweight	0.88	(0.68; 1.13)
Obese	1.08	(0.82; 1.41)
No hyp.	1	(Reference)
Hyp. contr.	0.88	(0.69; 1.12)
Hyp. uncontr.	0.94	(0.67; 1.32)
Untreat. hyp.	1.13	(0.66; 1.95)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.42	(1.00; 2.01)
No CVA	1	(Reference)
CVA	1.12	(0.87; 1.43)
No oth. co.	1	(Reference)
Other co.	1.79	(1.45; 2.21)
No diabetes	1	(Reference)
Diabetes	1.30	(1.02; 1.64)

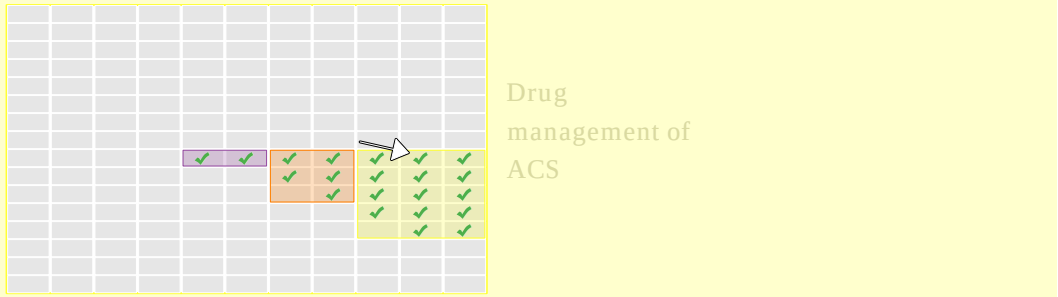
Number of clinical triggers 2764; Number of clinical actions 422. ICC for practice = 0.216. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'statin'. Drug cessation (triggers = 9211; actions = 1341)



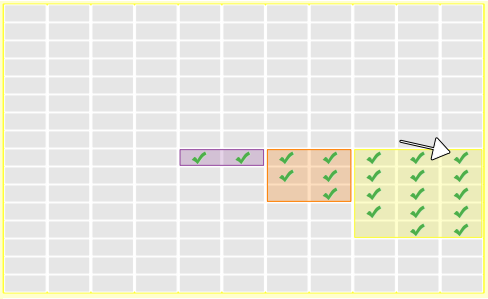


Mixed−effects model for 'unstable angina' and 'statin'. Drug cessation

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.02	(0.83; 1.25)
Quintile 3	1.07	(0.87; 1.30)
Quintile 4	0.89	(0.73; 1.10)
Quintile 5	1.04	(0.84; 1.27)
Age 35 to 39	1.79	(0.80; 4.01)
Age 40 to 44	2.44	(1.50; 3.95)
Age 45 to 49	1.37	(0.86; 2.18)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.14	(0.79; 1.64)
Age 60 to 64	1.39	(0.98; 1.95)
Age 65 to 69	1.17	(0.82; 1.66)
Age 70 to 74	1.82	(1.30; 2.54)
Age 75 to 79	1.91	(1.36; 2.68)
Age 80 to 84	2.90	(2.07; 4.07)
Age 85+	4.83	(3.44; 6.79)
Male	1	(Reference)
Female	1.03	(0.92; 1.16)
Non−smoker	1	(Reference)
Smoker	1.00	(0.85; 1.18)
BMI low / norm.	1	(Reference)
Overweight	0.91	(0.78; 1.06)
Obese	0.75	(0.63; 0.88)
No hyp.	1	(Reference)
Hyp. contr.	0.79	(0.69; 0.91)
Hyp. uncontr.	0.80	(0.66; 0.97)
Untreat. hyp.	1.09	(0.75; 1.58)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.04	(0.82; 1.32)
No CVA	1	(Reference)
CVA	1.16	(1.01; 1.33)
No oth. co.	1	(Reference)
Other co.	1.46	(1.30; 1.64)
No diabetes	1	(Reference)
Diabetes	1.05	(0.92; 1.19)
Elect. adm.	1	(Reference)
Emer. adm.	1.12	(0.87; 1.45)

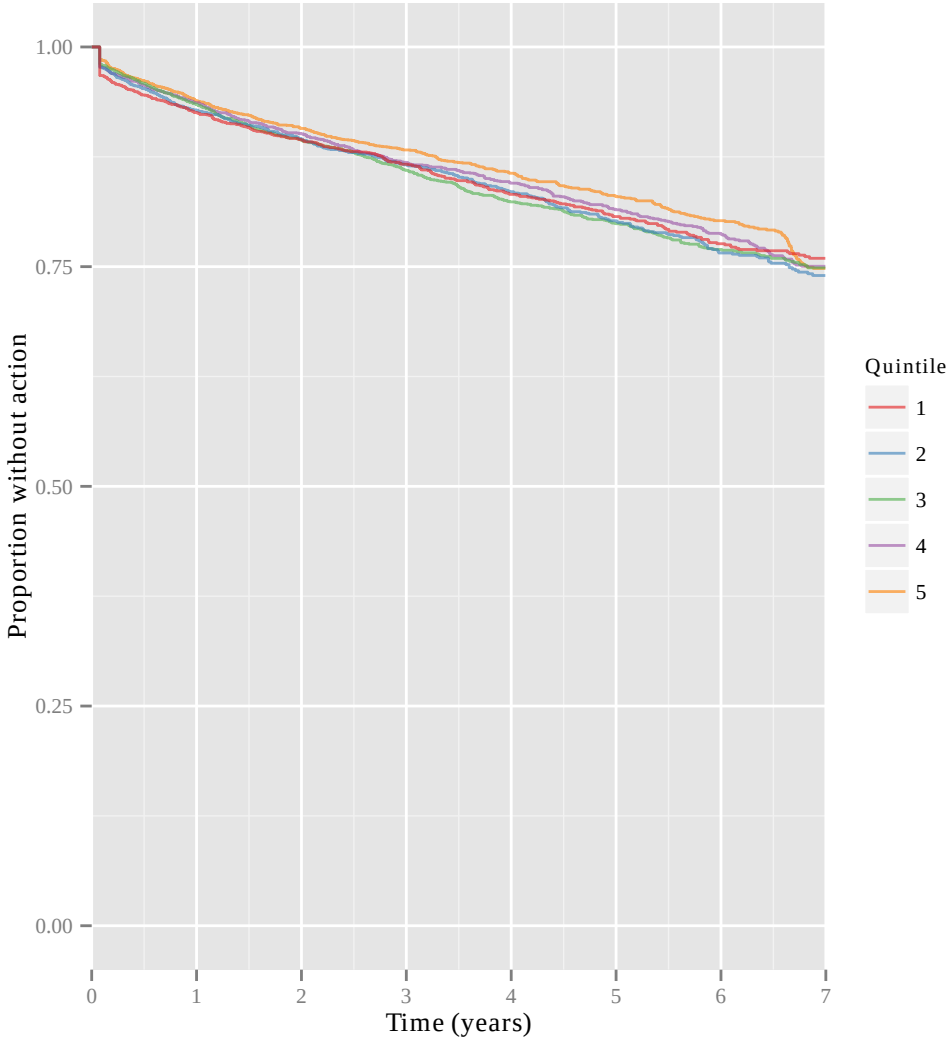
	HR	95% CI
Other adm.	1.03	(0.77; 1.38)
Cardiac cen.	1	(Reference)
Other cen.	1.18	(0.86; 1.61)
Cardiology	1	(Reference)
Med. spec.	1.15	(1.00; 1.33)
Other spec.	1.18	(0.94; 1.49)

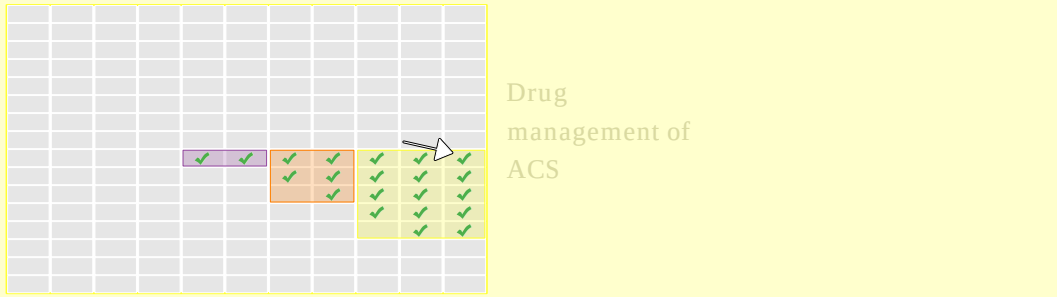
Number of clinical triggers 9211; Number of clinical actions 1341. ICC for practice = 0.159. ICC for hospital = 0.021. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'statin'. Drug cessation (triggers = 11380; actions = 1642)



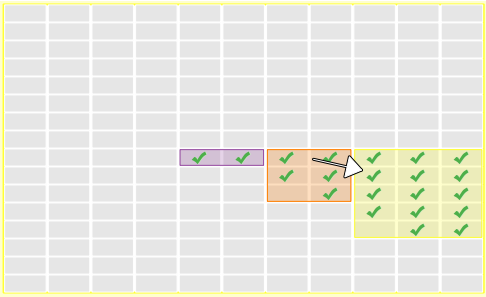


Mixed−effects model for 'MI' and 'statin'. Drug cessation

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.92	(0.77; 1.11)
Quintile 3	1.12	(0.94; 1.34)
Quintile 4	0.96	(0.80; 1.16)
Quintile 5	0.97	(0.80; 1.18)
Age 35 to 39	2.13	(1.23; 3.69)
Age 40 to 44	1.56	(0.96; 2.54)
Age 45 to 49	1.02	(0.63; 1.65)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.25	(0.87; 1.81)
Age 60 to 64	1.45	(1.03; 2.04)
Age 65 to 69	1.81	(1.30; 2.52)
Age 70 to 74	2.38	(1.73; 3.28)
Age 75 to 79	2.73	(1.98; 3.77)
Age 80 to 84	3.92	(2.85; 5.41)
Age 85+	5.47	(3.95; 7.58)
Male	1	(Reference)
Female	1.02	(0.92; 1.13)
Non−smoker	1	(Reference)
Smoker	0.94	(0.81; 1.09)
BMI low / norm.	1	(Reference)
Overweight	0.92	(0.81; 1.05)
Obese	0.80	(0.69; 0.93)
No hyp.	1	(Reference)
Hyp. contr.	0.99	(0.88; 1.12)
Hyp. uncontr.	0.91	(0.77; 1.09)
Untreat. hyp.	0.92	(0.67; 1.27)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.14	(1.00; 1.31)
No CVA	1	(Reference)
CVA	1.12	(0.98; 1.27)
No oth. co.	1	(Reference)
Other co.	1.69	(1.53; 1.88)
No diabetes	1	(Reference)
Diabetes	1.20	(1.07; 1.35)
Elect. adm.	1	(Reference)
Emer. adm.	1.39	(1.03; 1.88)

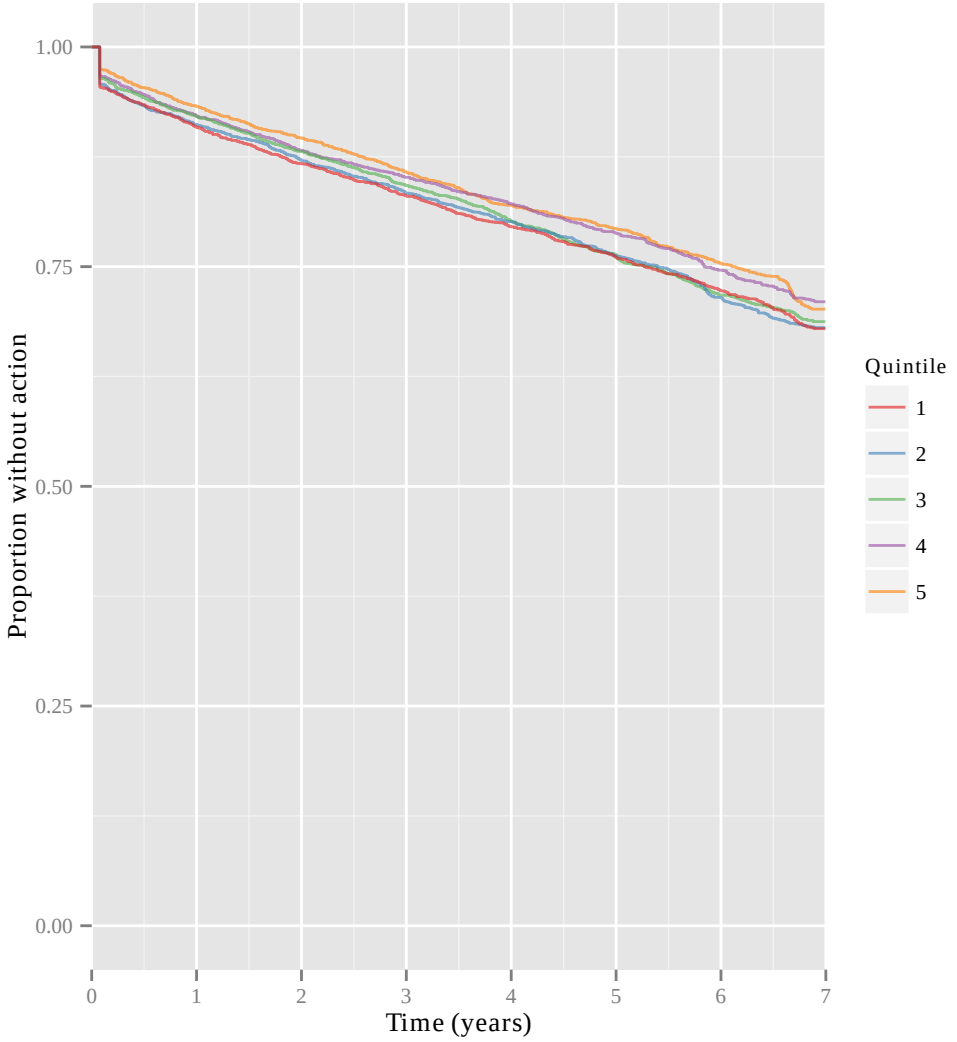
	HR	95% CI
Other adm.	1.19	(0.86; 1.64)
Cardiac cen.	1	(Reference)
Other cen.	1.13	(0.80; 1.60)
Cardiology	1	(Reference)
Med. spec.	1.11	(0.98; 1.26)
Other spec.	1.19	(0.96; 1.47)

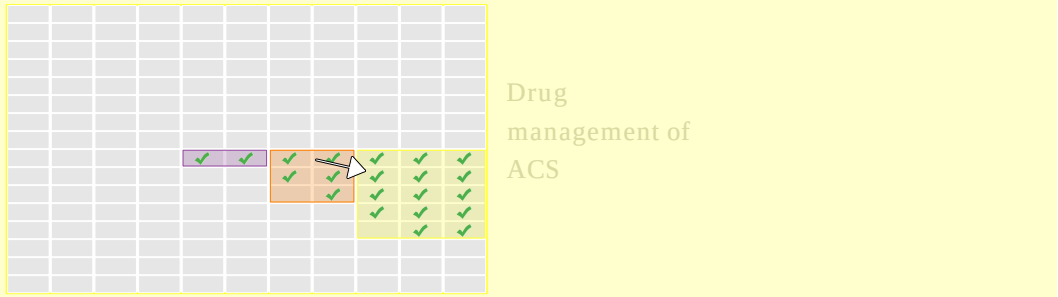
Number of clinical triggers 11380; Number of clinical actions 1642. ICC for practice = 0.144. ICC for hospital = 0.036. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'old ACS' and 'aspirin'. Drug cessation (triggers = 2692; actions = 537)

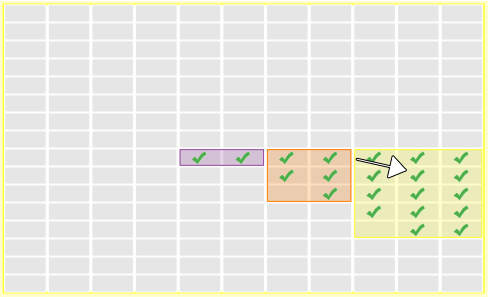




Mixed−effects model for 'old ACS' and 'aspirin'. Drug cessation

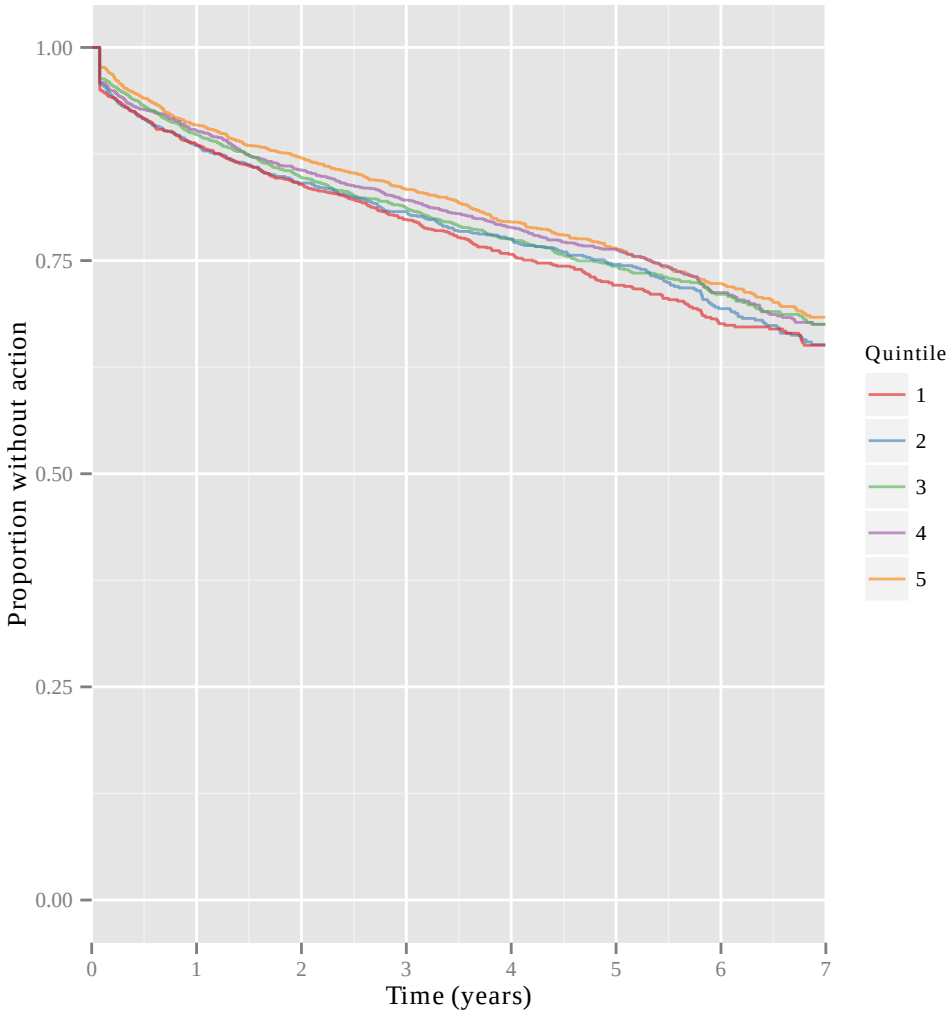
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.96	(0.72; 1.29)
Quintile 3	0.87	(0.65; 1.15)
Quintile 4	0.96	(0.72; 1.28)
Quintile 5	0.79	(0.59; 1.06)
Age 35 to 39	3.11	(1.06; 9.13)
Age 40 to 44	1.22	(0.60; 2.51)
Age 45 to 49	0.83	(0.42; 1.67)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.75	(0.44; 1.29)
Age 60 to 64	0.91	(0.55; 1.50)
Age 65 to 69	1.26	(0.79; 2.01)
Age 70 to 74	1.45	(0.92; 2.29)
Age 75 to 79	1.68	(1.07; 2.66)
Age 80 to 84	1.97	(1.24; 3.14)
Age 85+	2.52	(1.56; 4.07)
Male	1	(Reference)
Female	1.12	(0.93; 1.35)
Non−smoker	1	(Reference)
Smoker	1.18	(0.93; 1.51)
BMI low / norm.	1	(Reference)
Overweight	0.83	(0.65; 1.05)
Obese	1.01	(0.77; 1.32)
No hyp.	1	(Reference)
Hyp. contr.	0.91	(0.73; 1.12)
Hyp. uncontr.	0.91	(0.68; 1.21)
Untreat. hyp.	1.00	(0.62; 1.60)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.00	(0.79; 1.26)
No CVA	1	(Reference)
CVA	1.08	(0.86; 1.36)
No oth. co.	1	(Reference)
Other co.	1.47	(1.23; 1.77)
No diabetes	1	(Reference)
Diabetes	1.37	(1.11; 1.70)

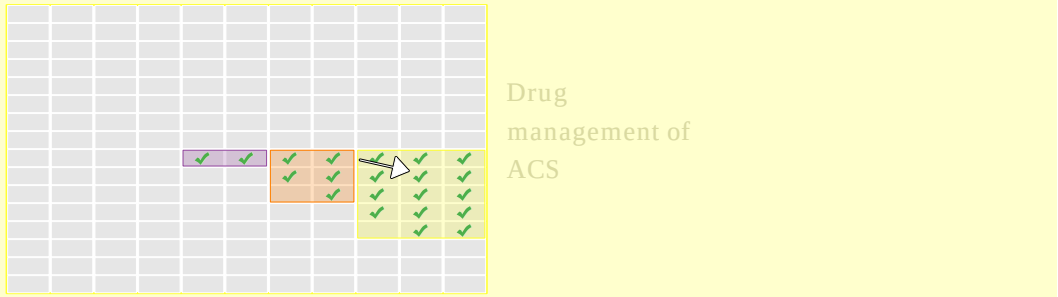
Number of clinical triggers 2692; Number of clinical actions 537. ICC for practice = 0.122. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'aspirin'. Drug cessation (triggers = 8663; actions = 1654)



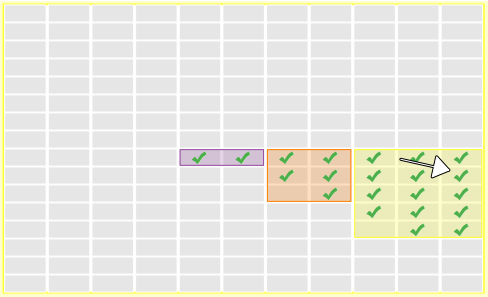


Mixed−effects model for 'unstable angina' and 'aspirin'. Drug cessation

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.92	(0.77; 1.10)
Quintile 3	0.95	(0.80; 1.14)
Quintile 4	0.95	(0.79; 1.13)
Quintile 5	0.85	(0.71; 1.02)
Age 35 to 39	1.28	(0.64; 2.58)
Age 40 to 44	1.25	(0.81; 1.92)
Age 45 to 49	0.98	(0.66; 1.45)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.02	(0.77; 1.35)
Age 60 to 64	0.92	(0.70; 1.21)
Age 65 to 69	1.00	(0.76; 1.31)
Age 70 to 74	1.39	(1.07; 1.80)
Age 75 to 79	1.45	(1.11; 1.89)
Age 80 to 84	1.81	(1.39; 2.37)
Age 85+	2.06	(1.56; 2.71)
Male	1	(Reference)
Female	1.05	(0.95; 1.17)
Non−smoker	1	(Reference)
Smoker	0.95	(0.82; 1.10)
BMI low / norm.	1	(Reference)
Overweight	0.92	(0.80; 1.06)
Obese	0.86	(0.73; 1.01)
No hyp.	1	(Reference)
Hyp. contr.	0.81	(0.72; 0.92)
Hyp. uncontr.	0.91	(0.77; 1.08)
Untreat. hyp.	0.83	(0.58; 1.17)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.04	(0.91; 1.19)
No CVA	1	(Reference)
CVA	1.03	(0.90; 1.18)
No oth. co.	1	(Reference)
Other co.	1.39	(1.26; 1.54)
No diabetes	1	(Reference)
Diabetes	0.94	(0.84; 1.06)
Elect. adm.	1	(Reference)
Emer. adm.	1.15	(0.92; 1.45)

