DRUG UTILISATION STUDIES ON THE IMPACT OF THE REDUCTION OF THE PRESCRIPTION CHARGE IN WALES AND THE RECLASSIFICATION OF MEDICINES

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SUMMARY

Since 2000 there have been a number of policy changes in the UK to remove barriers that limit access to medicines. Perhaps the most significant of these have been the phased reduction and abolition of the prescription charge in Wales and the efforts of the UK Government to encourage the reclassification of medicines. This thesis explored aspects of both these changes.

The percent change in the number of prescription items dispensed over the two year period before and after the first reduction of the prescription charge in October 2004 was determined. There was an increase in the percent change [median (interquartile range)] for non-sedating antihistamines [7.3 (5.0 – 10.7) to 13.7 (10.9 – 17.1), $p < 0.001$] and laxatives [2.2 (0.8 – 3.1) to 3.7 (1.4 – 6.4), $p = 0.04$], whilst no change was observed for loperamide [-1.2 (-3.3 – 3.2) to 2.6 (-0.9 – 5.2), $p = 0.11$] and fluconazole [-7.4 (-14.4 – 2.1) to -3.7 (-10.9 – 1.4), $p = 0.52$].

Over the counter (OTC) sales of omeprazole and simvastatin were monitored following reclassification and accounted for less than 1% of the volume of their prescription counterpart. In contrast, sales of OTC hyoscine butylbromide and chloramphenicol eye drops were more than 20% of the number of items dispensed. Twelve months after reclassification there was an increase in the percent change in the number of prescription items dispensed for hyoscine butylbromide in Wales [5.8 (0.2 – 12.6) to 20.7 (4.4 – 25.6), $p = 0.007$], whilst prescriptions for chloramphenicol eye drops decreased [10.0 (6.0 – 13.6) to -8.9 (-13.1 – -4.4), $p < 0.001$]. More OTC chloramphenicol was sold in less deprived areas ($r = -0.44$, $p = 0.04$).

The changes in prescription volume and OTC medicine sales varied from medicine to medicine and require a qualitative evaluation to better understand the reasons behind the differences observed.

CONTENTS

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ABBREVIATIONS

ACE	Angiotensin converting enzyme
ARB	Angiotensin receptor blocker
BNF	British National Formulary
CASPA	Comparative Analysis System for Prescribing Audit
CHD	Coronary heart disease
CHM	Commission on Human Medicines
CI	Confidence interval
COX-2	Cyclo-oxygenase-2
CSM	Committee on Safety of Medicines
DDD	Defined daily doses
DED	District Electoral Division
EHC	Emergency hormonal contraceptive
FDA	Food and Drug Administration
GORD	Gastro-oesophageal reflux disease
GP	General practitioner
GPRD	General practice research database
GSL	General sale list
HRT	Hormone replacement therapy
IBS	Irritable bowel syndrome
IMD	Index of Multiple Deprivation
IMS	Intercontinental Marketing Services
IQR	Interquartile range
LDL	Low density lipoprotein
LHB	Local Health Boards
LLTI	Limiting long term illness
LSOA	Lower Super Output Area

MeSH	Medical subject heading
MHRA	Medicines and Healthcare products Regulatory Agency
MPR	Medication possession ratio
NHS	National Health Service
NR	Nepali Rupees
NSAIDs	Non-steroidal anti-inflammatory drugs
OTC	Over the counter
P	Pharmacy medicine
PAGB	Proprietary Association of Great Britain
PCO	Primary Care Organisations
PCT	Primary Care Trusts
PMPM	Prescriptions filled per member per month
POM	Prescription only medicine
PPD	Prescription Pricing Division
PPI	Proton pump inhibitor
RPSGB	Royal Pharmaceutical Society of Great Britain
RSA	Regional sale analysis
SGA	Second generation antihistamine
SPR	Standardised prescription ratio
SPSS	Statistical Package for the Social Sciences
SSRI	Selective serotonin reuptake inhibitor
STAR-PU	Specific therapeutic group age-sex related prescribing unit
TCA	Tricyclic antidepressant
UPA	Under-privileged area
UK	United Kingdom
US	United States
WIMD	Welsh Index of Multiple Deprivation