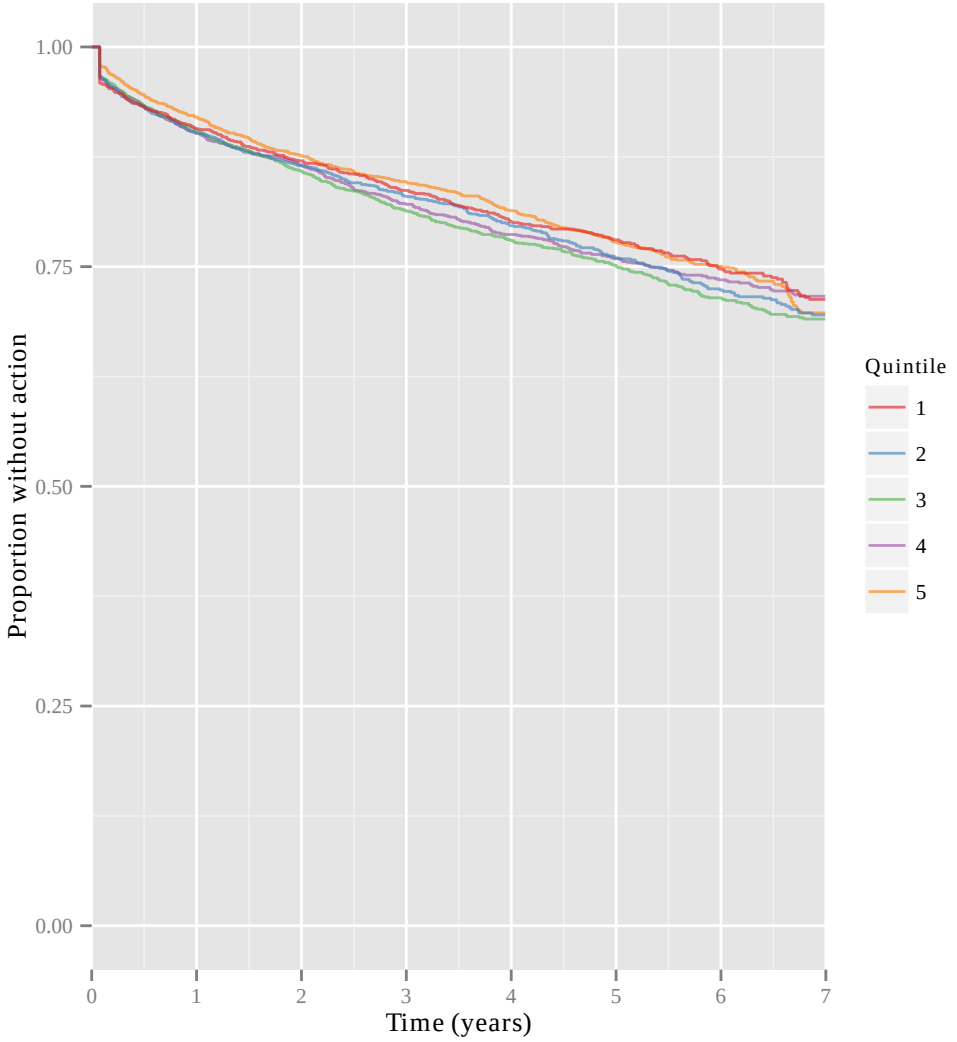
	HR	95% CI
Other adm.	0.91	(0.70; 1.17)
Cardiac cen.	1	(Reference)
Other cen.	1.10	(0.88; 1.37)
Cardiology	1	(Reference)
Med. spec.	1.21	(1.07; 1.38)
Other spec.	0.96	(0.77; 1.19)

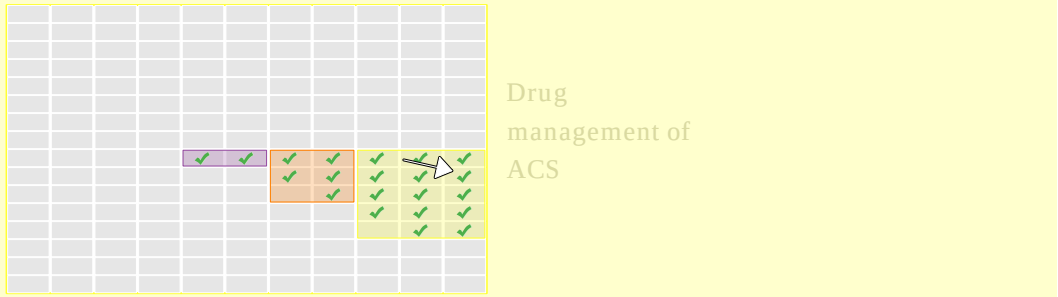
Number of clinical triggers 8663; Number of clinical actions 1654. ICC for practice = 0.134. ICC for hospital = 0.008. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'aspirin'. Drug cessation (triggers = 11011; actions = 1889)

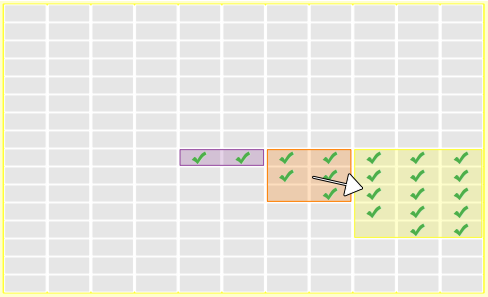




Mixed−effects model for 'MI' and 'aspirin'. Drug cessation

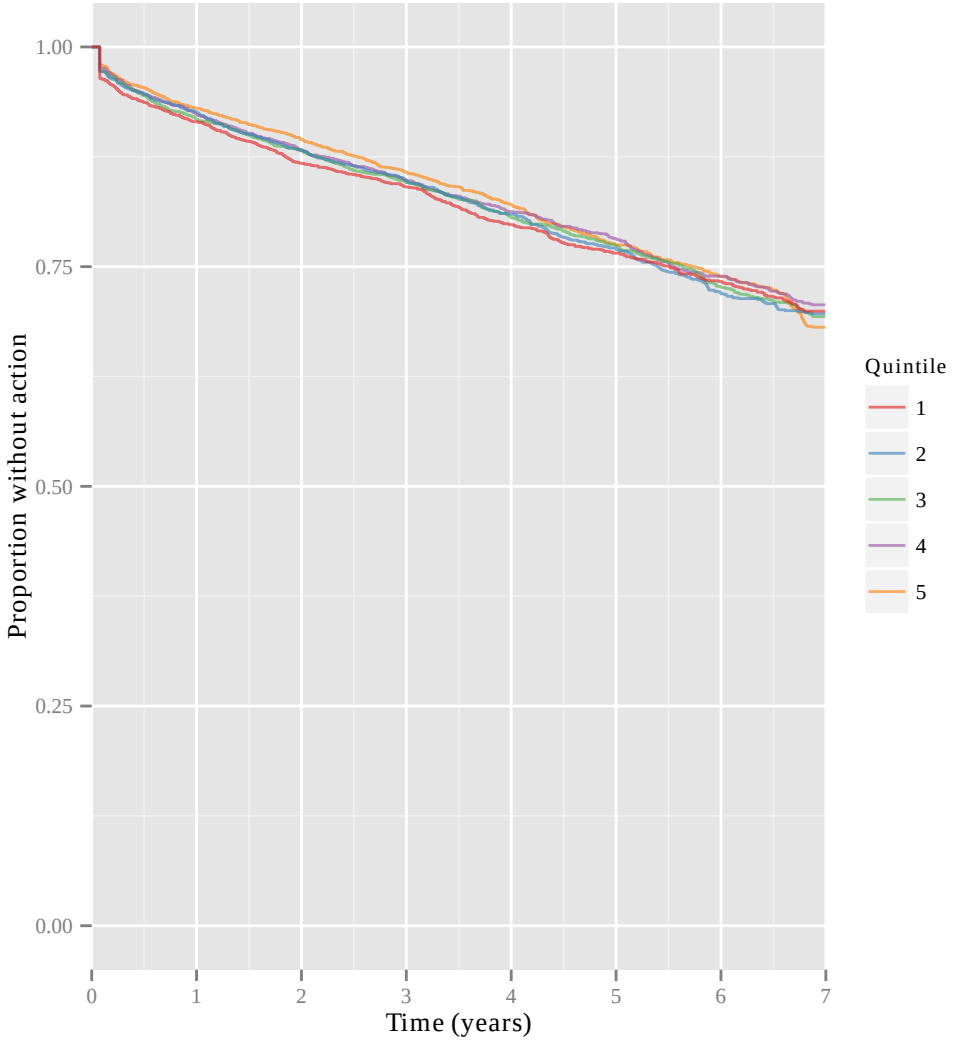
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.00	(0.84; 1.19)
Quintile 3	1.20	(1.01; 1.42)
Quintile 4	1.09	(0.92; 1.29)
Quintile 5	1.13	(0.94; 1.35)
Age 35 to 39	1.02	(0.58; 1.80)
Age 40 to 44	1.30	(0.87; 1.97)
Age 45 to 49	0.82	(0.54; 1.23)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.92	(0.67; 1.26)
Age 60 to 64	1.04	(0.78; 1.40)
Age 65 to 69	1.53	(1.16; 2.01)
Age 70 to 74	1.83	(1.39; 2.40)
Age 75 to 79	1.91	(1.45; 2.51)
Age 80 to 84	2.81	(2.14; 3.69)
Age 85+	3.16	(2.40; 4.17)
Male	1	(Reference)
Female	0.95	(0.86; 1.05)
Non−smoker	1	(Reference)
Smoker	1.04	(0.91; 1.18)
BMI low / norm.	1	(Reference)
Overweight	0.90	(0.81; 1.01)
Obese	0.93	(0.80; 1.07)
No hyp.	1	(Reference)
Hyp. contr.	1.06	(0.95; 1.19)
Hyp. uncontr.	1.00	(0.85; 1.17)
Untreat. hyp.	0.82	(0.60; 1.12)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.86	(0.75; 0.98)
No CVA	1	(Reference)
CVA	1.07	(0.95; 1.22)
No oth. co.	1	(Reference)
Other co.	1.60	(1.46; 1.77)
No diabetes	1	(Reference)
Diabetes	1.20	(1.07; 1.33)
Elect. adm.	1	(Reference)
Emer. adm.	1.09	(0.85; 1.40)
Other adm.	0.84	(0.64; 1.10)
Cardiac cen.	1	(Reference)
Other cen.	0.88	(0.63; 1.24)
Cardiology	1	(Reference)
Med. spec.	1.13	(1.00; 1.27)
Other spec.	1.19	(0.98; 1.45)

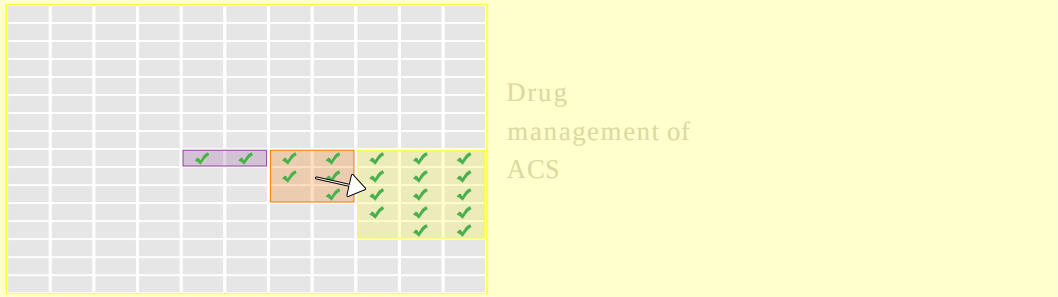
Number of clinical triggers 11011; Number of clinical actions 1889. ICC for practice = 0.132. ICC for hospital = 0.037. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'old ACS' and 'ACE inhibitor'. Drug cessation (triggers = 2441; actions = 466)

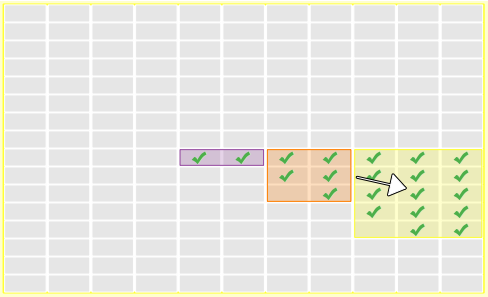




Mixed−effects model for 'old ACS' and 'ACE inhibitor'. Drug cessation

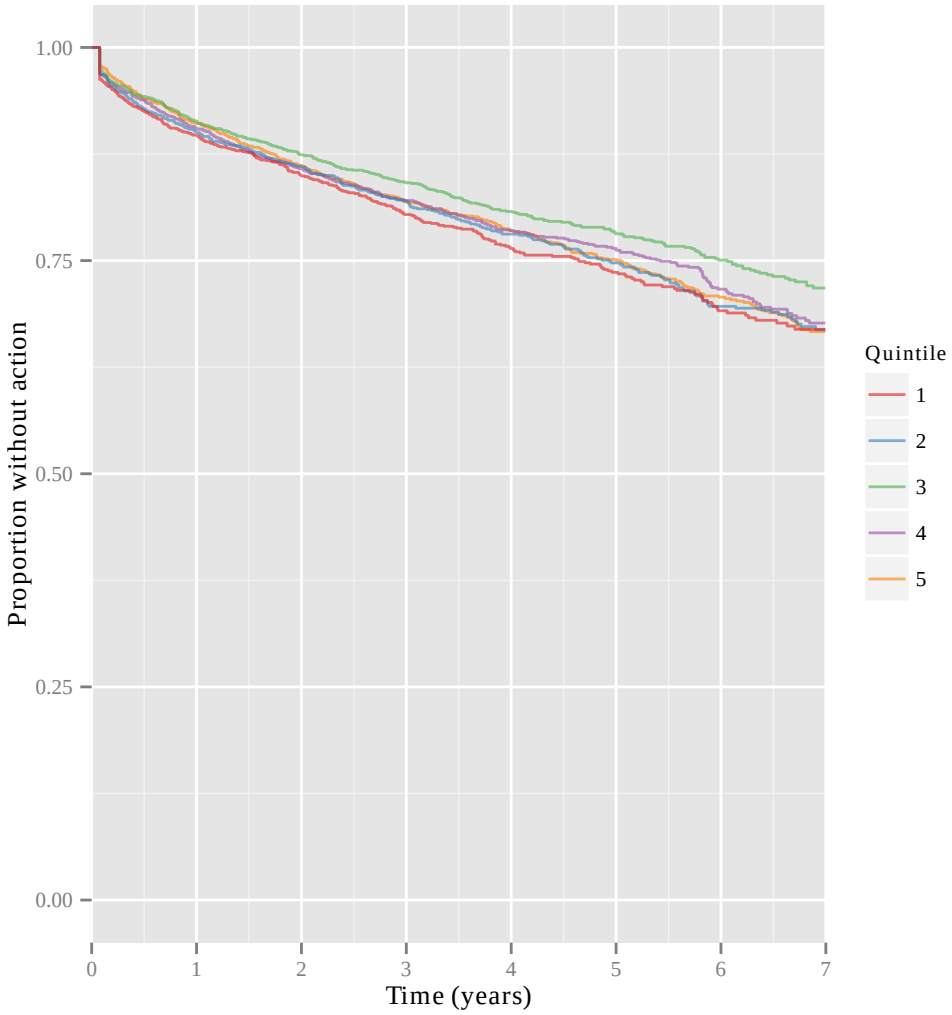
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.98	(0.70; 1.36)
Quintile 3	1.13	(0.82; 1.55)
Quintile 4	0.99	(0.72; 1.38)
Quintile 5	1.10	(0.80; 1.52)
Age 35 to 39	1.42	(0.18; 11.23)
Age 40 to 44	1.18	(0.44; 3.16)
Age 45 to 49	1.88	(0.85; 4.12)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.70	(0.32; 1.51)
Age 60 to 64	1.41	(0.73; 2.72)
Age 65 to 69	2.39	(1.29; 4.45)
Age 70 to 74	1.76	(0.95; 3.28)
Age 75 to 79	2.43	(1.30; 4.53)
Age 80 to 84	5.57	(3.03; 10.21)
Age 85+	6.18	(3.29; 11.63)
Male	1	(Reference)
Female	0.98	(0.81; 1.20)
Non−smoker	1	(Reference)
Smoker	1.35	(1.03; 1.77)
BMI low / norm.	1	(Reference)
Overweight	0.95	(0.75; 1.22)
Obese	0.96	(0.73; 1.25)
No hyp.	1	(Reference)
Hyp. contr.	0.83	(0.65; 1.06)
Hyp. uncontr.	0.77	(0.56; 1.05)
Untreat. hyp.	0.90	(0.49; 1.67)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.12	(0.88; 1.42)
No CVA	1	(Reference)
CVA	1.21	(0.96; 1.53)
No oth. co.	1	(Reference)
Other co.	1.73	(1.42; 2.11)
No diabetes	1	(Reference)
Diabetes	1.15	(0.92; 1.44)

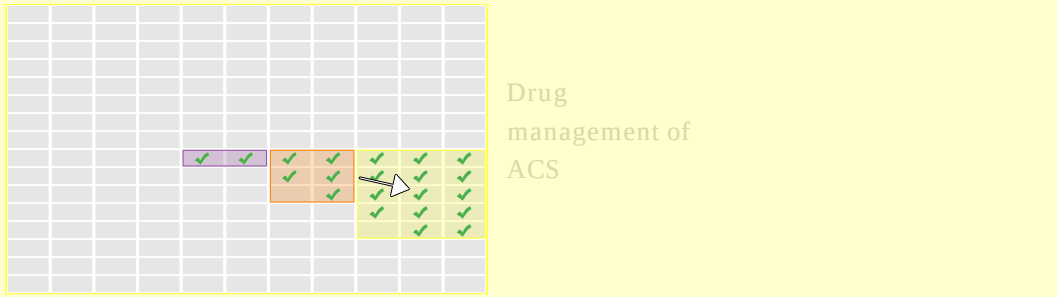
Number of clinical triggers 2441; Number of clinical actions 466. ICC for practice = 0.173. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'ACE inhibitor'. Drug cessation (triggers = 7860; actions = 1443)



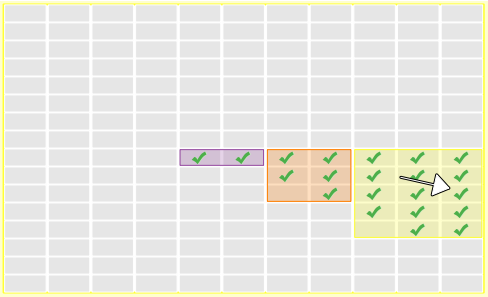


Mixed−effects model for 'unstable angina' and 'ACE inhibitor'. Drug cessation

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.03	(0.84; 1.25)
Quintile 3	0.98	(0.80; 1.20)
Quintile 4	1.16	(0.96; 1.42)
Quintile 5	1.14	(0.93; 1.38)
Age 35 to 39	0.41	(0.10; 1.68)
Age 40 to 44	1.16	(0.63; 2.13)
Age 45 to 49	1.20	(0.72; 2.00)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.08	(0.74; 1.57)
Age 60 to 64	1.30	(0.91; 1.86)
Age 65 to 69	1.26	(0.89; 1.80)
Age 70 to 74	1.84	(1.31; 2.58)
Age 75 to 79	2.66	(1.90; 3.72)
Age 80 to 84	3.54	(2.53; 4.96)
Age 85+	5.11	(3.63; 7.19)
Male	1	(Reference)
Female	1.10	(0.99; 1.23)
Non−smoker	1	(Reference)
Smoker	1.30	(1.11; 1.52)
BMI low / norm.	1	(Reference)
Overweight	0.78	(0.67; 0.92)
Obese	0.77	(0.66; 0.90)
No hyp.	1	(Reference)
Hyp. contr.	0.78	(0.68; 0.90)
Hyp. uncontr.	0.65	(0.54; 0.79)
Untreat. hyp.	0.85	(0.57; 1.28)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.01	(0.84; 1.21)
No CVA	1	(Reference)
CVA	1.13	(0.99; 1.29)
No oth. co.	1	(Reference)
Other co.	1.53	(1.37; 1.71)
No diabetes	1	(Reference)
Diabetes	1.14	(1.01; 1.29)
Elect. adm.	1	(Reference)
Emer. adm.	1.29	(0.99; 1.68)

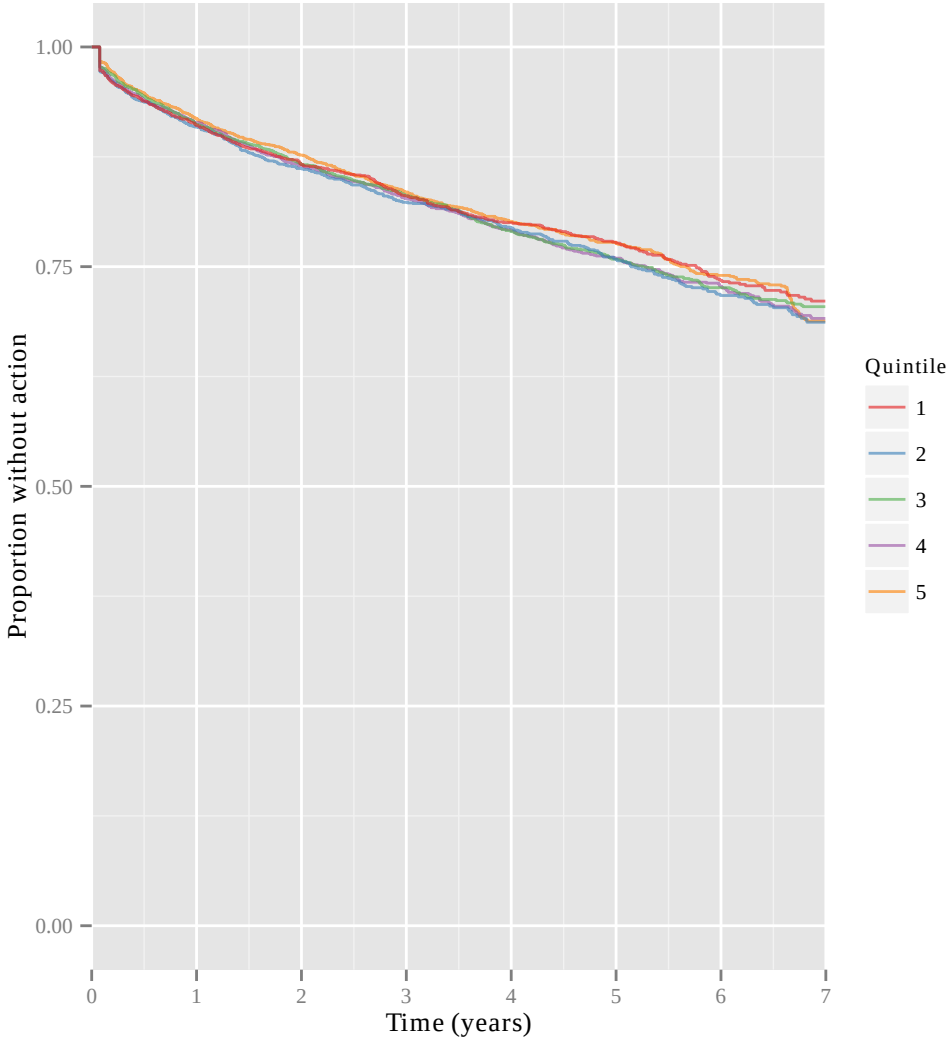
	HR	95% CI
Other adm.	1.19	(0.89; 1.59)
Cardiac cen.	1	(Reference)
Other cen.	1.22	(0.99; 1.50)
Cardiology	1	(Reference)
Med. spec.	1.24	(1.08; 1.42)
Other spec.	1.37	(1.10; 1.72)