GLOSSARY

Beneficiary	A person who is eligible for or receiving benefits under an insurance policy or plan.
Coinsurance	A cost sharing requirement under some health insurance policies in which the insured person pays some of the costs of covered services.
Copayment	Flat fees or payments that a patient pays for each doctor visit or prescription.
Cost sharing	An insurance policy requires the insured person to pay a portion of the costs of covered services. Deductibles, coinsurance, copayments and prescription charge are cost sharing.
Deductible	The amount of money, or value of certain services (such as one physician visit), a patient or family must pay before costs (or percentages of costs) are covered by the health plan or insurance company, usually per year.
Deprivation	Deprivation is a wider concept than poverty and refers to problems caused by a general lack of resources and opportunities (not just money).
Formulary	A list of medications that a managed care company encourages or requires physicians to prescribe as necessary in order to reduce costs.
Prescription charge	A flat rate charge per item made to patients for NHS prescription medicines.
Socioeconomic status	Broad based classification of a person or family's social or economic position based on income, occupation, wealth and education.

CHAPTER 1

INTRODUCTION

The desire to take medicine is perhaps the greatest feature which distinguishes man from animals (Sir William Osler, 1849 – 1919).

In the United Kingdom (UK), medicines are classified into three categories:[1] (1) Prescription Only Medicines (POM) which are available only on prescription; (2) Pharmacy (P) medicines which are available for sale in a pharmacy without a prescription when supplied under the supervision of a pharmacist; and (3) General Sale List (GSL) medicines which are freely available by self selection to the public from normal retail outlets such as supermarkets and garages but which may also be sold from a pharmacy. Collectively P and GSL medicines are often referred to as nonprescription or over the counter (OTC) medicines.[2]

Several factors are known as obstacles to the use of medicines including the prescription charge and the limitation of medicines that are available OTC. The policy on a prescription charge has been debated across the UK constituent countries.[3] As of 2007, Wales was the only country in the UK that has successfully abolished the prescription charge. This policy has been implemented in phases since October 2004. It is of interest to investigate if the phased reduction of the prescription charge had an impact on the use of medicine in Wales.

The purchase of OTC medicines is part of self care, which is a fundamental element for people to proactively manage their own health. However, the restricted number of OTC medicines available has limited the use of medicines for self care. To promote self care management, the UK Government has aimed to increase the number and range of medicines available OTC by supporting the reclassification of a number of medicines. This was presented in several of the Government's plans and policies such as the NHS (National Health Service) Plan,[4] Building on the Best,[5] and Self Care – a real choice.[6] The engagement of the public with the increasing range of medicines recently reclassified and their impact on NHS prescribing are examined in the present study.

1.1 Prescription charge – cost sharing

Healthcare costs, especially the escalating cost of prescription medicines, present major challenges to governments worldwide.[7] Cost sharing is one approach to control public expenditure on medicines.[8] It should be noted that cost sharing is a broad term used to describe a general set of financing arrangements in which a covered member must pay a portion of the costs associated with receiving care. In the UK, cost sharing for prescription medicines is known as the prescription charge. However, the term cost sharing has been used in the present study when referring to cost sharing in general or when the term is specifically used in other healthcare systems.

Cost sharing or prescription charge in the UK is a flat rate charge for each item on a prescription. The amount of medicine prescribed as a single item could range from a single use to several months supply. As of April 2007, the prescription charge in

England, Scotland and Northern Ireland was £6.85. In Wales, the prescription charge was reduced in steps from October 2004 and was abolished in April 2007.