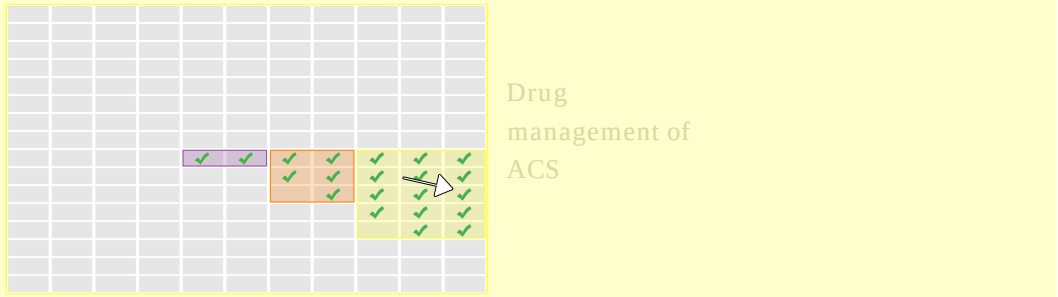
Number of clinical triggers 7860; Number of clinical actions 1443. ICC for practice = 0.141. ICC for hospital = < 0.005. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'ACE inhibitor'. Drug cessation (triggers = 10772; actions = 1916)



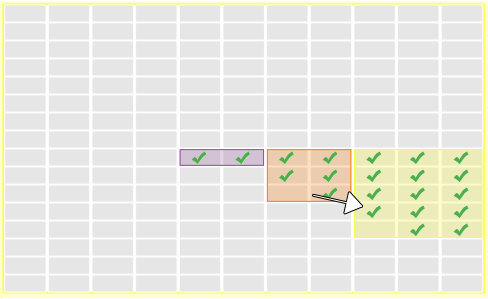


Mixed−effects model for 'MI' and 'ACE inhibitor'. Drug cessation

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.99	(0.84; 1.18)
Quintile 3	1.10	(0.93; 1.30)
Quintile 4	1.13	(0.96; 1.33)
Quintile 5	1.15	(0.96; 1.36)
Age 35 to 39	1.79	(1.03; 3.09)
Age 40 to 44	1.91	(1.26; 2.87)
Age 45 to 49	1.04	(0.68; 1.60)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.92	(0.65; 1.32)
Age 60 to 64	1.27	(0.92; 1.74)
Age 65 to 69	1.69	(1.25; 2.29)
Age 70 to 74	2.20	(1.64; 2.95)
Age 75 to 79	2.99	(2.23; 4.01)
Age 80 to 84	4.26	(3.18; 5.70)
Age 85+	6.03	(4.49; 8.10)
Male	1	(Reference)
Female	1.02	(0.93; 1.13)
Non−smoker	1	(Reference)
Smoker	1.06	(0.93; 1.22)
BMI low / norm.	1	(Reference)
Overweight	0.89	(0.80; 1.00)
Obese	0.85	(0.74; 0.98)
No hyp.	1	(Reference)
Hyp. contr.	0.96	(0.85; 1.07)
Hyp. uncontr.	0.77	(0.65; 0.91)
Untreat. hyp.	0.73	(0.53; 1.02)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.04	(0.92; 1.16)
No CVA	1	(Reference)
CVA	1.17	(1.04; 1.32)
No oth. co.	1	(Reference)
Other co.	1.69	(1.53; 1.86)
No diabetes	1	(Reference)
Diabetes	1.20	(1.08; 1.34)
Elect. adm.	1	(Reference)
Emer. adm.	1.07	(0.82; 1.40)

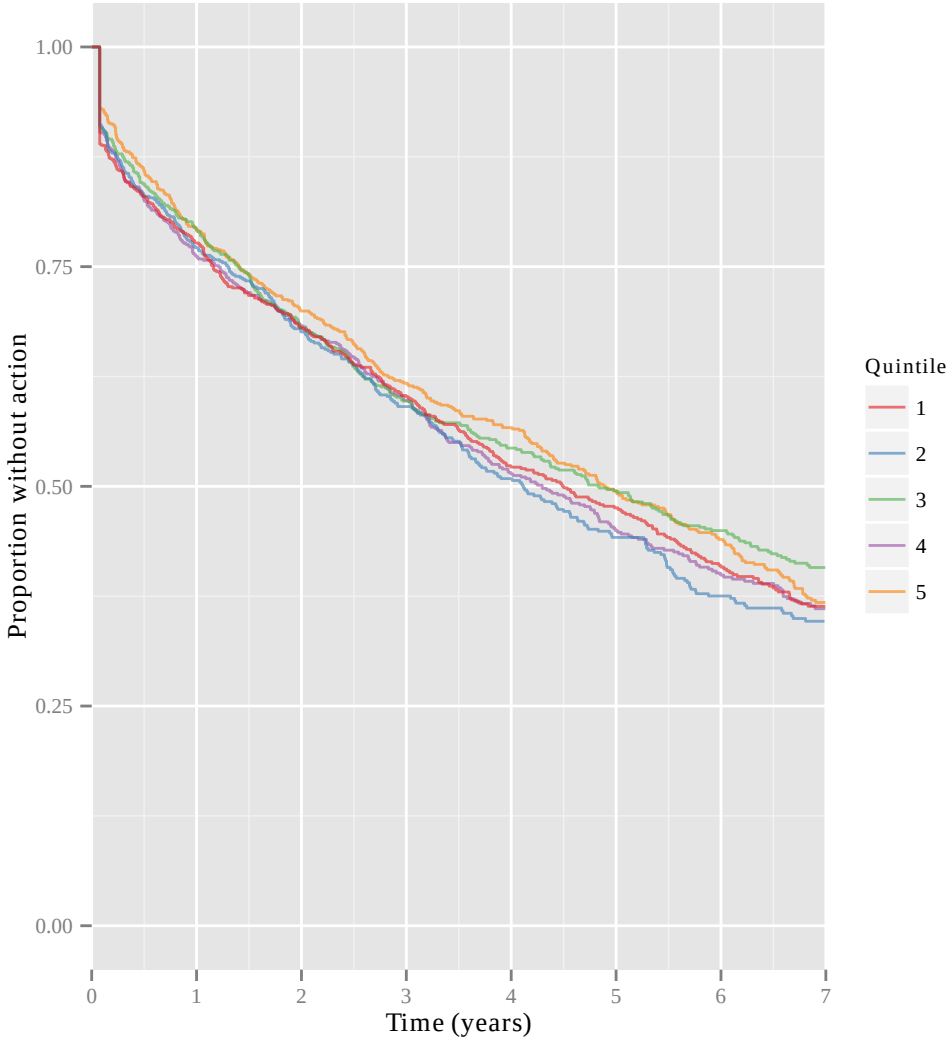
	HR	95% CI
Other adm.	1.00	(0.75; 1.34)
Cardiac cen.	1	(Reference)
Other cen.	1.13	(0.86; 1.48)
Cardiology	1	(Reference)
Med. spec.	1.10	(0.98; 1.23)
Other spec.	1.03	(0.83; 1.26)

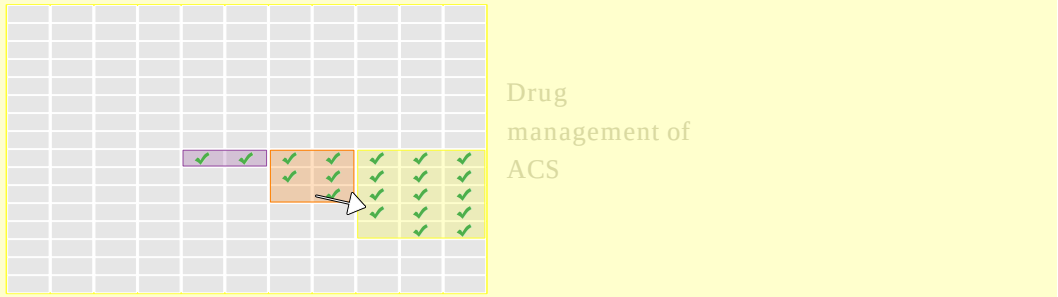
Number of clinical triggers 10772; Number of clinical actions 1916. ICC for practice = 0.083. ICC for hospital = 0.02. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'old ACS' and 'beta−blocker'. Drug cessation (triggers = 332; actions = 190)

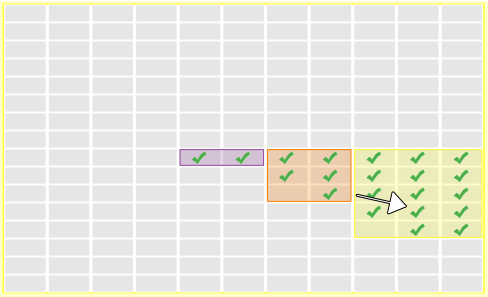




Mixed−effects model for 'old ACS' and 'beta−blocker'. Drug cessation

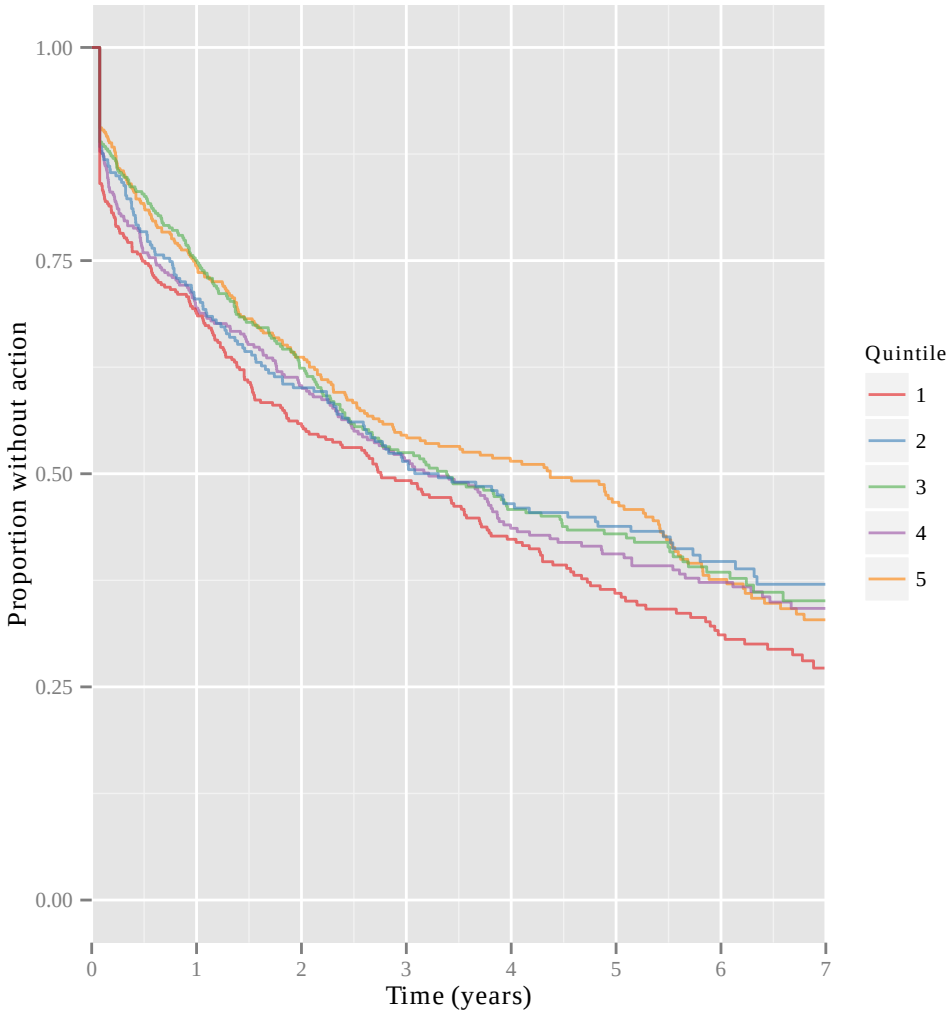
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.89	(0.56; 1.41)
Quintile 3	1.05	(0.68; 1.63)
Quintile 4	0.92	(0.57; 1.50)
Quintile 5	0.87	(0.54; 1.41)
Age 35 to 39	21.19	(2.42; >99)
Age 40 to 44	0.62	(0.21; 1.83)
Age 45 to 49	1.13	(0.42; 3.09)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.34	(0.70; 2.58)
Age 60 to 64	1.36	(0.69; 2.68)
Age 65 to 69	0.93	(0.46; 1.90)
Age 70 to 74	0.79	(0.40; 1.56)
Age 75 to 79	1.23	(0.60; 2.53)
Age 80 to 84	1.43	(0.68; 3.03)
Age 85+	1.25	(0.55; 2.84)
Male	1	(Reference)
Female	1.51	(1.10; 2.08)
Non−smoker	1	(Reference)
Smoker	1.10	(0.69; 1.74)
BMI low / norm.	1	(Reference)
Overweight	1.40	(0.94; 2.09)
Obese	0.87	(0.54; 1.41)
No hyp.	1	(Reference)
Hyp. contr.	0.59	(0.40; 0.85)
Hyp. uncontr.	0.84	(0.54; 1.32)
Untreat. hyp.	0.83	(0.33; 2.05)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.88	(0.58; 1.35)
No CVA	1	(Reference)
CVA	0.90	(0.57; 1.43)
No oth. co.	1	(Reference)
Other co.	1.15	(0.80; 1.67)
No diabetes	1	(Reference)
Diabetes	1.14	(0.77; 1.70)

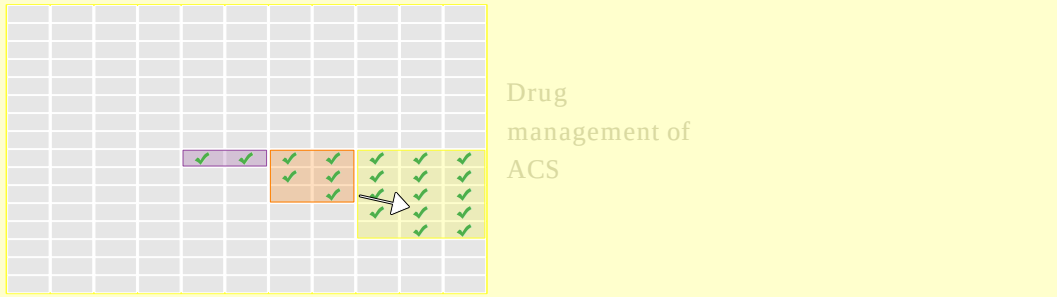
Number of clinical triggers 332; Number of clinical actions 190. ICC for practice < 0.005. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'beta−blocker'. Drug cessation (triggers = 968; actions = 506)



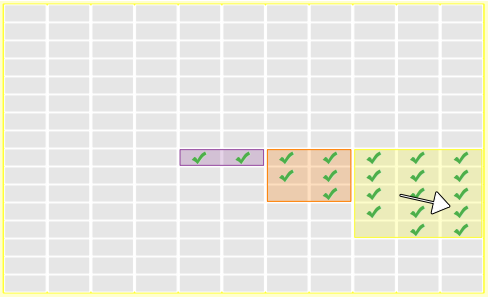


Mixed−effects model for 'unstable angina' and 'beta−blocker'. Drug cessation

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.75	(0.54; 1.06)
Quintile 3	0.71	(0.52; 0.97)
Quintile 4	0.91	(0.67; 1.24)
Quintile 5	0.82	(0.61; 1.11)
Age 35 to 39	1.39	(0.39; 4.98)
Age 40 to 44	1.49	(0.72; 3.07)
Age 45 to 49	1.03	(0.57; 1.86)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.97	(0.63; 1.52)
Age 60 to 64	1.09	(0.71; 1.69)
Age 65 to 69	0.90	(0.57; 1.40)
Age 70 to 74	1.44	(0.93; 2.23)
Age 75 to 79	1.02	(0.65; 1.62)
Age 80 to 84	1.71	(1.09; 2.66)
Age 85+	1.59	(0.93; 2.74)
Male	1	(Reference)
Female	1.08	(0.89; 1.32)
Non−smoker	1	(Reference)
Smoker	0.89	(0.67; 1.19)
BMI low / norm.	1	(Reference)
Overweight	1.00	(0.75; 1.33)
Obese	0.91	(0.68; 1.22)
No hyp.	1	(Reference)
Hyp. contr.	1.01	(0.76; 1.34)
Hyp. uncontr.	1.08	(0.77; 1.51)
Untreat. hyp.	1.12	(0.42; 2.98)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.76	(0.53; 1.08)
No CVA	1	(Reference)
CVA	0.91	(0.68; 1.22)
No oth. co.	1	(Reference)
Other co.	1.30	(1.05; 1.60)
No diabetes	1	(Reference)
Diabetes	1.36	(1.09; 1.69)
Elect. adm.	1	(Reference)
Emer. adm.	1.08	(0.72; 1.60)

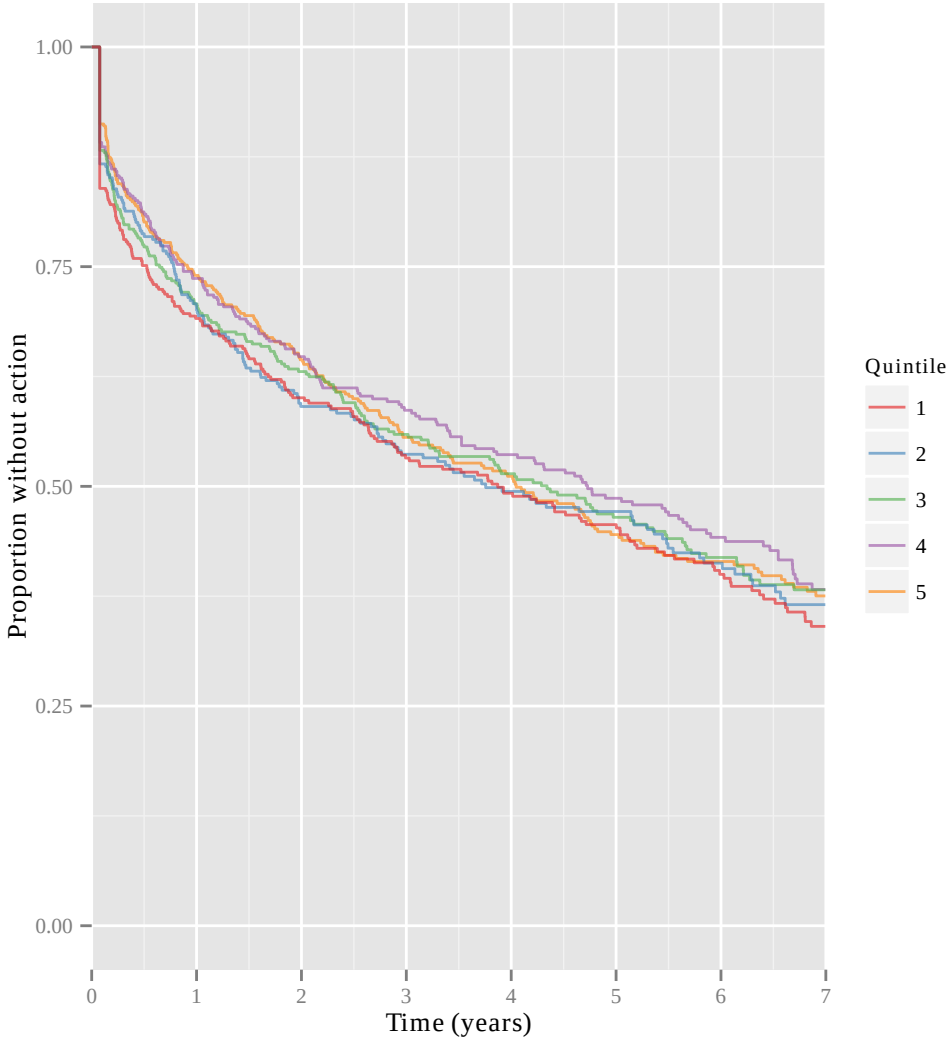
	HR	95% CI
Other adm.	1.22	(0.78; 1.91)
Cardiac cen.	1	(Reference)
Other cen.	1.33	(1.03; 1.71)
Cardiology	1	(Reference)
Med. spec.	0.91	(0.71; 1.18)
Other spec.	0.70	(0.47; 1.04)

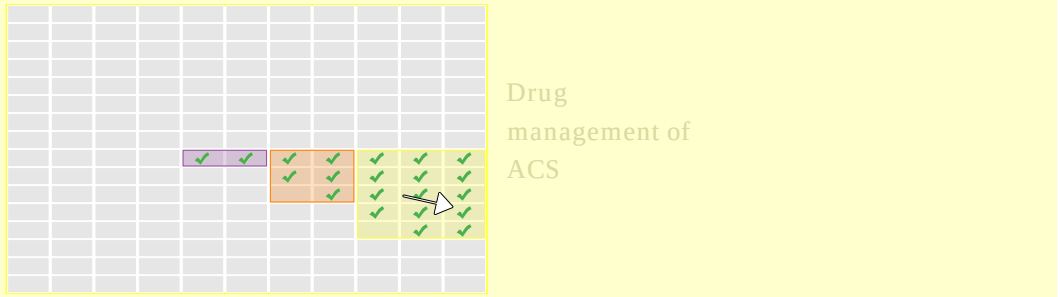
Number of clinical triggers 968; Number of clinical actions 506. ICC for practice = 0.133. ICC for hospital = < 0.005. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'beta−blocker'. Drug cessation (triggers = 820; actions = 458)

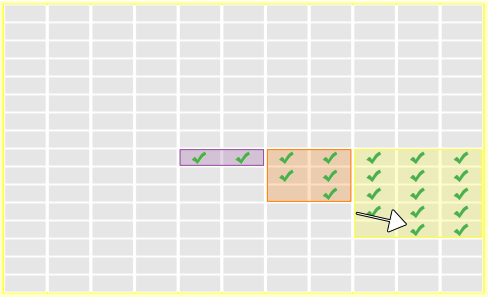




Mixed−effects model for 'MI' and 'beta−blocker'. Drug cessation

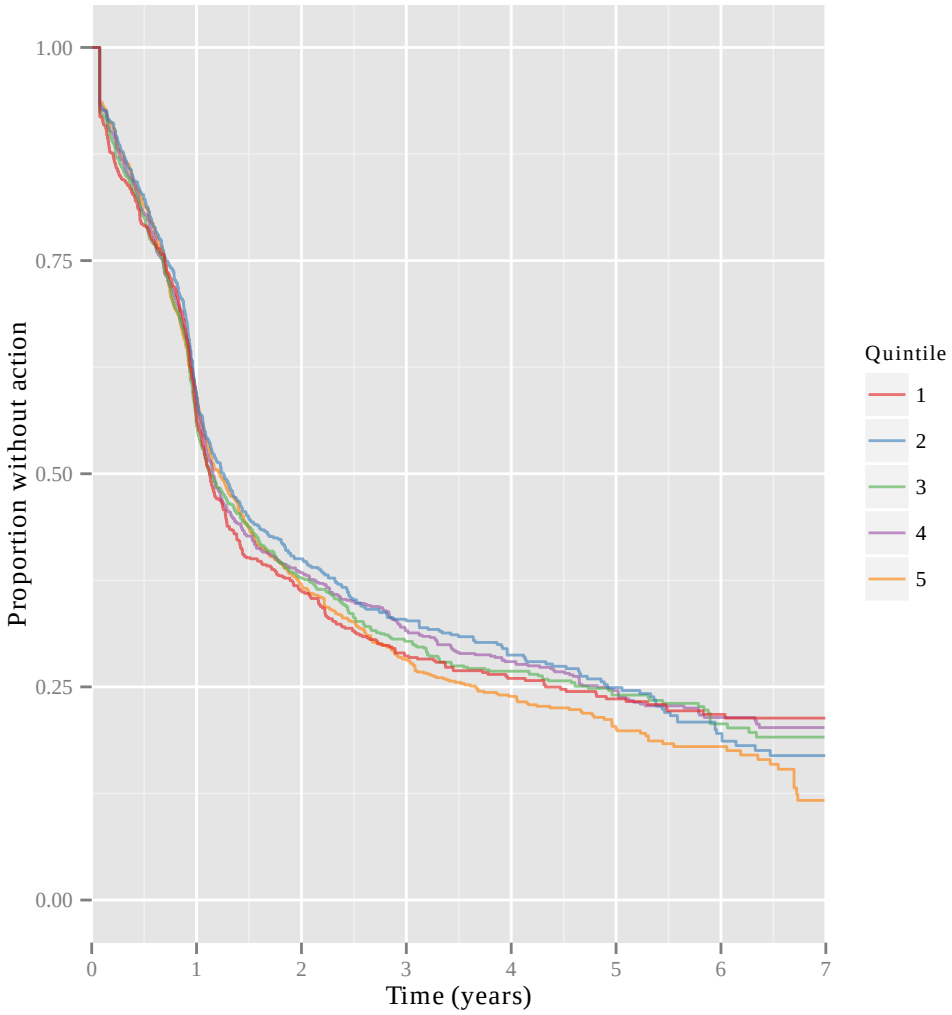
	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	1.06	(0.76; 1.48)
Quintile 3	1.17	(0.84; 1.63)
Quintile 4	0.94	(0.67; 1.32)
Quintile 5	1.09	(0.78; 1.51)
Age 35 to 39	0.46	(0.16; 1.34)
Age 40 to 44	1.02	(0.54; 1.92)
Age 45 to 49	0.72	(0.38; 1.33)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.02	(0.62; 1.66)
Age 60 to 64	0.68	(0.42; 1.09)
Age 65 to 69	1.59	(1.03; 2.45)
Age 70 to 74	1.26	(0.80; 1.99)
Age 75 to 79	1.53	(0.98; 2.41)
Age 80 to 84	1.39	(0.87; 2.22)
Age 85+	1.79	(1.08; 2.97)
Male	1	(Reference)
Female	0.98	(0.78; 1.22)
Non−smoker	1	(Reference)
Smoker	1.03	(0.78; 1.35)
BMI low / norm.	1	(Reference)
Overweight	1.05	(0.81; 1.36)
Obese	1.02	(0.77; 1.35)
No hyp.	1	(Reference)
Hyp. contr.	1.31	(0.99; 1.73)
Hyp. uncontr.	1.16	(0.83; 1.62)
Untreat. hyp.	0.85	(0.32; 2.25)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.94	(0.66; 1.32)
No CVA	1	(Reference)
CVA	1.06	(0.76; 1.46)
No oth. co.	1	(Reference)
Other co.	1.07	(0.85; 1.37)
No diabetes	1	(Reference)
Diabetes	1.08	(0.85; 1.37)
Elect. adm.	1	(Reference)
Emer. adm.	0.46	(0.28; 0.76)
Other adm.	0.41	(0.24; 0.71)
Cardiac cen.	1	(Reference)
Other cen.	1.05	(0.81; 1.35)
Cardiology	1	(Reference)
Med. spec.	0.92	(0.71; 1.19)
Other spec.	0.46	(0.27; 0.80)

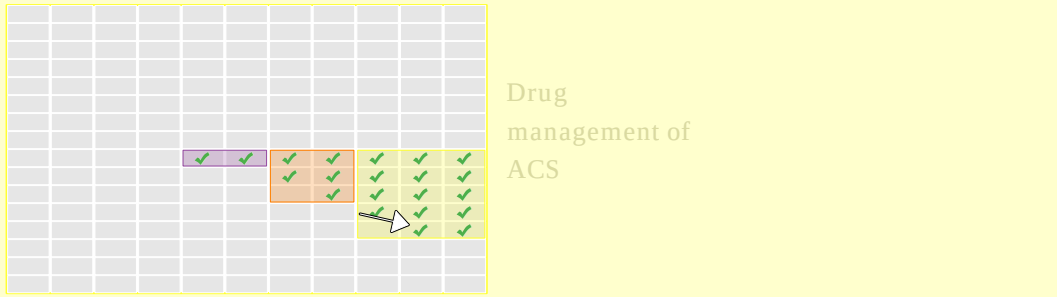
Number of clinical triggers 820; Number of clinical actions 458. ICC for practice = 0.104. ICC for hospital = < 0.005. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'unstable angina' and 'clopidogrel'. Drug cessation (triggers = 5783; actions = 3419)



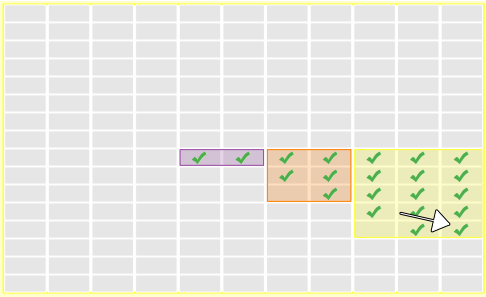


Mixed−effects model for 'unstable angina' and 'clopidogrel'. Drug cessation

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.95	(0.83; 1.09)
Quintile 3	0.96	(0.85; 1.09)
Quintile 4	0.97	(0.86; 1.11)
Quintile 5	1.03	(0.91; 1.17)
Age 35 to 39	0.55	(0.31; 0.97)
Age 40 to 44	1.25	(0.95; 1.64)
Age 45 to 49	1.01	(0.80; 1.27)
Age 50 to 54	1	(Reference)
Age 55 to 59	1.13	(0.95; 1.34)
Age 60 to 64	1.30	(1.10; 1.53)
Age 65 to 69	1.19	(1.01; 1.41)
Age 70 to 74	1.28	(1.09; 1.52)
Age 75 to 79	1.37	(1.15; 1.63)
Age 80 to 84	1.18	(0.98; 1.41)
Age 85+	1.57	(1.30; 1.89)
Male	1	(Reference)
Female	1.05	(0.97; 1.13)
Non−smoker	1	(Reference)
Smoker	1.00	(0.91; 1.10)
BMI low / norm.	1	(Reference)
Overweight	1.08	(0.98; 1.19)
Obese	1.00	(0.90; 1.11)
No hyp.	1	(Reference)
Hyp. contr.	0.89	(0.82; 0.98)
Hyp. uncontr.	0.93	(0.82; 1.05)
Untreat. hyp.	0.86	(0.66; 1.11)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	1.02	(0.92; 1.12)
No CVA	1	(Reference)
CVA	0.89	(0.81; 0.99)
No oth. co.	1	(Reference)
Other co.	0.88	(0.82; 0.95)
No diabetes	1	(Reference)
Diabetes	0.86	(0.79; 0.93)
Elect. adm.	1	(Reference)
Emer. adm.	0.87	(0.75; 1.01)

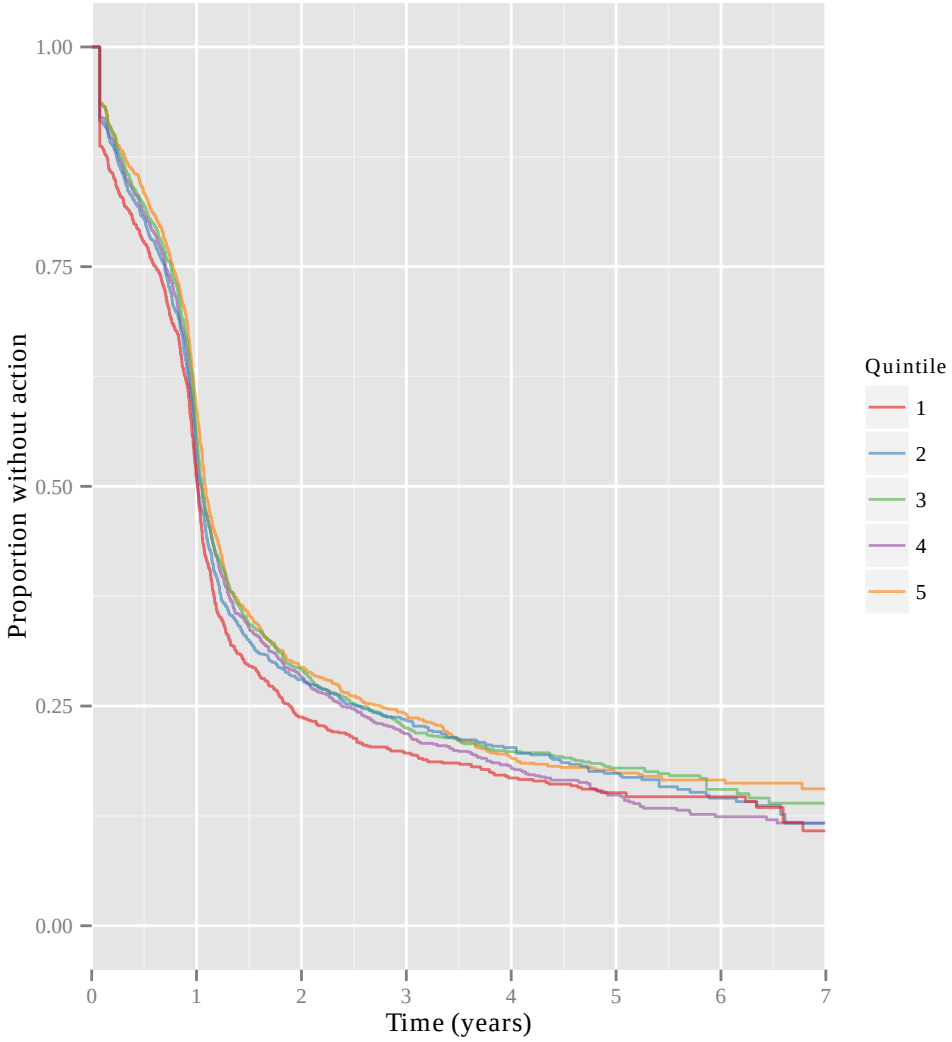
	HR	95% CI
Other adm.	0.88	(0.75; 1.04)
Cardiac cen.	1	(Reference)
Other cen.	0.97	(0.83; 1.14)
Cardiology	1	(Reference)
Med. spec.	1.04	(0.95; 1.13)
Other spec.	1.18	(1.00; 1.40)

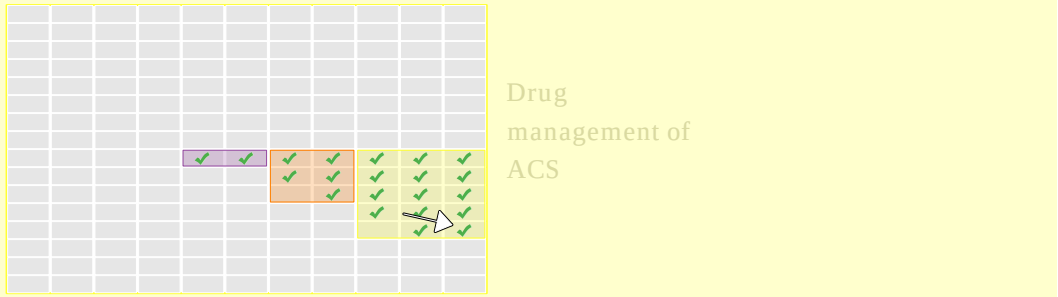
Number of clinical triggers 5783; Number of clinical actions 3419. ICC for practice = 0.072. ICC for hospital = 0.005. Missing values imputed using MICE.



Drug management of ACS

Kaplan−Meier plot for 'MI' and 'clopidogrel'. Drug cessation (triggers = 10133; actions = 6536)





Mixed−effects model for 'MI' and 'clopidogrel'. Drug cessation

	HR	95% CI
Quintile 1	1	(Reference)
Quintile 2	0.99	(0.90; 1.09)
Quintile 3	0.91	(0.83; 1.00)
Quintile 4	0.98	(0.89; 1.07)
Quintile 5	0.86	(0.78; 0.95)
Age 35 to 39	1.04	(0.83; 1.31)
Age 40 to 44	1.00	(0.85; 1.18)
Age 45 to 49	0.96	(0.84; 1.10)
Age 50 to 54	1	(Reference)
Age 55 to 59	0.94	(0.83; 1.05)
Age 60 to 64	0.93	(0.83; 1.04)
Age 65 to 69	1.05	(0.94; 1.17)
Age 70 to 74	1.11	(1.00; 1.25)
Age 75 to 79	1.22	(1.09; 1.37)
Age 80 to 84	1.03	(0.91; 1.17)
Age 85+	1.12	(0.98; 1.28)
Male	1	(Reference)
Female	0.99	(0.94; 1.05)
Non−smoker	1	(Reference)
Smoker	0.98	(0.92; 1.05)
BMI low / norm.	1	(Reference)
Overweight	1.05	(0.99; 1.12)
Obese	1.02	(0.95; 1.09)
No hyp.	1	(Reference)
Hyp. contr.	0.92	(0.87; 0.98)
Hyp. uncontr.	0.95	(0.87; 1.03)
Untreat. hyp.	0.91	(0.79; 1.05)
Chol:HDL < 4	1	(Reference)
Chol:HDL >= 4	0.98	(0.93; 1.04)
No CVA	1	(Reference)
CVA	0.88	(0.81; 0.95)
No oth. co.	1	(Reference)
Other co.	0.97	(0.92; 1.02)
No diabetes	1	(Reference)
Diabetes	0.88	(0.82; 0.94)
Elect. adm.	1	(Reference)
Emer. adm.	1.03	(0.86; 1.23)

	HR	95% CI
Other adm.	1.07	(0.89; 1.30)
Cardiac cen.	1	(Reference)
Other cen.	1.01	(0.85; 1.19)
Cardiology	1	(Reference)
Med. spec.	1.03	(0.97; 1.10)
Other spec.	1.08	(0.92; 1.26)

Number of clinical triggers 10133; Number of clinical actions 6536. ICC for practice = 0.068. ICC for hospital = 0.009. Missing values imputed using MICE.

E

CLINICAL CODES

In this electronic appendix, I have shown in tabular format the nature of the clinical codes that I used to define different clinical conditions. In the following table, I show the condition or state that I am defining, the code used in that definition, the coding system to which the code pertains, the text description relating to that code. I have also included a notes column, where, for example, I show which drugs have been included in the antihypertensive category.

Table E.1: Summary of clinical codes used for defining different conditions in this thesis

Defined	System	Code	Description	Notes
Diabetes	ICD-10	E10	Insulin-dependent diabetes mellitus	
Diabetes	ICD-10	E100	Insulin-dependent diabetes mellitus: With coma	
Diabetes	ICD-10	E101	Insulin-dependent diabetes mellitus: With ketoacidosis	
Diabetes	ICD-10	E102	Insulin-dependent diabetes mellitus: With renal complications	
Diabetes	ICD-10	E103	Insulin-dependent diabetes mellitus: With ophthalmic complications	
Diabetes	ICD-10	E104	Insulin-dependent diabetes mellitus: With neurological complications	
Diabetes	ICD-10	E105	Insulin-dependent diabetes mellitus: With peripheral circulatory complications	
Diabetes	ICD-10	E106	Insulin-dependent diabetes mellitus: With other specified complications	
Diabetes	ICD-10	E107	Insulin-dependent diabetes mellitus: With multiple complications	
Diabetes	ICD-10	E108	Insulin-dependent diabetes mellitus: With unspecified complications	
Diabetes	ICD-10	E109	Insulin-dependent diabetes mellitus: Without complications	
Diabetes	ICD-10	E11	Non-insulin-dependent diabetes mellitus	
Diabetes	ICD-10	E110	Non-insulin-dependent diabetes mellitus: With coma	
Diabetes	ICD-10	E111	Non-insulin-dependent diabetes mellitus: With ketoacidosis	
Diabetes	ICD-10	E112	Non-insulin-dependent diabetes mellitus: With renal complications	

Continued on next page

Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	ICD-10	E113	Non-insulin-dependent diabetes mellitus: With ophthalmic complications	
Diabetes	ICD-10	E114	Non-insulin-dependent diabetes mellitus: With neurological complications	
Diabetes	ICD-10	E115	Non-insulin-dependent diabetes mellitus: With peripheral circulatory complications	
Diabetes	ICD-10	E116	Non-insulin-dependent diabetes mellitus: With other specified complications	
Diabetes	ICD-10	E117	Non-insulin-dependent diabetes mellitus: With multiple complications	
Diabetes	ICD-10	E118	Non-insulin-dependent diabetes mellitus: With unspecified complications	
Diabetes	ICD-10	E119	Non-insulin-dependent diabetes mellitus: Without complications	
Diabetes	ICD-10	E14	Unspecified diabetes mellitus	
Diabetes	ICD-10	E140	Unspecified diabetes mellitus: With coma	
Diabetes	ICD-10	E141	Unspecified diabetes mellitus: With ketoacidosis	
Diabetes	ICD-10	E142	Unspecified diabetes mellitus: With renal complications	
Diabetes	ICD-10	E143	Unspecified diabetes mellitus: With ophthalmic complications	
Diabetes	ICD-10	E144	Unspecified diabetes mellitus: With neurological complications	
Diabetes	ICD-10	E145	Unspecified diabetes mellitus: With peripheral circulatory complications	
Diabetes	ICD-10	E146	Unspecified diabetes mellitus: With other specified complications	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	ICD-10	E147	Unspecified diabetes mellitus: With multiple complications	
Diabetes	ICD-10	E148	Unspecified diabetes mellitus: With unspecified complications	
Diabetes	ICD-10	E149	Unspecified diabetes mellitus: Without complications	
Diabetes	Read v2	66A..	Diabetic monitoring	
Diabetes	Read v2	66AS.	Diabetic annual review	
Diabetes	Read v2	68A7.	Diabetic retinopathy screening	
Diabetes	Read v2	9OL..	Diabetes monitoring admin.	
Diabetes	Read v2	9OL4.	Diabetes monitoring 1st letter	
Diabetes	Read v2	C10F.	Type 2 diabetes mellitus	
Diabetes	Read v2	66AP.	Diabetes: practice programme	
Diabetes	Read v2	66A4.	Diabetic on oral treatment	
Diabetes	Read v2	66A2.	Follow-up diabetic assessment	
Diabetes	Read v2	C10..	[X]Diabetes mellitus	
Diabetes	Read v2	Cyu2.	[X]Diabetes mellitus	
Diabetes	Read v2	66A3.	Diabetic on diet only	
Diabetes	Read v2	66Ac.	Diabetic periph neurop screen	
Diabetes	Read v2	9NND.	Under care of diab foot screen	
Diabetes	Read v2	2G5E.	O/E - R diab foot at low risk	
Diabetes	Read v2	2G5I.	O/E - L diab foot at low risk	
Diabetes	Read v2	66A5.	Diabetic on insulin	

Continued on next page

Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	Read v2	8B3l.	Diabetes medication review	
Diabetes	Read v2	13AB.	Diabetic lipid lowering diet	
Diabetes	Read v2	C109.	Non-insulin depd diabetes mell	
Diabetes	Read v2	9OLA.	Diabetes monitor. check done	
Diabetes	Read v2	9OL5.	Diabetes monitoring 2nd letter	
Diabetes	Read v2	66AD.	Fundoscopy - diabetic check	
Diabetes	Read v2	F4200	Background diabetic retinopath	
Diabetes	Read v2	66Aq.	Diabetic foot screen	
Diabetes	Read v2	66AZ.	Diabetic monitoring NOS	
Diabetes	Read v2	66A8.	Has seen dietician - diabetes	
Diabetes	Read v2	8BL2.	Pt on max tol ther for diabet	
Diabetes	Read v2	F420.	Diabetic retinopathy	
Diabetes	Read v2	C10E.	Type 1 diabetes mellitus	
Diabetes	Read v2	66Ab.	Diabetic foot examination	
Diabetes	Read v2	66AI.	Diabetic - good control	
Diabetes	Read v2	66AY.	Diabetic diet-good compliance	
Diabetes	Read v2	679L.	Health education - diabetes	
Diabetes	Read v2	66AU.	Diabetes care by hospital only	
Diabetes	Read v2	9OL6.	Diabetes monitoring 3rd letter	
Diabetes	Read v2	66AR.	Diabetes management plan given	
Diabetes	Read v2	13AC.	Diabetic weight reducing diet	
Diabetes	Read v2	66AJ.	Diabetic - poor control	