1.1.1 Impact of cost sharing

Since studies on the impact of the prescription charge in the UK are limited[3] an overview of the impact of cost sharing in general is thereby presented in this section. Cost sharing is a universal concept and it is anticipated that a better understanding of its impact may help interpret the impact of the reduction of the prescription charge in this study.

The imposition of cost sharing is seen as a major barrier to the access of prescription medicines for certain groups of patients, particularly those with low income.[9-11] Several strategies have been developed by patients to reduce the financial burden of cost sharing including requesting that not all prescribed medicines on a prescription are dispensed or delaying dispensing until they have enough money to pay.[12, 13] Doctors have also been known to take into account the patient's ability to afford the medicine prescribed when making prescribing decisions.[14-16] For example, they may choose to prescribe higher quantities on a single prescription to reduce the need for the patient to make a monthly payment.

Increasing cost sharing has been shown to decrease the use of prescription medicines.[17-27] The burden of cost sharing and the subsequent decision not to acquire a prescribed medicine has been linked to serious adverse events,[28] poorer clinical outcomes[29, 30] and higher referral rate[31] and hospital admissions.[32]

Some studies[33-35] have reported relatively small changes in medication utilisation in response to increases in cost sharing, but these have often focused on relatively small changes in cost sharing. Results from a Canadian study[36] have shown that use of essential medicines including beta blockers, angiotensin converting enzyme (ACE) inhibitors and lipid lowering drugs in vulnerable patients, such as elderly patients who had experienced an acute myocardial infarction, did not change following an introduction of cost sharing. It is likely that an association between increased cost sharing and a decline in medical utilization depends on the medicine studied and the size of the increase in the patient's contribution.

1.1.2 Review of relevant literature

Relevant published articles that have examined the effects of prescription cost sharing schemes were identified using a strategic search[37] of a Medline database (via Ovid system). During the period January 1996 to September 2007, two hundred and ninety two articles in English language were identified under the following standard medical subject headings (MeSH): "insurance, pharmaceutical services or deductibles and coinsurance or cost sharing or prescription fee or prescription charge (keyword)" and "physician's practice patterns or prescriptions, drug or drug utilization".

The articles identified were screened by title and/or abstract. Abstracts and, in some cases, the full text of the 77 articles that passed the screening stage were examined to identify articles with a similar design to the present study. However, because the majority of these studies were observational they were classified according to whether the association between cost sharing and the outcome of interest was measured as follows:[38]

- Aggregated time series: analysed changes over time in data aggregated at the geographic or plan level
- Cross sectional: analysed individual level data at a single time point for multiple cost sharing plan
- Repeated cross sectional: analysed cross sectional data from multiple time periods
- Longitudinal: analysed individual level data with repeated observations for the same beneficiaries over time
- Before and after without control group: compared outcomes at 2 points in time, before and after a change in cost sharing with no control group
- Before and after with control group: compared outcomes before and after a change in cost sharing with control group of stable cost sharing policy

Of the 77 articles identified, 11 had a "before and after with control group" design and were included in the review. The level of evidence presented (Tables 1.1, 1.2 and 1.3) was based on the traditional hierarchy of evidence suggested by the Evidence-Based Medicine Working Group[39] in the following order:

1. Systemic reviews and meta-analyses
2. Randomised controlled trials with definitive results
3. Randomised controlled trials with non-definitive results
4. Cohort studies
5. Case controlled studies
6. Cross sectional surveys
7. Case reports

Table 1.1 Studies examining the association between cost sharing policies and drug utilisation or prescribing