Continued on next page

Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	Read v2	C1001	Diab.mell.no comp. - adult	
Diabetes	Read v2	2BBF.	Retina abnormal - diabet relat	
Diabetes	Read v2	C109J	Insul treated Type 2 diab mell	
Diabetes	Read v2	C10FJ	Insul treated Type 2 diab mell	
Diabetes	Read v2	8Hl1.	Ref diabetc retinopathy screen	
Diabetes	Read v2	2G5F.	O/E - R diab foot at mod risk	
Diabetes	Read v2	2G5J.	O/E - L diab foot at mod risk	
Diabetes	Read v2	66A9.	Understands diet - diabetes	
Diabetes	Read v2	9OL7.	Diabetes monitor.verbal invite	
Diabetes	Read v2	66AW.	Diabetic foot risk assessment	
Diabetes	Read v2	9OL8.	Diabetes monitor.phone invite	
Diabetes	Read v2	C108.	Insulin depnd diabetes melitus	
Diabetes	Read v2	F4204	Diabetic maculopathy	
Diabetes	Read v2	66AT.	Annual diabetic blood test	
Diabetes	Read v2	1434.	H/O: diabetes mellitus	
Diabetes	Read v2	66Aa.	Diabetic diet-poor compliance	
Diabetes	Read v2	8I3W.	Diabetic foot exam declined	
Diabetes	Read v2	8HBG.	Diab retinopathy 12 mth review	
Diabetes	Read v2	2G5G.	O/E - R diab foot at high risk	
Diabetes	Read v2	F372.	Polyneuropathy in diabetes	
Diabetes	Read v2	2G5K.	O/E - L diab foot at high risk	
Diabetes	Read v2	9OLZ.	Diabetes monitoring admin.NOS	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	Read v2	68A9.	Diabetic retinopathy scr offer	
Diabetes	Read v2	C1000	Diab.mell.no comp. - juvenile	
Diabetes	Read v2	F4201	Proliferative diabetic retinop	
Diabetes	Read v2	66AV.	Diabetic on insulin+oral treat	
Diabetes	Read v2	9h4..	Except report: diabet qual ind	
Diabetes	Read v2	8I3X.	Diab retinopath screen refused	
Diabetes	Read v2	9OLD.	Diabet pt unsuit dig ret photo	
Diabetes	Read v2	9OL3.	Diabetes monitoring default	
Diabetes	Read v2	C101.	Diab.mell.with ketoacidosis	
Diabetes	Read v2	9360.	Pt held diabetic record issued	
Diabetes	Read v2	F4202	Preproliferative diabetic ret	
Diabetes	Read v2	C104.	Diab.mell. with nephropathy	
Diabetes	Read v2	66AH.	Diabetic treatment changed	
Diabetes	Read v2	2G5B.	O/E-Left diabet foot at risk	
Diabetes	Read v2	66AK.	Diabetic - cooperative patient	
Diabetes	Read v2	2G5A.	O/E-Right diabet foot at risk	
Diabetes	Read v2	2BBL.	O/E - diabet maculop both eyes	
Diabetes	Read v2	7276.	Pan retinal photocoag diabetes	
Diabetes	Read v2	C106.	Diab.mell. with neuropathy	
Diabetes	Read v2	F4206	Non prolif diab retinop	
Diabetes	Read v2	F4640	Diabetic cataract	
Diabetes	Read v2	9Non.	Seen community diab spec clin	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	Read v2	66A0.	Diabetes type 2 review	
Diabetes	Read v2	9NM0.	Attending diabetes clinic	
Diabetes	Read v2	8Hj4.	Refer to DESMOND diab st ed pr	
Diabetes	Read v2	66AJz	Diabetic - poor control NOS	
Diabetes	Read v2	C100.	Diab.mell. - no complication	
Diabetes	Read v2	679L0	Educa self management diabetes	
Diabetes	Read v2	8HHy.	Referral to diabetic register	
Diabetes	Read v2	66Af.	Pt diabetes education review	
Diabetes	Read v2	C1097	Type 2 diab mell+poor control	
Diabetes	Read v2	C10F7	Type 2 diab mell+poor control	
Diabetes	Read v2	F420z	Diabetic retinopathy NOS	
Diabetes	Read v2	9OL2.	Refuses diabetes monitoring	
Diabetes	Read v2	8H2J.	Admit diabetic emergency	
Diabetes	Read v2	F3722	Asymptomatic diab neuropathy	
Diabetes	Read v2	679R.	Pt offered diab struct ed prog	
Diabetes	Read v2	66AN.	Date diabetic treatment start	
Diabetes	Read v2	M2711	Neuropathic diab ulcer - foot	
Diabetes	Read v2	9m0A.	Declined diabetic retinop scrn	
Diabetes	Read v2	F1711	Autonomic neuropathy-diabetes	
Diabetes	Read v2	M2712	Mixed diabetic ulcer - foot	
Diabetes	Read v2	8A13.	Diabetic stabilisation	
Diabetes	Read v2	F3721	Chron painful diab neuropathy	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	Read v2	M2710	Ischaemic ulcer diabetic foot	
Diabetes	Read v2	2G5H.	O/E - R diab foot - ulcerated	
Diabetes	Read v2	F4203	Advanced diabetic maculopathy	
Diabetes	Read v2	2G5L.	O/E - L diab foot - ulcerated	
Diabetes	Read v2	2G510	Foot abnormal-diabetes related	
Diabetes	Read v2	2G5C.	Foot abnormal-diabetes related	
Diabetes	Read v2	C1096	Type 2 diab mell + retinopathy	
Diabetes	Read v2	C10F6	Type 2 diab mell + retinopathy	
Diabetes	Read v2	C10FC	Type 2 diab mell + nephropathy	
Diabetes	Read v2	9OLM.	Diabetes struc edu prog declin	
Diabetes	Read v2	66AL.	Diabetic-uncooperative patient	
Diabetes	Read v2	M0372	Cellulitis in diabetic foot	
Diabetes	Read v2	C105.	Diab.mell.+ eye manifestation	
Diabetes	Read v2	C1099	Non-insul-dep diab mel no comp	
Diabetes	Read v2	N0301	Diabetic Charcot arthropathy	
Diabetes	Read v2	8HBH.	Diab retinopathy 6 mth review	
Diabetes	Read v2	C107.	Diab.mell.+periph.circul.dis	
Diabetes	Read v2	C1087	Type 1 diab mell + retinopathy	
Diabetes	Read v2	C10E7	Type 1 diab mell + retinopathy	
Diabetes	Read v2	8CR2.	Diabetes clin management plan	
Diabetes	Read v2	C1088	Type 1 diab mell poor control	
Diabetes	Read v2	C10E8	Type 1 diab mell poor control	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	Read v2	C1090	Type 2 diab mell + renal compl	
Diabetes	Read v2	C10F0	Type 2 diab mell + renal compl	
Diabetes	Read v2	C10F9	Type 2 diab mell without comp	
Diabetes	Read v2	N0300	Diabetic cheiroarthropathy	
Diabetes	Read v2	C1089	Type 1 diab mell matur onset	
Diabetes	Read v2	C10E9	Type 1 diab mell matur onset	
Diabetes	Read v2	66AJ1	Brittle diabetes	
Diabetes	Read v2	68AB.	Diabtic dig retnpthy scrn offd	
Diabetes	Read v2	F3720	Acute painful diab neuropathy	
Diabetes	Read v2	66At1	Type II diabetic dietary revie	
Diabetes	Read v2	F3y0.	Diabetic mononeuropathy	
Diabetes	Read v2	8CS0.	Diabetes care plan agreed	
Diabetes	Read v2	C101z	Diab.mell.+ketoacid -onset NOS	
Diabetes	Read v2	C106z	Diab.mell.+neuropathy NOS	
Diabetes	Read v2	C10ED	Type 1 diab mell + nephropathy	
Diabetes	Read v2	F3813	Myasthenic syndrome+diabetes	
Diabetes	Read v2	8A12.	Diabetic crisis monitoring	
Diabetes	Read v2	C104z	Diab.mell.+nephropathy NOS	
Diabetes	Read v2	C1094	Type 2 diab mell with ulcer	
Diabetes	Read v2	C10F4	Type 2 diab mell with ulcer	
Diabetes	Read v2	C1061	Diab.mell.+neuropathy - adult	
Diabetes	Read v2	K01x1	Nephrotic syndrome+diabetes M.	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	Read v2	C1011	Diab.mell.+ketoacid - adult	
Diabetes	Read v2	F35z0	Diabetic mononeuritis NOS	
Diabetes	Read v2	F4205	Advanced diabetic retinal dis	
Diabetes	Read v2	R0542	[D]Gangrene of toe in diabetic	
Diabetes	Read v2	C1092	Type 2 diab mell + neurol comp	
Diabetes	Read v2	C10F2	Type 2 diab mell + neurol comp	
Diabetes	Read v2	C10ER	Latent autoimm diab mell adult	
Diabetes	Read v2	C103.	Diab.mell. + ketoacidotic coma	
Diabetes	Read v2	C10EE	Type 1 diab mell + hypo coma	
Diabetes	Read v2	C1085	Type 1 diab mell with ulcer	
Diabetes	Read v2	C10E5	Type 1 diab mell with ulcer	
Diabetes	Read v2	C109E	NIDDM with diabetic cataract	
Diabetes	Read v2	9OLF.	Diabetes struc ed prog complet	
Diabetes	Read v2	C100z	Diab.mell.no comp. - onset NOS	
Diabetes	Read v2	F4407	Diabetic iritis	
Diabetes	Read v2	8H3O.	Non-urgent diabetic admission	
Diabetes	Read v2	C10C.	Diab mell aut dom	
Diabetes	Read v2	C10z.	Diab.mell. + unspec comp	
Diabetes	Read v2	C1095	Type 2 diab mell + gangrene	
Diabetes	Read v2	C10F5	Type 2 diab mell + gangrene	
Diabetes	Read v2	C10FH	Type 2 diab mell neurop+arthr	
Diabetes	Read v2	C10E4	Unstab type 1 diabet mellitus	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	Read v2	G73y0	Diabetic peripheral angiopathy	
Diabetes	Read v2	C1081	Type 1 diab mell + ophth comps	
Diabetes	Read v2	C10E1	Type 1 diab mell + ophth comps	
Diabetes	Read v2	C1091	Type 2 diab mell+ophthal comp	
Diabetes	Read v2	C10F1	Type 2 diab mell+ophthal comp	
Diabetes	Read v2	L1806	Pre-ex diab mel non insuln-dep	
Diabetes	Read v2	C10FG	Type 2 diab mell + arthropathy	
Diabetes	Read v2	2G5V.	O/E - R chron diab foot ulcer	
Diabetes	Read v2	C10FE	Type 2 diab mell+diab catarct	
Diabetes	Read v2	2G5W.	O/E - L chron diab foot ulcer	
Diabetes	Read v2	C10FB	Type 2 diab mell + polyneurop	
Diabetes	Read v2	C10FD	Type 2 diab mell+hypogly coma	
Diabetes	Read v2	8HLE.	Diabetology D.V. done	
Diabetes	Read v2	C1084	Unstab insul depend diab mell	
Diabetes	Read v2	C1041	Diab.mell.+nephropathy - adult	
Diabetes	Read v2	C10D.	Diab mell aut dom type 2	
Diabetes	Read v2	C1051	Diab.mell.+eye manif - adult	
Diabetes	Read v2	C10N1	Cyst fibro relat diab mellitus	
Diabetes	Read v2	C1086	Type 1 diab mell with gangrene	
Diabetes	Read v2	C10E6	Type 1 diab mell with gangrene	
Diabetes	Read v2	C10FA	Type 2 diab mell mononeurop	
Diabetes	Read v2	C10EJ	Type 1 diab mell+neuro arthrop	

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Defined	System	Code	Description	Notes
Diabetes	Read v2	C10N.	Secondary diabetes mellitus	
Diabetes	Read v2	C102.	Diab.mell. + hyperosmolar coma	
Diabetes	Read v2	C10EC	Type 1 diab mell + polyneurop	
Diabetes	Read v2	C10y.	Diab.mell.+other manifestation	
Diabetes	Read v2	C1080	Insuln-dep diab mel+renal comp	
Diabetes	Read v2	C101y	Oth specfd diab mel+ketoacidos	
Diabetes	Read v2	C1083	Type 1 diab mell + mult comps	
Diabetes	Read v2	C10E3	Type 1 diab mell + mult comps	
Diabetes	Read v2	F3450	Diabet mononeuritis multiplex	
Diabetes	Read v2	C103z	Diab.mell.+ketoac coma NOS	
Diabetes	Read v2	C10z1	Diab.mell.+comp NOS - adult	
Diabetes	Read v2	C10EA	Type 1 diab mell without comp	
Diabetes	Read v2	C10F3	Type 2 diab mell + multip comp	
Diabetes	Read v2	C1072	Diabetic gangrene - adult	
Diabetes	Read v2	C10y1	Diab.mell.+other manif. -adult	
Diabetes	Read v2	C108F	IDDM with diabetic cataract	
Diabetes	Read v2	C103y	Oth specif diab mell with coma	
Diabetes	Read v2	C1021	Diab.mell.+hyperosm.coma-adult	
Diabetes	Read v2	C10A.	Malnutritn-relat diab mellitus	
Diabetes	Read v2	C1082	Type 1 diab mell + neuro comps	
Diabetes	Read v2	C10E2	Type 1 diab mell + neuro comps	
Diabetes	Read v2	C1050	Diab.mell.+eye manif -juvenile	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Diabetes	Read v2	Cyu20	[X]Oth specf diabetes mellitus	
Diabetes	Read v2	C102z	Diabetes+hyperosmolar coma NOS	
Diabetes	Read v2	C109F	NIDDM with periph angiopath	
Diabetes	Read v2	TJ23z	AR - insulins/antidiabetic NOS	
Diabetes	Read v2	6761.	Diabetic pre-pregnancy counsel	
Diabetes	Read v2	C10yy	Oth spec diab mel+oth spec cmp	
Diabetes	Read v2	C108G	IDDM with peripheral angiopath	
Diabetes	Read v2	C10EH	Type 1 diab mell + arthropathy	
Diabetes	Read v2	R0543	[D]Widespread diab foot gangr	
Diabetes	Read v2	C10zz	Diab.mell. + unspec comp NOS	
Diabetes	Read v2	C10EB	Type 1 diab mell + mononeurop	
Diabetes	Read v2	3883.	Diabetes treatmt satisf quest	
Diabetes	Read v2	9M00.	Informd consent diab nat audit	
Diabetes	Read v2	L1800	Preg.+diabetes mellitus unspec	
Diabetes	Read v2	C10z0	Diab.mell.+comp NOS - juvenile	
Diabetes	Read v2	2BBr.	Impair vision due diab retinop	
Diabetes	Read v2	C105y	Oth specfd diab mel+ophth comp	
Smoking ascertainment	Read v2	1371.	Never smoked tobacco	
Smoking ascertainment	Read v2	137S.	Ex smoker	
Smoking ascertainment	Read v2	137P.	Cigarette smoker	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Smoking ascertainment	Read v2	137L.	Current non-smoker	
Smoking ascertainment	Read v2	137R.	Current smoker	
Smoking ascertainment	Read v2	1374.	Moderate smoker - 10-19 cigs/d	
Smoking ascertainment	Read v2	1373.	Light smoker - 1-9 cigs/day	
Smoking ascertainment	Read v2	1379.	Ex-moderate smoker (10-19/day)	
Smoking ascertainment	Read v2	1375.	Heavy smoker - 20-39 cigs/day	
Smoking ascertainment	Read v2	137K.	Stopped smoking	
Smoking ascertainment	Read v2	1378.	Ex-light smoker (1-9/day)	
Smoking ascertainment	Read v2	137G.	Trying to give up smoking	
Smoking ascertainment	Read v2	137A.	Ex-heavy smoker (20-39/day)	
Smoking ascertainment	Read v2	137F.	Ex-smoker - amount unknown	
Smoking ascertainment	Read v2	1372.	Trivial smoker - < 1 cig/day	
Smoking ascertainment	Read v2	137M.	Rolls own cigarettes	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Smoking ascertainment	Read v2	137Z.	Tobacco consumption NOS	
Smoking ascertainment	Read v2	1377.	Ex-trivial smoker (<1/day)	
Smoking ascertainment	Read v2	137T.	Date ceased smoking	
Smoking ascertainment	Read v2	137H.	Pipe smoker	
Smoking ascertainment	Read v2	137J.	Cigar smoker	
Smoking ascertainment	Read v2	137B.	Ex-very heavy smoker (40+/day)	
Smoking ascertainment	Read v2	1376.	Very heavy smoker - 40+cigs/d	
Smoking ascertainment	Read v2	137X.	Cigarette consumption	
Smoking ascertainment	Read v2	137N.	Ex pipe smoker	
Smoking ascertainment	Read v2	137Q.	Smoking started	
Smoking ascertainment	Read v2	137O.	Ex cigar smoker	
Smoking ascertainment	Read v2	137Y.	Cigar consumption	
Smoking ascertainment	Read v2	137V.	Smoking reduced	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Smoking ascertainment	Read v2	137K0	Recently stopped smoking	
Smoking ascertainment	Read v2	9kn..	Non-smoker annual review - enhanced services administration	
Smoking ascertainment	Read v2	9ko..	Current smoker annual review - enhanced services administration	
Smoking advice	Read v2	8CAL.	Smoking cessation advice	
Smoking advice	Read v2	6791.	Health ed. - smoking	
Smoking advice	Read v2	67H1.	Lifestyle adv re smoking	
Smoking advice	Read v2	67H6.	Brf intervention smoking cessn	
Smoking cessation referral	Read v2	8H7i.	Referral: smok cessatn advisor	
Smoking cessation referral	Read v2	8HTK.	Referl to stop-smoking clinic	
Smoking cessation referral	Read v2	9N2k.	Seen by smoking cesstn advisor	
Smoking cessation referral	Read v2	9N4M.	DNA - Smoking cessation clinic	
Smoking cessation referral	Read v2	13p5.	Smoking cessn progm start date	

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Defined	System	Code	Description	Notes
Smoking cessation referral	Read v2	8HkQ.	Refer to NHS stop smoking srvc	
Chronic renal disease	Read v2	66i..	CKD monitoring	
Chronic renal disease	Read v2	9Oto.	CKD monitoring first letter	
Chronic renal disease	Read v2	K05..	Chronic renal failure	
Chronic renal disease	Read v2	1Z1..	Chronic renal impairment	
Chronic renal disease	Read v2	K060.	Renal impairment	
Chronic renal disease	Read v2	1Z1B.	CKD stage 3 with proteinuria	
Chronic renal disease	Read v2	9Ot1.	CKD monitoring second letter	
Chronic renal disease	Read v2	9Ot..	CKD monitoring administration	
Chronic renal disease	Read v2	9Ot4.	CKD monitoring telephone invte	
Chronic renal disease	Read v2	9Ot2.	CKD monitoring third letter	
Chronic renal disease	Read v2	K08..	Impaired renal function disord	
Chronic renal disease	Read v2	K050.	End stage renal failure	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Chronic renal disease	Read v2	9Ot3.	CKD monitoring verbal invite	
Chronic renal disease	Read v2	1Z1H.	CKD stage 4 with proteinuria	
Chronic renal disease	Read v2	1Z1D.	CKD stage 3A with proteinuria	
Chronic renal disease	Read v2	1Z1F.	CKD stage 3B with proteinuria	
Chronic renal disease	Read v2	1Z19.	CKD stage 2 with proteinuria	
Chronic renal disease	Read v2	Kyu2.	[X]Renal failure	
Chronic renal disease	Read v2	K08z.	Impaired renal funct.dis.NOS	
Chronic renal disease	Read v2	D2150	Anaemia secondary to CRF	
Chronic renal disease	Read v2	D215.	Anaemia second renal failure	
Chronic renal disease	Read v2	1Z1K.	CKD stage 5 with proteinuria	
Chronic renal disease	Read v2	K0E..	Acute-on-chronic renal failure	
Chronic renal disease	Read v2	Kyu21	[X]Other chronic renal failure	
Chronic renal disease	Read v2	G222.	Hypertens renal dis+renal fail	

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Defined	System	Code	Description	Notes
Chronic renal disease	Read v2	G233.	Hypertn hrt+ren dis+renal fail	
Lipid disorders	Read v2	C3200	LDL hyperlipoproteinaemia	
Peripheral vascular disease	ICD-10	I702	Atherosclerosis of arteries of extremities	
Peripheral vascular disease	ICD-10	I708	Atherosclerosis of other arteries	
Peripheral vascular disease	ICD-10	I709	Generalized and unspecified atherosclerosis	
Peripheral vascular disease	ICD-10	I739	Peripheral vascular disease, unspecified	
Peripheral vascular disease	ICD-10	I792	Peripheral angiopathy in diseases classified elsewhere	
Old MI	ICD-10	I252	Old myocardial infarction	
Old MI	Read v2	G30..	Acute myocardial infarction	
Old MI	Read v2	G3115	Acute coronary syndrome	
Old MI	Read v2	G3111	Unstable angina	
Old MI	Read v2	G32..	Old myocardial infarction	
Old MI	Read v2	G308.	Inferior myocard. infarct NOS	
Old MI	Read v2	14A3.	H/O: myocardial infarct <60	
Old MI	Read v2	G30z.	Acute myocardial infarct. NOS	
Old MI	Read v2	G301z	Anterior myocard.infarct NOS	
Old MI	Read v2	G301.	Anterior myocard. infarct OS	
Old MI	Read v2	323..	ECG: myocardial infarction	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Old MI	Read v2	G31y0	Acute coronary insufficiency	
Old MI	Read v2	G3112	Angina at rest	
Old MI	Read v2	14A4.	H/O: myocardial infarct >60	
Old MI	Read v2	3232.	ECG: old myocardial infarction	
Old MI	Read v2	G304.	Posterior myocard.infarct NOS	
Old MI	Read v2	G305.	Lateral myocardial infarct NOS	
Old MI	Read v2	G35..	Subseqnt myocardial infarction	
Old MI	Read v2	G30y.	Other acute myocardial infarct	
Old MI	Read v2	323Z.	ECG: myocardial infarct NOS	
Old MI	Read v2	14AT.	H/O: myocardial infarction	
Old MI	Read v2	G30yz	Other acute myocardial inf.NOS	
Old MI	Read v2	14AH.	H/O: Myoc infarct in last year	
Old MI	Read v2	G351.	Subsqnt myocrd infarc/inf wall	
Old MI	Read v2	ZV719	[V]Obs/suspct myocard infarctn	
Old MI	Read v2	G306.	True posterior myocard.infarct	
Old MI	Read v2	G350.	Subsqnt myocrd infarc/ant wall	
Old MI	Read v2	G30B.	Acute posterol myocard infarct	
Old MI	Read v2	G33z0	Status anginosus	
MI	ICD-10	I21	Acute myocardial infarction	
MI	ICD-10	I210	Acute transmural myocardial infarction of anterior wall	
MI	ICD-10	I211	Acute transmural myocardial infarction of inferior wall	
MI	ICD-10	I212	Acute transmural myocardial infarction of other sites	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
MI	ICD-10	I213	Acute transmural myocardial infarction of unspecified site	
MI	ICD-10	I214	Acute subendocardial myocardial infarction	
MI	ICD-10	I219	Acute myocardial infarction, unspecified	
MI	ICD-10	I22	Subsequent myocardial infarction	
MI	ICD-10	I220	Subsequent myocardial infarction of anterior wall	
MI	ICD-10	I221	Subsequent myocardial infarction of inferior wall	
MI	ICD-10	I228	Subsequent myocardial infarction of other sites	
MI	ICD-10	I229	Subsequent myocardial infarction of unspecified site	
Unstable angina	ICD-10	I200	Unstable angina	
Hypertension diagnosis	ICD-10	I110	Hypertensive heart disease with (congestive) heart failure	
Hypertension diagnosis	ICD-10	I119	Hypertensive heart disease without (congestive) heart failure	
Hypertension diagnosis	ICD-10	I120	Hypertensive renal disease with renal failure	
Hypertension diagnosis	ICD-10	I129	Hypertensive renal disease without renal failure	
Hypertension diagnosis	ICD-10	I130	Hypertensive heart and renal disease with (congestive) heart failure	
Hypertension diagnosis	ICD-10	I131	Hypertensive heart and renal disease with renal failure	
Hypertension diagnosis	ICD-10	I132	Hypertensive heart and renal disease with both (congestive) heart failure and renal failure	
Hypertension diagnosis	ICD-10	I139	Hypertensive heart and renal disease, unspecified	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Hypertension diagnosis	ICD-10	I150	Renovascular hypertension	
Hypertension diagnosis	ICD-10	I151	Hypertension secondary to other renal disorders	
Hypertension diagnosis	ICD-10	I152	Hypertension secondary to endocrine disorders	
Hypertension diagnosis	ICD-10	I158	Other secondary hypertension	
Hypertension diagnosis	ICD-10	I159	Secondary hypertension, unspecified	
Hypertension diagnosis	Read v2	G20..	Essential hypertension	
Hypertension diagnosis	Read v2	G2...	Hypertensive disease	
Hypertension diagnosis	Read v2	14A2.	H/O: hypertension	
Hypertension diagnosis	Read v2	G20z.	Essential hypertension NOS	
Hypertension diagnosis	Read v2	G201.	Benign essential hypertension	
Hypertension diagnosis	Read v2	G2z..	Hypertensive disease NOS	
Hypertension diagnosis	Read v2	G202.	Systolic hypertension	
Hypertension diagnosis	Read v2	G2y..	Hypertensive disease OS	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Hypertension diagnosis	Read v2	G200.	Malignant essential hypertension	
Hypertension diagnosis	Read v2	G203.	Diastolic hypertension	
Hypertension diagnosis	Read v2	Gyu2.	[X]Hypertensive diseases	
CVA	ICD-10	I110	Hypertensive heart disease with (congestive) heart failure	
CVA	ICD-10	I119	Hypertensive heart disease without (congestive) heart failure	
CVA	ICD-10	I120	Hypertensive renal disease with renal failure	
CVA	ICD-10	I129	Hypertensive renal disease without renal failure	
CVA	ICD-10	I130	Hypertensive heart and renal disease with (congestive) heart failure	
CVA	ICD-10	I131	Hypertensive heart and renal disease with renal failure	
CVA	ICD-10	I132	Hypertensive heart and renal disease with both (congestive) heart failure and renal failure	
CVA	ICD-10	I139	Hypertensive heart and renal disease, unspecified	
CVA	ICD-10	I150	Renovascular hypertension	
CVA	ICD-10	I151	Hypertension secondary to other renal disorders	
CVA	ICD-10	I152	Hypertension secondary to endocrine disorders	
CVA	ICD-10	I158	Other secondary hypertension	
CVA	ICD-10	I159	Secondary hypertension, unspecified	
CVA	Read v2	G65..	Transient cerebral ischaemia	
CVA	Read v2	G66..	Stroke/CVA unspecified	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
CVA	Read v2	662M.	Stroke monitoring	
CVA	Read v2	9Omo.	Stroke/TIA monitor 1st letter	
CVA	Read v2	662e.	Stroke/CVA annual review	
CVA	Read v2	G6...	[X]Cerebrovascular diseases	
CVA	Read v2	Gyu6.	[X]Cerebrovascular diseases	
CVA	Read v2	9h21.	Except stroke qual ind: Pt uns	
CVA	Read v2	G64..	Cerebral arterial occlusion	
CVA	Read v2	14A7.	H/O: CVA/stroke	
CVA	Read v2	9h22.	Exc stroke qual ind: Infor dis	
CVA	Read v2	8HBJ.	Stroke / TIA referral	
CVA	Read v2	9Om1.	Stroke/TIA monitor 2nd letter	
CVA	Read v2	8HTQ.	Referral to stroke clinic	
CVA	Read v2	G64z.	Cerebral infarction NOS	
CVA	Read v2	9Nop.	Seen in stroke clinic	
CVA	Read v2	14AB.	H/O: TIA	
CVA	Read v2	9N4X.	Did not attend stroke clinic	
CVA	Read v2	9Om2.	Stroke/TIA monitor 3rd letter	
CVA	Read v2	G667.	Left sided CVA	
CVA	Read v2	388I.	Stroke risk	
CVA	Read v2	9h2..	Except report: stroke qual ind	
CVA	Read v2	G668.	Right sided CVA	
CVA	Read v2	G65z.	Transient cerebral ischaem.NOS	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
CVA	Read v2	G65zz	Transient cerebral ischaem.NOS	
CVA	Read v2	9Om..	Stroke/TIA monitoring admin	
CVA	Read v2	1JA1.	Suspect cerebrovasculr disease	
CVA	Read v2	9Om4.	Stroke/TIA monitr phone invite	
CVA	Read v2	9Om3.	Stroke/TIA monitor verb invit	
CVA	Read v2	G6z..	Cerebrovascular disease NOS	
CVA	Read v2	G64z2	Left sided cerebral infarction	
CVA	Read v2	G640.	Cerebral thrombosis	
CVA	Read v2	6F...	Stroke prevention	
CVA	Read v2	G64z3	Right sided cerebral infarct	
CVA	Read v2	G63y0	Cerebr infct/throm/precere art	
CVA	Read v2	G6711	Chronic cerebral ischaemia	
CVA	Read v2	G663.	Brain stem stroke syndrome	
CVA	Read v2	G641.	Cerebral embolism	
CVA	Read v2	G664.	Cerebellar stroke syndrome	
CVA	Read v2	G67..	Other cerebrovascular disease	
CVA	Read v2	7A252	Embolisation cerebral art NEC	
CVA	Read v2	Gyu64	[X]Other cerebral infarction	
CVA	Read v2	G670.	Cerebral atherosclerosis	
CVA	Read v2	1JK..	Suspected TIA	
CVA	Read v2	G660.	Middle cerebral artery syndrm	
CVA	Read v2	7A250	PC TL embolisation cerebr art	

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Defined	System	Code	Description	Notes
CVA	Read v2	1477.	H/O: cerebrovascular disease	
CVA	Read v2	G6400	Cerebr infct/throm/cerebrl art	
CVA	Read v2	G65y.	Other transient cerebral isch.	
CVA	Read v2	1JA10	Suspct cerebrovasclar accident	
CVA	Read v2	G6y..	Cerebrovascular disease OS	
CVA	Read v2	Fyu55	[X]Oth cerebral TIA's+rel synd	
CVA	Read v2	G63y1	Cerebr infct/embol/precere art	
CVA	Read v2	G63..	Precerebral arterial occlusion	
CVA	Read v2	G68X.	Seql/strok,n spc/h'm,infarc	
CVA	Read v2	G65z1	Intermittent CVA	
CVA	Read v2	38DM.	ABCD2 stroke risk score	
CVA	Read v2	G68..	Cerebrovasc.dis.-late effects	
CVA	Read v2	G6410	Cerebr infct/embol/cerebrl art	
CVA	Read v2	G661.	Anterior cerebral artery syn	
CVA	Read v2	G67z.	Other cerebrovasc.disease NOS	
CVA	Read v2	14AK.	H/O: Stroke in last year	
CVA	Read v2	7A246	Open embolisation cerebral art	
CVA	Read v2	G63z.	Precerebral artery occlus. NOS	
CVA	Read v2	G683.	Sequelae/cerebral infarction	
CVA	Read v2	G63y.	Other precerebral artery occl.	
CVA	Read v2	8HHM.	Ref to stroke func improv serv	
CVA	Read v2	1M4..	Central post-stroke pain	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
CVA	Read v2	Gyu66	[X]Oc+sten/o cerebral arteries	
CVA	Read v2	7A244	Open embolectomy cerebral art	
CVA	Read v2	G65z0	Impending CVA	
CVA	Read v2	Gyu65	[X]Oc+steno/o precerebral artr	
CVA	Read v2	G654.	Multi+bilat precerebrl art syn	
CVA	Read v2	Gyu67	[X]Other spcfd cerebrovasc dis	
CVA	Read v2	Gyu6A	[X]Oth cerebrovasc diso/dis CE	
Beta-blocker	Read v2	G65..	Transient cerebral ischaemia	Antihypertensive
Beta-blocker	Read v2	G66..	Stroke/CVA unspecified	Antihypertensive
Beta-blocker	Read v2	662M.	Stroke monitoring	Antihypertensive
Beta-blocker	Read v2	9Om0.	Stroke/TIA monitor 1st letter	Antihypertensive
Beta-blocker	Read v2	662e.	Stroke/CVA annual review	Antihypertensive
Beta-blocker	Read v2	G6...	[X]Cerebrovascular diseases	Antihypertensive
Beta-blocker	Read v2	Gyu6.	[X]Cerebrovascular diseases	Antihypertensive
Beta-blocker	Read v2	9h21.	Except stroke qual ind: Pt uns	Antihypertensive
Beta-blocker	Read v2	G64..	Cerebral arterial occlusion	Antihypertensive
Beta-blocker	Read v2	14A7.	H/O: CVA/stroke	Antihypertensive
Beta-blocker	Read v2	9h22.	Exc stroke qual ind: Infor dis	Antihypertensive
Beta-blocker	Read v2	8HBJ.	Stroke / TIA referral	Antihypertensive
Beta-blocker	Read v2	9Om1.	Stroke/TIA monitor 2nd letter	Antihypertensive
Beta-blocker	Read v2	8HTQ.	Referral to stroke clinic	Antihypertensive
Beta-blocker	Read v2	G64z.	Cerebral infarction NOS	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Beta-blocker	Read v2	9N0p.	Seen in stroke clinic	Antihypertensive
Beta-blocker	Read v2	14AB.	H/O: TIA	Antihypertensive
Beta-blocker	Read v2	9N4X.	Did not attend stroke clinic	Antihypertensive
Beta-blocker	Read v2	9Om2.	Stroke/TIA monitor 3rd letter	Antihypertensive
Beta-blocker	Read v2	G667.	Left sided CVA	Antihypertensive
Beta-blocker	Read v2	388I.	Stroke risk	Antihypertensive
Beta-blocker	Read v2	9h2..	Except report: stroke qual ind	Antihypertensive
Beta-blocker	Read v2	G668.	Right sided CVA	Antihypertensive
Beta-blocker	Read v2	G65z.	Transient cerebral ischaem.NOS	Antihypertensive
Beta-blocker	Read v2	G65zz	Transient cerebral ischaem.NOS	Antihypertensive
Beta-blocker	Read v2	9Om..	Stroke/TIA monitoring admin	Antihypertensive
Beta-blocker	Read v2	1JA1.	Suspect cerebrovasculr disease	Antihypertensive
Beta-blocker	Read v2	9Om4.	Stroke/TIA monitr phone invite	Antihypertensive
Beta-blocker	Read v2	9Om3.	Stroke/TIA monitor verb invit	Antihypertensive
Beta-blocker	Read v2	G6z..	Cerebrovascular disease NOS	Antihypertensive
Beta-blocker	Read v2	G64z2	Left sided cerebral infarction	Antihypertensive
Beta-blocker	Read v2	G640.	Cerebral thrombosis	Antihypertensive
Beta-blocker	Read v2	6F...	Stroke prevention	Antihypertensive
Beta-blocker	Read v2	G64z3	Right sided cerebral infarct	Antihypertensive
Beta-blocker	Read v2	G63y0	Cerebr infct/throm/precere art	Antihypertensive
Beta-blocker	Read v2	G6711	Chronic cerebral ischaemia	Antihypertensive
Beta-blocker	Read v2	G663.	Brain stem stroke syndrome	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Beta-blocker	Read v2	G641.	Cerebral embolism	Antihypertensive
Beta-blocker	Read v2	G664.	Cerebellar stroke syndrome	Antihypertensive
Beta-blocker	Read v2	G67..	Other cerebrovascular disease	Antihypertensive
Beta-blocker	Read v2	7A252	Embolisation cerebral art NEC	Antihypertensive
Beta-blocker	Read v2	Gyu64	[X]Other cerebral infarction	Antihypertensive
Beta-blocker	Read v2	G670.	Cerebral atherosclerosis	Antihypertensive
Beta-blocker	Read v2	1JK..	Suspected TIA	Antihypertensive
Beta-blocker	Read v2	G660.	Middle cerebral artery syndrm	Antihypertensive
Beta-blocker	Read v2	7A250	PC TL embolisation cerebr art	Antihypertensive
Beta-blocker	Read v2	1477.	H/O: cerebrovascular disease	Antihypertensive
Beta-blocker	Read v2	G6400	Cerebr infct/throm/cerebrl art	Antihypertensive
Beta-blocker	Read v2	G65y.	Other transient cerebral isch.	Antihypertensive
Beta-blocker	Read v2	1JA10	Suspct cerebrovasclar accident	Antihypertensive
Beta-blocker	Read v2	G6y..	Cerebrovascular disease OS	Antihypertensive
Beta-blocker	Read v2	Fyu55	[X]Oth cerebral TIA's+rel synd	Antihypertensive
Beta-blocker	Read v2	G63y1	Cerebr infct/embol/precere art	Antihypertensive
Beta-blocker	Read v2	G63..	Precerebral arterial occlusion	Antihypertensive
Beta-blocker	Read v2	G68X.	Seql/strok,n spc/h'm,infarc	Antihypertensive
Beta-blocker	Read v2	G65z1	Intermittent CVA	Antihypertensive
Beta-blocker	Read v2	38DM.	ABCD2 stroke risk score	Antihypertensive
Beta-blocker	Read v2	G68..	Cerebrovasc.dis.-late effects	Antihypertensive
Beta-blocker	Read v2	G6410	Cerebr infct/embol/cerebrl art	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Beta-blocker	Read v2	G661.	Anterior cerebral artery syn	Antihypertensive
Beta-blocker	Read v2	G67z.	Other cerebrovasc.disease NOS	Antihypertensive
Beta-blocker	Read v2	14AK.	H/O: Stroke in last year	Antihypertensive
Beta-blocker	Read v2	7A246	Open embolisation cerebral art	Antihypertensive
Beta-blocker	Read v2	G63z.	Precerebral artery occlus. NOS	Antihypertensive
Beta-blocker	Read v2	G683.	Sequelae/cerebral infarction	Antihypertensive
Beta-blocker	Read v2	G63y.	Other precerebral artery occl.	Antihypertensive
Beta-blocker	Read v2	8HHM.	Ref to stroke func improv serv	Antihypertensive
Beta-blocker	Read v2	1M4..	Central post-stroke pain	Antihypertensive
Beta-blocker	Read v2	Gyu66	[X]Oc+sten/o cerebral arteries	Antihypertensive
Beta-blocker	Read v2	7A244	Open embolectomy cerebral art	Antihypertensive
Beta-blocker	Read v2	G65z0	Impending CVA	Antihypertensive
Beta-blocker	Read v2	Gyu65	[X]Oc+steno/o precerebral artr	Antihypertensive
Beta-blocker	Read v2	G654.	Multi+bilat precerebrl art syn	Antihypertensive
Beta-blocker	Read v2	Gyu67	[X]Other spcfd cerebrovasc dis	Antihypertensive
Beta-blocker	Read v2	Gyu6A	[X]Oth cerebrovasc diso/dis CE	Antihypertensive
Clopidogrel	Read v2	bu51.	CLOPIDOGREL 75mg tablets	
Clopidogrel	Read v2	bu52.	PLAVIX 75mg tablets	
Clopidogrel	Read v2	bu54.	CLOPIDOGREL 300mg tablets	
Cholesterol	Read v2	44P..	Serum cholesterol	
Cholesterol	Read v2	44P3.	Serum cholesterol raised	
Cholesterol	Read v2	44PJ.	Serum total cholesterol level	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Cholesterol	Read v2	44P1.	Serum cholesterol normal	
Cholesterol	Read v2	44OE.	Plasma total cholesterol level	
Cholesterol	Read v2	44P2.	Serum cholesterol borderline	
Cholesterol	Read v2	44PZ.	Serum cholesterol NOS	
Cholesterol	Read v2	44PH.	Total cholesterol measurement	
Cholesterol	Read v2	44P4.	Serum cholesterol very high	
Cholesterol	Read v2	44P9.	Serum cholesterol studies	
Cholesterol	Read v2	44PK.	Serum fastng total cholesterol	
Cholesterol	Read v2	662a.	Pre-treatmnt serum cholest lev	
BMI	Read v2	22K..	Body Mass Index	
BMI	Read v2	22K5.	Body mass index 30+ - obesity	
BMI	Read v2	22K1.	Body Mass Index normal K/M2	
BMI	Read v2	22K2.	Body Mass Index high K/M2	
BMI	Read v2	22K4.	BMI 25-29 - overweight	
BMI	Read v2	22K8.	Body mass index 20-24 - normal	
BMI	Read v2	22K7.	BMI 40+ - severely obese	
BMI	Read v2	22K3.	Body Mass Index low K/M2	
BMI	Read v2	22K6.	Body mass index less than 20	
Blood pressure measurement	Read v2	246..	O/E - blood pressure	
Blood pressure measurement	Read v2	2464.	O/E - BP reading normal	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Blood pressure measurement	Read v2	2466.	O/E - BP reading raised	
Blood pressure measurement	Read v2	2469.	O/E - Systolic BP reading	
Blood pressure measurement	Read v2	662L.	24 hr blood pressure monitor.	
Blood pressure measurement	Read v2	2465.	O/E - BP borderline raised	
Blood pressure measurement	Read v2	246E.	Sitting blood pressure reading	
Blood pressure measurement	Read v2	246Z.	O/E-blood pressure reading NOS	
Blood pressure measurement	Read v2	246M.	White coat hypertension	
Blood pressure measurement	Read v2	246D.	Standing blood pressure reading	
Blood pressure measurement	Read v2	246W.	Ave 24h systol blood pressure	
Blood pressure measurement	Read v2	246Y.	Average day interval systolic blood pressure	
Blood pressure measurement	Read v2	246b.	Average night interval systolic blood pressure	
Blood pressure measurement	Read v2	2467.	O/E - BP reading very high	
Blood pressure measurement	Read v2	2462.	O/E - BP reading low	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Blood pressure measurement	Read v2	246N.	Standing systolic blood pressure	
Blood pressure measurement	Read v2	246C.	Lying blood pressure reading	
Blood pressure measurement	Read v2	246F.	O/E - blood pressure decreased	
Blood pressure measurement	Read v2	246V.	Ave 24h diastol blood pressure	
Blood pressure measurement	Read v2	2463.	O/E - BP borderline low	
Blood pressure measurement	Read v2	246Q.	Sitting systolic blood pressure	
Blood pressure measurement	Read v2	246X.	Ave day diastol blood pressure	
Blood pressure measurement	Read v2	246a.	Ave night diast blood pressure	
Blood pressure measurement	Read v2	246S.	Lying systolic blood pressure	
Blood pressure measurement	Read v2	246T.	Lying diastolic blood pressure	
HDL reading	Read v2	44P5.	Serum HDL cholesterol level	
HDL reading	Read v2	44PB.	Serum fast HDL cholesterol lev	
HDL reading	Read v2	44PC.	Ser random HDL cholesterol lev	
HDL reading	Read v2	44d3.	Plasma fast HDL cholest level	
HDL reading	Read v2	44R3.	Lipoprotein electroph. - HDL	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
HDL reading	Read v2	44dA.	Plasma HDL cholesterol level	
HDL reading	Read v2	44d2.	Plasma rndm HDL cholest level	
Cholesterol HDL ratio reading	Read v2	44lF.	Serum cholesterol/HDL ratio	
Cholesterol HDL ratio reading	Read v2	44PF.	Total cholesterol:HDL ratio	
Cholesterol HDL ratio reading	Read v2	44l2.	Cholesterol/HDL ratio	
Cholesterol HDL ratio reading	Read v2	44lG.	Plasma cholesterol/HDL ratio	
Calcium channel blocker	Read v2	blb1.	AMLODIPINE 5mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	blb2.	AMLODIPINE 10mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8i.	ADALAT LA 30mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8j.	ADALAT LA 60mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	blh1.	LERCANIDIPINE HCL 10mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8M.	ADALAT LA 20mg m/r tablets	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Calcium channel blocker	Read v2	bl5Z.	TILDIEM LA 200mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl83.	ADALAT RETARD 20mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	ble2.	LACIDIPINE 4mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl84.	ADALAT RETARD 10mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3k.	SECURON SR 240mg m/r tabs 28CP	Antihypertensive only
Calcium channel blocker	Read v2	ble1.	LACIDIPINE 2mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5I.	ADIZEM-XL 240mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl5A.	TILDIEM LA 300mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl8A.	ADIPINE MR 20 m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl58.	TILDIEM RETARD 90mg m/r tabs	Antihypertensive only
Calcium channel blocker	Read v2	blb3.	ISTIN 5mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5K.	ADIZEM-XL 120mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb3j.	SECURON SR 240mg m/r tablets	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Calcium channel blocker	Read v2	bl8z.	NIFEDIPINE 20mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb31.	VERAPAMIL 40mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5E.	ADIZEM-XL 300mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl8B.	ADIPINE MR 10 m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5J.	ADIZEM-XL 180mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl5B.	ADIZEM-SR 90mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl59.	TILDIEM RETARD 120mg m/r tabs	Antihypertensive only
Calcium channel blocker	Read v2	bl86.	NIFEDIPINE 10mg capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl51.	TILDIEM 60mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5R.	ANGITIL SR 90 m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl8e.	CORACTEN SR 20mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb3A.	VERAPAMIL 240mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8X.	CORACTEN XL 30mg m/r capsules	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Calcium channel blocker	Read v2	bl85.	NIFEDIPINE 5mg capsules	Antihypertensive only
Calcium channel blocker	Read v2	blb4.	ISTIN 10mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8w.	NIFEDIPINE 10mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5Q.	SLOZEM 240mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl8k.	CORACTEN SR 10mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb32.	VERAPAMIL 80mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5C.	ADIZEM-SR 120mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb33.	VERAPAMIL 120mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5F.	DILZEM SR 60mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl5S.	ANGITIL SR 120 m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb3F.	HALF-SECURON SR 120mg 28CP	Antihypertensive only
Calcium channel blocker	Read v2	blh3.	LERCANIDIPINE HCl 20mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3y.	VERAPAMIL 240mg m/r capsules	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Calcium channel blocker	Read v2	bl8Y.	CORACTEN XL 60mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl5D.	ADIZEM-SR 180mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl5G.	DILZEM SR 90mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl82.	ADALAT 10mg capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb3s.	VERTAB SR 240 m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5O.	SLOZEM 120mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	ble3.	MOTENS 2mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5P.	SLOZEM 180mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl8u.	NIFEDIPINE 10mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl8v.	NIFEDIPINE 20mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	ble4.	MOTENS 4mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3n.	UNIVER 240mg m/r capsules x28	Antihypertensive only
Calcium channel blocker	Read v2	bl5M.	DILZEM-XL 180mg m/r capsules	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Calcium channel blocker	Read v2	bl5U.	ANGITIL SR 180 m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl5L.	DILZEM-XL 120mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl81.	ADALAT 5mg capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb3C.	VERAPAMIL 120mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl7y.	NICARDIPINE 20mg capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb3l.	UNIVER 120mg m/r capsules x28	Antihypertensive only
Calcium channel blocker	Read v2	bl54.	ADIZEM-SR 120mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl7z.	NICARDIPINE 30mg capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl5x.	ANGITIL XL 240 m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	blh2.	ZANIDIP 10mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5N.	DILZEM-XL 240mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb3v.	VERAPAMIL 120mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl5h.	DILTIAZEM HCL 200mg m/r caps	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Calcium channel blocker	Read v2	bb3B.	HALF SECURON SR 120mg m/r tabs	Antihypertensive only
Calcium channel blocker	Read v2	bl5y.	ANGITIL XL 300 m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl55.	DILTIAZEM HCL 120mg m/r tabs	Antihypertensive only
Calcium channel blocker	Read v2	bl71.	CARDENE 20mg capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl7x.	NICARDIPINE 30mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl8L.	FORTIPINE LA40 m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3w.	VERAPAMIL 160mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl5t.	VIAZEM XL 360mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bb3m.	UNIVER 180mg m/r capsules x56	Antihypertensive only
Calcium channel blocker	Read v2	bl5V.	CALCICARD CR 90mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3g.	*SECURON 120mg tablets 56CP	Antihypertensive only
Calcium channel blocker	Read v2	bl73.	CARDENE SR 30mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl7w.	NICARDIPINE 45mg m/r capsules	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Calcium channel blocker	Read v2	bl72.	CARDENE 30mg capsules	Antihypertensive only
Calcium channel blocker	Read v2	bla1.	ISRADIPINE 2.5mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3z.	VERAPAMIL 180mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl8h.	*NIFENSAR XL 20mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bla2.	PRESCAL 2.5mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl74.	CARDENE SR 45mg m/r capsules	Antihypertensive only
Calcium channel blocker	Read v2	bl5W.	CALCICARD CR 120mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8S.	NIFEDIPRESS MR 10 m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8F.	NIFEDIPINE 40mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb39.	*CORDILOX 80mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb38.	*CORDILOX 40mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3D.	VERAPAMIL 40mg/5mL s/f soln	Antihypertensive only
Calcium channel blocker	Read v2	bl57.	*ADIZEM 60mg tablets	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Calcium channel blocker	Read v2	bb3e.	*SECURON 80mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	blh4.	ZANIDIP 20mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8P.	*ANGIOPINE MR 10mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8t.	*NIFOPRESS RETRD 20mg m/r tabs	Antihypertensive only
Calcium channel blocker	Read v2	bl8D.	*NIMODREL MR 10 m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8q.	HYPOLAR RETARD 20 m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl53.	*BRITIAZIM 60mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3Q.	VERA-TIL SR 120mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3P.	VERA-TIL SR 240mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	dt13.	NIMODIPINE 30mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	blb5.	AMLOSTIN 5mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3i.	*SECURON 160mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3x.	*VERPAMIL HCL 120mg tabs x56	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Calcium channel blocker	Read v2	blb6.	AMLOSTIN 10mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8C.	*UNIPINE XL 30mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl56.	*ANGIOZEM 60mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	dt14.	NIMOTOP 30mg tablets	Antihypertensive only
Calcium channel blocker	Read v2	bl8R.	*GENALAT RETARD 20mg m/r tabs	Antihypertensive only
Calcium channel blocker	Read v2	bl8G.	*ANGIOPINE 40 LA m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb30.	SECURON IV 5mg/2mL injection	Antihypertensive only
Calcium channel blocker	Read v2	bl8O.	*SLOFEDIPINE 20mg m/r tablets	Antihypertensive only
Calcium channel blocker	Read v2	bb3h.	*SECURON 160mg tablets 56CP	Antihypertensive only
Calcium channel blocker	Read v2	bl52.	*CALCICARD 60mg tablets	Antihypertensive only
ACE inhibitor	Read v2	bi67.	RAMIPRIL 10mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi63.	RAMIPRIL 5mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi62.	RAMIPRIL 2.5mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi34.	LISINOPRIL 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi33.	LISINOPRIL 10mg tablets	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bi52.	PERINDOPRIL ERBUMINE 4mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi32.	LISINOPRIL 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi51.	PERINDOPRIL ERBUMINE 2mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk42.	VALSARTAN 80mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi61.	RAMIPRIL 1.25mg capsules	Antihypertensive
ACE inhibitor	Read v2	bk32.	LOSARTAN POTASSIUM 50mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi57.	PERINDOPRIL ERBUMINE 8mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi31.	LISINOPRIL 2.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk43.	VALSARTAN 160mg capsules	Antihypertensive
ACE inhibitor	Read v2	bk52.	IRBESARTAN 150mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk37.	LOSARTAN POTASSIUM 100mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi2z.	ENALAPRIL MAL 20mg tabs x28	Antihypertensive
ACE inhibitor	Read v2	bk53.	IRBESARTAN 300mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk73.	CANDESARTAN CILEXETIL 8mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi2x.	ENALAPRIL MAL 10mg tabs x28	Antihypertensive
ACE inhibitor	Read v2	bk41.	VALSARTAN 40mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi2y.	ENALAPRIL MALEATE 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk31.	LOSARTAN POTASSIUM 25mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi2v.	ENALAPRIL MALEATE 5mg tabs x28	Antihypertensive
ACE inhibitor	Read v2	bk72.	CANDESARTAN CILEXETIL 4mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi2w.	ENALAPRIL MALEATE 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk74.	CANDESARTAN CILEXET 16mg tabs	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bk51.	IRBESARTAN 75mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi93.	TRANDOLAPRIL 2mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi2u.	ENALAPRIL MALEATE 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi72.	FOSINOPRIL 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1v.	CAPTOPRIL 12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi6D.	RAMIPRIL 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi2t.	ENALAPRIL MALEATE 2.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi6E.	RAMIPRIL 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk81.	TELMISARTAN 40mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1x.	CAPTOPRIL 25mg tablets x56	Antihypertensive
ACE inhibitor	Read v2	bi6C.	RAMIPRIL 2.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1z.	CAPTOPRIL 50mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1w.	CAPTOPRIL 25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk82.	TELMISARTAN 80mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi43.	QUINAPRIL 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi54.	*COVERSYL 4mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi71.	FOSINOPRIL 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkB2.	OLMESARTAN MEDOXOMIL 20mg tabs	Antihypertensive
ACE inhibitor	Read v2	bkB1.	OLMESARTAN MEDOXOMIL 10mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi3p.	LISINO+HYDROCHL 20/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi42.	QUINAPRIL 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi4A.	QUINAPRIL 40mg tablets	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bk71.	CANDESARTAN CILEXETIL 2mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi92.	TRANDOLAPRIL 1mg capsules	Antihypertensive
ACE inhibitor	Read v2	bk45.	DIOVAN 80mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi3h.	ZESTRIL 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk9z.	EPROSARTAN 600mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk8z.	TELMISARTAN 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1y.	CAPTOPRIL 50mg tablets x56	Antihypertensive
ACE inhibitor	Read v2	bi53.	*COVERSYL 2mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi3f.	ZESTRIL 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi3j.	ZESTRIL 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi3t.	LISINO+HYDROCHL 10/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk34.	COZAAR 50mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk7z.	CANDESARTAN CILEXETL 32mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi55.	*PERIND ERB+INDAP 4/1.25mg tab	Antihypertensive
ACE inhibitor	Read v2	bi6B.	RAMIPRIL 1.25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi41.	QUINAPRIL 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkB3.	OLMESARTAN MEDOXOMIL 40mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi25.	INNOVACE 10mg tablets x28	Antihypertensive
ACE inhibitor	Read v2	bi3n.	ZESTORETIC 20/12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk9y.	EPROSARTAN 400mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk35.	LOSART+HYDROCHLTHZ 50/12.5 tab	Antihypertensive
ACE inhibitor	Read v2	bi27.	INNOVACE 20mg tablets x28	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bk5y.	IRBES+HYDROCHL 300/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk46.	DIOVAN 160mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi9z.	TRANDOLAPRIL 4mg capsules	Antihypertensive
ACE inhibitor	Read v2	bk36.	COZAAR-COMP 50mg/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk9x.	EPROSARTAN 300mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1c.	*CAPOZIDE 50mg tablets x28	Antihypertensive
ACE inhibitor	Read v2	bk5z.	IRBES+HYDROCHL 150/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk55.	APROVEL 150mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi91.	TRANDOLAPRIL 500mcg capsules	Antihypertensive
ACE inhibitor	Read v2	bi3g.	ZESTRIL 10mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bi23.	INNOVACE 5mg tablets x28	Antihypertensive
ACE inhibitor	Read v2	bi3e.	ZESTRIL 5mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bi3d.	ZESTRIL 2.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi74.	*STARIL 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk4w.	VALSARTAN 40mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi73.	*STARIL 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi24.	INNOVACE 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi56.	*COVERSYL PLUS 4mg/1.25mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk58.	COAPROVEL 300mg/12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi96.	GOPTEN 2mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi26.	INNOVACE 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi22.	INNOVACE 5mg tablets	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bi18.	CAPOTEN 25mg tablets x56	Antihypertensive
ACE inhibitor	Read v2	bi16.	*CAPOTEN 12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi28.	INNOZIDE 20/12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk44.	DIOVAN 40mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi17.	CAPOTEN 25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi45.	ACCUPRO 10mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bk4z.	VALSRT+HYDROCHL 160/12.5mg tab	Antihypertensive
ACE inhibitor	Read v2	bi3i.	ZESTRIL 20mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bk8y.	TELMIS+HYDROCHL 80/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi69.	*RAMIPRIL 2.5mg+5mg+10mg caps	Antihypertensive
ACE inhibitor	Read v2	bi66.	*TRITACE 5mg capsules	Antihypertensive
ACE inhibitor	Read v2	bk3z.	LOSART+HYDROCHLTHZ 100/25 tabs	Antihypertensive
ACE inhibitor	Read v2	bi1G.	*CO-ZIDOCAPT 50mg/25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk56.	APROVEL 300mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk4x.	VALSART+HYDROCHL 80/12.5mg tab	Antihypertensive
ACE inhibitor	Read v2	bk77.	AMIAS 8mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1a.	CAPOTEN 50mg tablets x56	Antihypertensive
ACE inhibitor	Read v2	bi44.	ACCUPRO 5mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bk57.	COAPROVEL 150mg/12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi46.	ACCUPRO 20mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bi1s.	CAPOZIDE 50mg/25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk54.	APROVEL 75mg tablets	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bk76.	AMIAS 4mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi2b.	ENALAP+HYDROCHL 20/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi65.	*TRITACE 2.5mg capsules	Antihypertensive
ACE inhibitor	Read v2	biC8.	PERIND ARG+INDAP 5/1.25mg tabs	Antihypertensive
ACE inhibitor	Read v2	biBz.	IMIDAPRIL HCL 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi3s.	ZESTORETIC 10/12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk4y.	VALSART+HYDROCHL 160/25mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk33.	COZAAR HALF-STRENGTH 25mg tabs	Antihypertensive
ACE inhibitor	Read v2	bkB4.	OLMETEC 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi3m.	*ZESTORETIC tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bk8x.	TELMIS+HYDROCHL 40/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi21.	INNOVACE 2.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi39.	*CARACE 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi95.	GOPTEN 1mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi3k.	CARACE 20 PLUS tablets	Antihypertensive
ACE inhibitor	Read v2	bk83.	MICARDIS 40mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk78.	AMIAS 16mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk87.	MICARDISPLUS 80mg/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi47.	ACCURETIC tablets	Antihypertensive
ACE inhibitor	Read v2	bi3b.	*CARACE 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi3q.	*ZESTRIL 2.5mg starter pack	Antihypertensive
ACE inhibitor	Read v2	bi64.	*TRITACE 1.25mg capsules	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bk38.	COZAAR 100mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi49.	ACCUPRO 40mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi35.	*CARACE 2.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi8a.	CILAZAPRIL 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi38.	*CARACE 10mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bk4v.	VALSARTAN 320mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi19.	CAPOTEN 50mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi3c.	ZESTRIL 2.5mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bi36.	*CARACE 5mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bkD1.	AMLODIPNE+VALSARTN 5/80mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi68.	*TRITACE 10mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi37.	*CARACE 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkFy.	ALISKIREN 300mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi58.	*COVERSYL 8mg tablets	Antihypertensive
ACE inhibitor	Read v2	biBy.	IMIDAPRIL HCL 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk62.	TARKA 2mg/180mg m/r capsules	Antihypertensive
ACE inhibitor	Read v2	bi3a.	*CARACE 20mg tablets 28CP	Antihypertensive
ACE inhibitor	Read v2	bk84.	MICARDIS 80mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk93.	TEVETEN 600mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi3l.	CARACE 10 PLUS tablets	Antihypertensive
ACE inhibitor	Read v2	bk47.	CO-DIOVAN 160mg/12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk49.	CO-DIOVAN 80mg/12.5mg tablets	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bA1z.	FELODIPINE+RAMIPRIL 5/5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bkD2.	AMLODPNE+VALSARTN 5/160mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi13.	ACEPRIL 25mg tablets x56	Antihypertensive
ACE inhibitor	Read v2	bkB5.	OLMETEC 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi2a.	*ENALAPRIL MAL tabs titre pack	Antihypertensive
ACE inhibitor	Read v2	bi15.	ACEPRIL 50mg tablets x56	Antihypertensive
ACE inhibitor	Read v2	bi6x.	TRITACE 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bA12.	TRIAPIN 5mg/5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk86.	MICARDISPLUS 40mg/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bkCz.	OLMESAR+HYDROCH 20/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi6w.	TRITACE 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkD3.	AMLODPNE+VALSRTN 10/160mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi6y.	TRITACE 2.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	biBx.	IMIDAPRIL HCL 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi3r.	*LISINOPRIL 2.5mg tabs starter	Antihypertensive
ACE inhibitor	Read v2	bk75.	AMIAS 2mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk3C.	LOSARTAN POTASSIUM 12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi11.	ACEPRIL 12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi82.	CILAZAPRIL 500mcg tablets	Antihypertensive
ACE inhibitor	Read v2	bi94.	GOPTEN 500micrograms capsules	Antihypertensive
ACE inhibitor	Read v2	bk39.	COZAAR-COMP 100mg/25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi89.	VASCACE 5mg tablets	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bk48.	CO-DIOVAN 160mg/25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk85.	MICARDIS 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi88.	VASCACE 2.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	biC7.	COVRSYL ARGIN PLS 5/1.25mg tab	Antihypertensive
ACE inhibitor	Read v2	bi48.	QUINAPRIL+HYDROCHLOROTHIAZIDE	Antihypertensive
ACE inhibitor	Read v2	bi1d.	CAPOZIDE LS 25mg tablets x28CP	Antihypertensive
ACE inhibitor	Read v2	biC2.	PERINDOPRIL ARGININE 2.5mg tab	Antihypertensive
ACE inhibitor	Read v2	biC4.	PERINDOPRIL ARGININE 5mg tabs	Antihypertensive
ACE inhibitor	Read v2	biC6.	PERINDOPRIL ARGININE 10mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi1b.	ACEZIDE 50mg tablets x56	Antihypertensive
ACE inhibitor	Read v2	bi87.	VASCACE 1mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkDx.	EXFORGE 10mg/160mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi84.	CILAZAPRIL 2.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk3y.	LOSART+HYDRCHL 100/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi6A.	*TRITACE Titration Pack caps	Antihypertensive
ACE inhibitor	Read v2	bA1y.	FELODIP+RAMIPRL 2.5/2.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	biA1.	MOEXIPRIL HCL 7.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk91.	TEVETEN 300mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1f.	CAPTOP+HYDROCHL 50/25mg tabs	Antihypertensive
ACE inhibitor	Read v2	bkDy.	EXFORGE 5mg/160mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi12.	ACEPRIL 25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi6F.	RAMIPRIL 2.5+5+10mg tabs pack	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bk5x.	IRBES+HYDROCHL 300mg/25mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk92.	TEVETEN 400mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkDz.	EXFORGE 5mg/80mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi6z.	TRITACE 1.25mg tablets	Antihypertensive
ACE inhibitor	Read v2	biB1.	TANATRIL 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkCy.	OLMESART+HYDROCHL 20/25mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi83.	CILAZAPRIL 1mg tablets	Antihypertensive
ACE inhibitor	Read v2	biB2.	TANATRIL 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk61.	TRANDOL+VERAP 2/180mg m/r caps	Antihypertensive
ACE inhibitor	Read v2	bi86.	VASCACE 500micrograms tablets	Antihypertensive
ACE inhibitor	Read v2	biA3.	PERDIX 7.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi14.	ACEPRIL 50mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkB6.	OLMETEC 40mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkC1.	OLMETEC PLUS 20mg/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk8w.	TELMIS+HYDROCHL 80mg/25mg tabs	Antihypertensive
ACE inhibitor	Read v2	biA2.	MOEXIPRIL HCL 15mg tablets	Antihypertensive
ACE inhibitor	Read v2	biC3.	COVERSYL ARGININE 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk4A.	DIOVAN 40mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi9A.	GOPTEN 4mg capsules	Antihypertensive
ACE inhibitor	Read v2	bkHz.	OLMESART+AMLODIPNE 20/5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk59.	COAPROVEL 300mg/25mg tablets	Antihypertensive
ACE inhibitor	Read v2	biC5.	COVERSYL ARGININE 10mg tablets	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bkHy.	OLMESART+AMLODIPNE 40/5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bA11.	TRIAPIN MITE 2.5mg/2.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	biA4.	PERDIX 15mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1p.	*TENSOPRIL 12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk3A.	COZAAR-COMP 100mg/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi6o.	TRITACE Titration Pack tablets	Antihypertensive
ACE inhibitor	Read v2	bkHx.	OLMESART+AMLODIPN 40/10mg tabs	Antihypertensive
ACE inhibitor	Read v2	bk79.	AMIAS 32mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi6v.	*LOPACE 10mg capsules	Antihypertensive
ACE inhibitor	Read v2	bkH3.	SEVIKAR 40mg/10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk88.	MICARDISPLUS 80mg/25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi2F.	*INNOVACE MELT 5mg wafer	Antihypertensive
ACE inhibitor	Read v2	bi2G.	*INNOVACE MELT 10mg wafer	Antihypertensive
ACE inhibitor	Read v2	bkH2.	SEVIKAR 40mg/5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkH1.	SEVIKAR 20mg/5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkC3.	OLMETEC PLUS 40mg/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi2D.	*ENALAPRIL MALEATE 20mg wafer	Antihypertensive
ACE inhibitor	Read v2	biC1.	COVERSYL ARGININE 2.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi2L.	*PRALENAL 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi81.	*CILAZAPRIL 250mcg tablets	Antihypertensive
ACE inhibitor	Read v2	bi2E.	*INNOVACE MELT 2.5mg wafer	Antihypertensive
ACE inhibitor	Read v2	bi6u.	*LOPACE 5mg capsules	Antihypertensive

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
ACE inhibitor	Read v2	bi29.	*INNOVACE tabs titration pack	Antihypertensive
ACE inhibitor	Read v2	bi2M.	*PRALENAL 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi2C.	*ENALAPRIL MALEATE 10mg wafer	Antihypertensive
ACE inhibitor	Read v2	bi1q.	*TENSOPRIL 25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkCx.	OLMESAR+HYDROCH 40/12.5mg tabs	Antihypertensive
ACE inhibitor	Read v2	bi4D.	QUINIL 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	biB3.	TANATRIL 20mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1k.	*KAPLON 25mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi1j.	*KAPLON 12.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi2K.	*PRALENAL 5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bi6t.	*LOPACE 2.5mg capsules	Antihypertensive
ACE inhibitor	Read v2	bi2J.	*PRALENAL 2.5mg tablets	Antihypertensive
ACE inhibitor	Read v2	bkGy.	AMBRISENTAN 10mg tablets	Antihypertensive
ACE inhibitor	Read v2	bk3E.	LOSARTAN POTASS 2.5mg/mL susp	Antihypertensive
ACE inhibitor	Read v2	bkGz.	AMBRISENTAN 5mg tablets	Antihypertensive
Thiazide diuretic	Read v2	b211.	BENDROFLUMETHIAZIDE 2.5mg tabs	Antihypertensive only
Thiazide diuretic	Read v2	b212.	BENDROFLUMETHIAZIDE 5mg tablet	Antihypertensive only
Thiazide diuretic	Read v2	b28z.	INDAPAMIDE 2.5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b285.	INDAPAMIDE 1.5mg m/r tablets	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Thiazide diuretic	Read v2	b281.	NATRILIX 2.5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b286.	NATRILIX SR 1.5mg m/r tablets	Antihypertensive only
Thiazide diuretic	Read v2	b2bz.	METOLAZONE 5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b25z.	CYCLOPENTHIAZIDE 500mcg tabs	Antihypertensive only
Thiazide diuretic	Read v2	b23y.	CHLORTALIDONE 50mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b2d1.	DIUREXAN 20mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b2dz.	XIPAMIDE 20mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b214.	APRINOX 5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b231.	HYGROTON 50mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b251.	NAVIDREX 500micrograms tablets	Antihypertensive only
Thiazide diuretic	Read v2	b26z.	*HYDROCHLOROTHIAZIDE 25mg tabs	Antihypertensive only
Thiazide diuretic	Read v2	b213.	APRINOX 2.5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b26y.	*HYDROCHLOROTHIAZIDE 50mg tabs	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Thiazide diuretic	Read v2	b219.	NEO-NACLEX 5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b2b1.	METENIX-5 5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b283.	*NATRAMID 2.5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b2c1.	*NEPHRIL 1mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b2b2.	*XURET 500micrograms tablets	Antihypertensive only
Thiazide diuretic	Read v2	b263.	*HYDROSALURIC 25mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b216.	*BERKOZIDE 5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b232.	*HYGROTON 100mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b22y.	CHLOROTHIAZIDE 250mg/5mL susp	Antihypertensive only
Thiazide diuretic	Read v2	b291.	*BAYCARON 25mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b22z.	*CHLOROTHIAZIDE 500mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b215.	*BERKOZIDE 2.5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b221.	*SALURIC 500mg tablets	Antihypertensive only

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Thiazide diuretic	Read v2	b2cz.	*POLYTHIAZIDE 1mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b264.	*HYDROSALURIC 50mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b21A.	*NEO-BENDROMAX 2.5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b23z.	*CHLORTHALIDONE 100mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b2b3.	*METOLAZONE 500mcg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b29z.	*MEFRUSIDE 25mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b271.	*HYDRENOX 50mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b21B.	*NEO-BENDROMAX 5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b218.	*CENTYL 5mg tablets	Antihypertensive only
Thiazide diuretic	Read v2	b217.	*CENTYL 2.5mg tablets	Antihypertensive only
Aspirin	Read v2	bu23.	ASPIRIN 75mg disp tabs	
Aspirin	Read v2	bu25.	*ASPIRIN 75mg tablets	
Aspirin	Read v2	bu2B.	ASPIRIN 75mg e/c tablets	
Aspirin	Read v2	di1f.	ASPIRIN 300mg e/c tablets	
Aspirin	Read v2	di13.	*ASPIRIN 75mg disp tabs	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Aspirin	Read v2	j112.	ASPIRIN 300mg disp tablets	
Aspirin	Read v2	j111.	ASPIRIN 300mg tablets	
Aspirin	Read v2	bu2A.	NU-SEALS ASPIRIN 75mg e/c tabs	
Aspirin	Read v2	di1m.	ASPIRIN 300mg soluble tablets	
Aspirin	Read v2	bu27.	*ASPIRIN 300mg eff tabs	
Aspirin	Read v2	bu2c.	ASPIRIN 75mg soluble tablets	
Aspirin	Read v2	di1c.	NU-SEALS ASPIRIN 300mg e/ctabs	
Aspirin	Read v2	di11.	ASPIRIN [CNS] 300mg tablets	
Aspirin	Read v2	bu2F.	CAPRIN 75mg e/c tablets	
Aspirin	Read v2	bu28.	*DISPRIN CV 100mg m/r tablets	
Aspirin	Read v2	bu29.	*ASPIRIN 100mg m/r tablets	
Aspirin	Read v2	di12.	ASPIRIN [CNS] 300mg disp tabs	
Aspirin	Read v2	bu2E.	*POSTMI 75mg e/c tablets	
Aspirin	Read v2	bu2K.	MICROPIRIN 75mg e/c tablets	
Aspirin	Read v2	bu2G.	*NU-SEALS CARDIO 75 e/c tabs	
Aspirin	Read v2	di1g.	*ASPIRIN 600mg e/c tablets	
Aspirin	Read v2	bu21.	*ASPIRIN 100mg eff tabs	
Aspirin	Read v2	di1h.	*ASPIRIN 324mg e/c tablets	
Aspirin	Read v2	di1r.	DISPRIN 300mg disp tabs	
Aspirin	Read v2	bu24.	*ANGETTES 75mg tablets	
Aspirin	Read v2	di1k.	CAPRIN 300mg e/c tablets	
Aspirin	Read v2	di1e.	*PALAPRIN FORTE 600mg tablets	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Aspirin	Read v2	di1d.	*NU-SEALS ASPIRIN 600mg tabs	
Aspirin	Read v2	di1o.	ASPIRIN 150mg suppositories	
Aspirin	Read v2	di1n.	ASPIRIN 300mg suppositories	
Aspirin	Read v2	bu2H.	*ENPRIN 75mg e/c tablets	
Aspirin	Read v2	bu2I.	ASPIRIN 162.5mg m/r capsules	
Aspirin	Read v2	di14.	*ASPERGUM 227mg chewing gum	
Aspirin	Read v2	di18.	*SOLPRIN 300mg disp tabs	
CABG	OPCS	K401	SAPHENOUS VEIN GRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K402	SAPHENOUS VEIN GRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K403	SAPHENOUS VEIN GRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K404	SAPHENOUS VEIN GRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K408	SAPHENOUS VEIN GRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K409	SAPHENOUS VEIN GRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K411	OTHER AUTOGRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K412	OTHER AUTOGRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K413	OTHER AUTOGRAFT REPLACEMENT OF CORONARY ARTERY	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
CABG	OPCS	K414	OTHER AUTOGRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K419	OTHER AUTOGRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K421	ALLOGRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K423	ALLOGRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K424	ALLOGRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K429	ALLOGRAFT REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K431	PROSTHETIC REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K433	PROSTHETIC REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K434	PROSTHETIC REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K441	OTHER REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K442	OTHER REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K448	OTHER REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K449	OTHER REPLACEMENT OF CORONARY ARTERY	
CABG	OPCS	K451	CONNECTION OF THORACIC ARTERY TO CORONARY ARTERY	
CABG	OPCS	K452	CONNECTION OF THORACIC ARTERY TO CORONARY ARTERY	
CABG	OPCS	K453	CONNECTION OF THORACIC ARTERY TO CORONARY ARTERY	
CABG	OPCS	K454	CONNECTION OF THORACIC ARTERY TO CORONARY ARTERY	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
CABG	OPCS	K455	CONNECTION OF THORACIC ARTERY TO CORONARY ARTERY	
CABG	OPCS	K456	CONNECTION OF THORACIC ARTERY TO CORONARY ARTERY	
CABG	OPCS	K458	CONNECTION OF THORACIC ARTERY TO CORONARY ARTERY	
CABG	OPCS	K459	CONNECTION OF THORACIC ARTERY TO CORONARY ARTERY	
CABG	OPCS	K463	OTHER BYPASS OF CORONARY ARTERY	
CABG	OPCS	K468	OTHER BYPASS OF CORONARY ARTERY	
CABG	OPCS	K473	REPAIR OF CORONARY ARTERY	
CABG	OPCS	K475	REPAIR OF CORONARY ARTERY	
CABG	OPCS	K478	REPAIR OF CORONARY ARTERY	
CABG	OPCS	K479	REPAIR OF CORONARY ARTERY	
CABG	OPCS	K482	OTHER OPEN OPERATIONS ON CORONARY ARTERY	
CABG	OPCS	K484	OTHER OPEN OPERATIONS ON CORONARY ARTERY	
CABG	OPCS	K488	OTHER OPEN OPERATIONS ON CORONARY ARTERY	
PCI	OPCS	K491	TRANSLUMINAL BALLOON ANGIOPLASTY OF CORONARY ARTERY	
PCI	OPCS	K492	TRANSLUMINAL BALLOON ANGIOPLASTY OF CORONARY ARTERY	
PCI	OPCS	K493	TRANSLUMINAL BALLOON ANGIOPLASTY OF CORONARY ARTERY	
PCI	OPCS	K494	TRANSLUMINAL BALLOON ANGIOPLASTY OF CORONARY ARTERY	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
PCI	OPCS	K498	TRANSLUMINAL BALLOON ANGIOPLASTY OF CORONARY ARTERY	
PCI	OPCS	K499	TRANSLUMINAL BALLOON ANGIOPLASTY OF CORONARY ARTERY	
PCI	OPCS	K501	OTHER THERAPEUTIC TRANSLUMINAL OPERATIONS ON CORONARY	
PCI	OPCS	K502	OTHER THERAPEUTIC TRANSLUMINAL OPERATIONS ON CORONARY	
PCI	OPCS	K503	OTHER THERAPEUTIC TRANSLUMINAL OPERATIONS ON CORONARY	
PCI	OPCS	K508	OTHER THERAPEUTIC TRANSLUMINAL OPERATIONS ON CORONARY	
PCI	OPCS	K509	OTHER THERAPEUTIC TRANSLUMINAL OPERATIONS ON CORONARY	
PCI	OPCS	K751	PERCUTANEOUS TRANSLUMINAL BALLOON ANGIOPLASTY AND INSER	
PCI	OPCS	K752	PERCUTANEOUS TRANSLUMINAL BALLOON ANGIOPLASTY AND INSER	
PCI	OPCS	K753	PERCUTANEOUS TRANSLUMINAL BALLOON ANGIOPLASTY AND INSER	
PCI	OPCS	K754	PERCUTANEOUS TRANSLUMINAL BALLOON ANGIOPLASTY AND INSER	
PCI	OPCS	K758	PERCUTANEOUS TRANSLUMINAL BALLOON ANGIOPLASTY AND INSER	
PCI	OPCS	K759	PERCUTANEOUS TRANSLUMINAL BALLOON ANGIOPLASTY AND INSER	
Charlson	ICD-10	F00	Dementia in Alzheimer disease	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	F01	Vascular dementia	
Charlson	ICD-10	F02	Dementia in other diseases classified elsewhere	
Charlson	ICD-10	F03	Unspecified dementia	
Charlson	ICD-10	F051	Delirium superimposed on dementia	
Charlson	ICD-10	G30	Alzheimer disease	
Charlson	ICD-10	G311	Senile degeneration of brain, not elsewhere classified	
Charlson	ICD-10	I278	Other specified pulmonary heart diseases	
Charlson	ICD-10	I279	Pulmonary heart disease, unspecified	
Charlson	ICD-10	J40	Bronchitis, not specified as acute or chronic	
Charlson	ICD-10	J41	Simple and mucopurulent chronic bronchitis	
Charlson	ICD-10	J42	Unspecified chronic bronchitis	
Charlson	ICD-10	J43	Emphysema	
Charlson	ICD-10	J44	Other chronic obstructive pulmonary disease	
Charlson	ICD-10	J45	Asthma	
Charlson	ICD-10	J46	Status asthmaticus	
Charlson	ICD-10	J47	Bronchiectasis	
Charlson	ICD-10	J60	Coalworker pneumoconiosis	
Charlson	ICD-10	J61	Pneumoconiosis due to asbestos and other mineral fibres	
Charlson	ICD-10	J62	Pneumoconiosis due to dust containing silica	
Charlson	ICD-10	J63	Pneumoconiosis due to other inorganic dusts	
Charlson	ICD-10	J64	Unspecified pneumoconiosis	
Charlson	ICD-10	J65	Pneumoconiosis associated with tuberculosis	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	J66	Airway disease due to specific organic dust	
Charlson	ICD-10	J67	Hypersensitivity pneumonitis due to organic dust	
Charlson	ICD-10	J684	Chronic respiratory conditions due to chemicals, gases, fumes and vapours	
Charlson	ICD-10	J701	Chronic and other pulmonary manifestations due to radiation	
Charlson	ICD-10	J703	Chronic drug-induced interstitial lung disorders	
Charlson	ICD-10	M05	Seropositive rheumatoid arthritis	
Charlson	ICD-10	M06	Other rheumatoid arthritis	
Charlson	ICD-10	M315	Giant cell arteritis with polymyalgia rheumatica	
Charlson	ICD-10	M32	Systemic lupus erythematosus	
Charlson	ICD-10	M33	Dermatopolymyositis	
Charlson	ICD-10	M34	Systemic sclerosis	
Charlson	ICD-10	M351	Other overlap syndromes	
Charlson	ICD-10	M353	Polymyalgia rheumatica	
Charlson	ICD-10	M360	Dermato(poly)myositis in neoplastic disease	
Charlson	ICD-10	K25	Gastric ulcer	
Charlson	ICD-10	K26	Duodenal ulcer	
Charlson	ICD-10	K27	Peptic ulcer, site unspecified	
Charlson	ICD-10	K28	Gastrojejunal ulcer	
Charlson	ICD-10	B18	Chronic viral hepatitis	
Charlson	ICD-10	K700	Alcoholic fatty liver	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	K701	Alcoholic hepatitis	
Charlson	ICD-10	K702	Alcoholic fibrosis and sclerosis of liver	
Charlson	ICD-10	K703	Alcoholic cirrhosis of liver	
Charlson	ICD-10	K709	Alcoholic liver disease, unspecified	
Charlson	ICD-10	K713	Toxic liver disease with chronic persistent hepatitis	
Charlson	ICD-10	K714	Toxic liver disease with chronic lobular hepatitis	
Charlson	ICD-10	K715	Toxic liver disease with chronic active hepatitis	
Charlson	ICD-10	K717	Toxic liver disease with fibrosis and cirrhosis of liver	
Charlson	ICD-10	K73	Chronic hepatitis, not elsewhere classified	
Charlson	ICD-10	K74	Fibrosis and cirrhosis of liver	
Charlson	ICD-10	K760	Fatty (change of) liver, not elsewhere classified	
Charlson	ICD-10	K762	Central haemorrhagic necrosis of liver	
Charlson	ICD-10	K763	Infarction of liver	
Charlson	ICD-10	K744	Secondary biliary cirrhosis	
Charlson	ICD-10	K768	Other specified diseases of liver	
Charlson	ICD-10	K769	Liver disease, unspecified	
Charlson	ICD-10	Z944	Liver transplant status	
Charlson	ICD-10	G041	Tropical spastic paraplegia	
Charlson	ICD-10	G114	Hereditary spastic paraplegia	
Charlson	ICD-10	G801	Spastic diplegic cerebral palsy	
Charlson	ICD-10	G802	Spastic hemiplegic cerebral palsy	
Charlson	ICD-10	G81	Hemiplegia	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	G82	Paraplegia and tetraplegia	
Charlson	ICD-10	G830	Diplegia of upper limbs	
Charlson	ICD-10	G831	Monoplegia of lower limb	
Charlson	ICD-10	G832	Monoplegia of upper limb	
Charlson	ICD-10	G833	Monoplegia, unspecified	
Charlson	ICD-10	G834	Cauda equina syndrome	
Charlson	ICD-10	G839	Paralytic syndrome, unspecified	
Charlson	ICD-10	I120	Hypertensive renal disease with renal failure	
Charlson	ICD-10	I131	Hypertensive heart and renal disease with renal failure	
Charlson	ICD-10	N032	Chronic nephritic syndrome: Diffuse membranous glomerulonephritis	
Charlson	ICD-10	N033	Chronic nephritic syndrome: Diffuse mesangial proliferative glomerulonephritis	
Charlson	ICD-10	N034	Chronic nephritic syndrome: Diffuse endocapillary proliferative glomerulonephritis	
Charlson	ICD-10	N035	Chronic nephritic syndrome: Diffuse mesangiocapillary glomerulonephritis	
Charlson	ICD-10	N036	Chronic nephritic syndrome: Dense deposit disease	
Charlson	ICD-10	N037	Chronic nephritic syndrome: Diffuse crescentic glomerulonephritis	
Charlson	ICD-10	N052	Unspecified nephritic syndrome: Diffuse membranous glomerulonephritis	
Charlson	ICD-10	N053	Unspecified nephritic syndrome: Diffuse mesangial proliferative glomerulonephritis	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	N054	Unspecified nephritic syndrome: Diffuse endocapillary proliferative glomerulonephritis	
Charlson	ICD-10	N055	Unspecified nephritic syndrome: Diffuse mesangiocapillary glomerulonephritis	
Charlson	ICD-10	N056	Unspecified nephritic syndrome: Dense deposit disease	
Charlson	ICD-10	N057	Unspecified nephritic syndrome: Diffuse crescentic glomerulonephritis	
Charlson	ICD-10	N18	Chronic kidney disease	
Charlson	ICD-10	N19	Unspecified kidney failure	
Charlson	ICD-10	N250	Renal osteodystrophy	
Charlson	ICD-10	Z490	Preparatory care for dialysis	
Charlson	ICD-10	Z491	Extracorporeal dialysis	
Charlson	ICD-10	Z492	Other dialysis	
Charlson	ICD-10	Z940	Kidney transplant status	
Charlson	ICD-10	Z992	Dependence on renal dialysis	
Charlson	ICD-10	C00	Malignant neoplasm of lip	
Charlson	ICD-10	C01	Malignant neoplasm of base of tongue	
Charlson	ICD-10	C02	Malignant neoplasm of other and unspecified parts of tongue	
Charlson	ICD-10	C03	Malignant neoplasm of gum	
Charlson	ICD-10	C04	Malignant neoplasm of floor of mouth	
Charlson	ICD-10	C05	Malignant neoplasm of palate	
Charlson	ICD-10	C06	Malignant neoplasm of other and unspecified parts of mouth	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	C07	Malignant neoplasm of parotid gland	
Charlson	ICD-10	C08	Malignant neoplasm of other and unspecified major salivary glands	
Charlson	ICD-10	C09	Malignant neoplasm of tonsil	
Charlson	ICD-10	C10	Malignant neoplasm of oropharynx	
Charlson	ICD-10	C11	Malignant neoplasm of nasopharynx	
Charlson	ICD-10	C12	Malignant neoplasm of piriform sinus	
Charlson	ICD-10	C13	Malignant neoplasm of hypopharynx	
Charlson	ICD-10	C14	Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx	
Charlson	ICD-10	C15	Malignant neoplasm of oesophagus	
Charlson	ICD-10	C16	Malignant neoplasm of stomach	
Charlson	ICD-10	C17	Malignant neoplasm of small intestine	
Charlson	ICD-10	C18	Malignant neoplasm of colon	
Charlson	ICD-10	C19	Malignant neoplasm of rectosigmoid junction	
Charlson	ICD-10	C20	Malignant neoplasm of rectum	
Charlson	ICD-10	C21	Malignant neoplasm of anus and anal canal	
Charlson	ICD-10	C22	Malignant neoplasm of liver and intrahepatic bile ducts	
Charlson	ICD-10	C23	Malignant neoplasm of gallbladder	
Charlson	ICD-10	C24	Malignant neoplasm of other and unspecified parts of biliary tract	
Charlson	ICD-10	C25	Malignant neoplasm of pancreas	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	C26	Malignant neoplasm of other and ill-defined digestive organs	
Charlson	ICD-10	C30	Malignant neoplasm of nasal cavity and middle ear	
Charlson	ICD-10	C31	Malignant neoplasm of accessory sinuses	
Charlson	ICD-10	C32	Malignant neoplasm of larynx	
Charlson	ICD-10	C33	Malignant neoplasm of trachea	
Charlson	ICD-10	C34	Malignant neoplasm of bronchus and lung	
Charlson	ICD-10	C37	Malignant neoplasm of thymus	
Charlson	ICD-10	C38	Malignant neoplasm of heart, mediastinum and pleura	
Charlson	ICD-10	C39	Malignant neoplasm of other and ill-defined sites in the respiratory system and intrathoracic organs	
Charlson	ICD-10	C40	Malignant neoplasm of bone and articular cartilage of limbs	
Charlson	ICD-10	C41	Malignant neoplasm of bone and articular cartilage of other and unspecified sites	
Charlson	ICD-10	C43	Malignant melanoma of skin	
Charlson	ICD-10	C45	Mesothelioma	
Charlson	ICD-10	C46	Kaposi sarcoma	
Charlson	ICD-10	C47	Malignant neoplasm of peripheral nerves and autonomic nervous system	
Charlson	ICD-10	C48	Malignant neoplasm of retroperitoneum and peritoneum	
Charlson	ICD-10	C49	Malignant neoplasm of other connective and soft tissue	
Charlson	ICD-10	C50	Malignant neoplasm of breast	
Charlson	ICD-10	C51	Malignant neoplasm of vulva	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	C52	Malignant neoplasm of vagina	
Charlson	ICD-10	C53	Malignant neoplasm of cervix uteri	
Charlson	ICD-10	C54	Malignant neoplasm of corpus uteri	
Charlson	ICD-10	C55	Malignant neoplasm of uterus, part unspecified	
Charlson	ICD-10	C56	Malignant neoplasm of ovary	
Charlson	ICD-10	C57	Malignant neoplasm of other and unspecified female genital organs	
Charlson	ICD-10	C58	Malignant neoplasm of placenta	
Charlson	ICD-10	C60	Malignant neoplasm of penis	
Charlson	ICD-10	C61	Malignant neoplasm of prostate	
Charlson	ICD-10	C62	Malignant neoplasm of testis	
Charlson	ICD-10	C63	Malignant neoplasm of other and unspecified male genital organs	
Charlson	ICD-10	C64	Malignant neoplasm of kidney, except renal pelvis	
Charlson	ICD-10	C65	Malignant neoplasm of renal pelvis	
Charlson	ICD-10	C66	Malignant neoplasm of ureter	
Charlson	ICD-10	C67	Malignant neoplasm of bladder	
Charlson	ICD-10	C68	Malignant neoplasm of other and unspecified urinary organs	
Charlson	ICD-10	C69	Malignant neoplasm of eye and adnexa	
Charlson	ICD-10	C70	Malignant neoplasm of meninges	
Charlson	ICD-10	C71	Malignant neoplasm of brain	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	C72	Malignant neoplasm of spinal cord, cranial nerves and other parts of central nervous system	
Charlson	ICD-10	C73	Malignant neoplasm of thyroid gland	
Charlson	ICD-10	C74	Malignant neoplasm of adrenal gland	
Charlson	ICD-10	C75	Malignant neoplasm of other endocrine glands and related structures	
Charlson	ICD-10	C76	Malignant neoplasm of other and ill-defined sites	
Charlson	ICD-10	C81	Hodgkin lymphoma	
Charlson	ICD-10	C82	Follicular lymphoma	
Charlson	ICD-10	C83	Non-follicular lymphoma	
Charlson	ICD-10	C84	Mature T/NK-cell lymphomas	
Charlson	ICD-10	C85	Other and unspecified types of non-Hodgkin lymphoma	
Charlson	ICD-10	C88	Malignant immunoproliferative diseases	
Charlson	ICD-10	C90	Multiple myeloma and malignant plasma cell neoplasms	
Charlson	ICD-10	C91	Lymphoid leukaemia	
Charlson	ICD-10	C92	Myeloid leukaemia	
Charlson	ICD-10	C93	Monocytic leukaemia	
Charlson	ICD-10	C94	Other leukaemias of specified cell type	
Charlson	ICD-10	C95	Leukaemia of unspecified cell type	
Charlson	ICD-10	C96	Other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue	
Charlson	ICD-10	C97	Malignant neoplasms of independent (primary) multiple sites	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	I850	Oesophageal varices with bleeding	
Charlson	ICD-10	I859	Oesophageal varices without bleeding	
Charlson	ICD-10	I864	Gastric varices	
Charlson	ICD-10	I982	Oesophageal varices without bleeding in diseases classified elsewhere	
Charlson	ICD-10	K704	Alcoholic hepatic failure	
Charlson	ICD-10	K711	Toxic liver disease with hepatic necrosis	
Charlson	ICD-10	K721	Chronic hepatic failure	
Charlson	ICD-10	K729	Hepatic failure, unspecified	
Charlson	ICD-10	K765	Hepatic veno-occlusive disease	
Charlson	ICD-10	K766	Portal hypertension	
Charlson	ICD-10	K767	Hepatorenal syndrome	
Charlson	ICD-10	C77	Secondary and unspecified malignant neoplasm of lymph nodes	
Charlson	ICD-10	C78	Secondary malignant neoplasm of respiratory and digestive organs	
Charlson	ICD-10	C79	Secondary malignant neoplasm of other and unspecified sites	
Charlson	ICD-10	C80	Malignant neoplasm, without specification of site	
Charlson	ICD-10	B20	Human immunodeficiency virus [HIV] disease resulting in infectious and parasitic diseases	
Charlson	ICD-10	B21	Human immunodeficiency virus [HIV] disease resulting in malignant neoplasms	

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Table E.1 – *Continued from previous page*

Defined	System	Code	Description	Notes
Charlson	ICD-10	B22	Human immunodeficiency virus [HIV] disease resulting in other specified diseases	
Charlson	ICD-10	B24	Unspecified human immunodeficiency virus [HIV] disease	

F

CALCULATION OF ILLUSTRATIVE EXAMPLE IN DISCUSSION CHAPTER

I acknowledge the help and advice that I have had from statisticians with the methods outlined in this section

In order to calculate the necessary information for the initiative example shown in chapter 10, I use the following definitions and method of calculation for each quintile Q_i where i is quintile numbers 1 to 5:

$$n_i = \text{number at risk in} \quad Q_i$$

$$p_i = \text{number with PCI in} \quad Q_i$$

$$h_i = \text{fully adjusted hazard ratio for} \quad Q_i$$

$$q_i = \text{number who would have had a PCI rate were as for} \quad Q_1$$

$$= p_i // h_i$$

$$m_i = \text{mortality rate in those at risk, no PCI in} \quad Q_i$$

$$r_i = \text{mortality rate in those at risk, PCI in} \quad Q_i$$

$$\text{number of deaths in} \quad Q_i = (n_i - p_i)m_i + p_i r_i = D1_i$$

$$\text{number of deaths if quintile 1 rate used for} \quad Q_i = (n_i - q_i)m_i + q_i r_i = D2_i$$

$$\text{number of deaths prevented or postponed in} \quad Q_i = D1_i - D2_i$$