Source	Study design	Sample	Setting	Cost sharing variation	Unit of measure	Outcomes	Level of evidence
Gibson et al,[40] 2005	7 quarters before and 9 quarters after (except the 4th quarter of 1997 and the 3rd quarter of 1998) increasing copayment; with control group	18767 employees in 2 firms (medical claims data, 1995 – 1998)	US	Copayment level in one firm changed from $2 to $7 for brand name drugs (generic drugs remained at $2); co-payment in other firm remained unchanged ($5 for generic drugs, $8 for brand name drugs if a generic substitute was not available, otherwise $15 for brand name drugs)	Number of filled prescriptions; drug spending	Copayment increase in brand drugs was associated with 4% ($p < 0.001$) decrease in total drug use, and 27% ($p < 0.001$) decrease in use of brand drugs; total drug expenditure decreased by about 10% ($p < 0.10$) of average quarterly expenditure	4
Huskamp et al,[41] 2005	Approximately 9 months before and more than 1 year after 3-tier adoption and 9 months after tier changes; with control group	36102 children as dependents in 2 employer-sponsored managed care plans (pharmacy claims data, 1999 – 2001)	US	One employer changed formulary from 1-tier ($7) to 3-tier ($8 for generic, $15 for preferred branded, and $30 for nonpreferred branded drugs); the other employer had a stable 2-tier formulary ($8 for generic and $15 for preferred branded drugs)	Initiation of drug therapy; drug spending	Relative to the control group, adding a third tier with a $30 copayment decreased probability that children would receive a drug for attention-deficit/hyperactivity disorder by 17% ($p < 0.001$), and decreased total medication spending by 20% ($p < 0.001$)	4

Table 1.1 (cont) Studies examining the association between cost sharing policies and drug utilisation or prescribing

Source	Study design	Sample	Setting	Cost sharing variation	Unit of measure	Outcomes	Level of evidence
Landsman et al,[42] 2005	12 months before and 12 months after benefit change; with control group	Users of 9 drug classes in 1 of 4 managed care plans with 1630000 total members (enrolment and pharmacy claims data, 1999 – 2001)	US	Three plans changed from 2-tier formulary (generic/preferred brand) to 3-tier formulary (generic/preferred brand/nonpreferred brand): \$5/\$10 to \$5/\$15/\$25, \$10/\$20 to \$10/\$20/\$40, and \$5/\$10 to \$5/\$20/\$35; one plan had a stable 2-tier formulary (\$10/\$20)	Medication possession ratio (MPR); discontinuation rates	Compared with the control group, intervention group showed lower MPR for the following drugs: TCAs* (1.4% v -4.0%; $p < 0.05$), SSRIs† (0.1% v -4.9%; $p < 0.01$), NSAIDs‡ (1.9% v -6.8%; $p < 0.01$), statins (-0.1% v -4.1%; $p < 0.05$), and ACE¶ inhibitors (0.5% v -4.1%; $p < 0.01$); changes in discontinuation rates were greater in intervention group for the following drugs: ACE inhibitors, ARBs,§ statins, SSRIs, and TCAs (all $p < 0.05$)	4
Liu et al,[43] 2004	8 months before and 8 months after the introduction of cost sharing; with control group	Over 3 million prescriptions for elderly patients from 21 hospitals (administrative data, 1998 – 2000)	Taipei, Taiwan	Since 1999, prescription drug policy in Taiwan changed from full coverage to 20% coinsurance with a maximum of US \$15.63 per prescription for prescriptions costing more than \$3.13; selected groups were exempt	Average prescription cost; prescription duration	Following the cost sharing program, cost sharing group showed lower growth of average prescription cost (7.8%; $p = 0.0001$) and prescription duration (1.6%; $p = 0.0001$) compared with exempt group (22.1%; $p = 0.0001$ and 42.6%; $p = 0.0001$)	4

*Tricyclic antidepressants, †selective serotonin reuptake inhibitors, ‡nonsteroidal anti-inflammatory drugs, ¶angiotensin converting enzyme inhibitors, §angiotensin receptor blockers

Table 1.1 (cont) Studies examining the association between cost sharing policies and drug utilisation or prescribing

Source	Study design	Sample	Setting	Cost sharing variation	Unit of measure	Outcomes	Level of evidence
Fairman et al,[44] 2003	12 months before and 30 months after benefit change; with control group	7709 employees whose employers were clients of the preferred provider organisation (medical and pharmacy claims data, 1997 – 2000)	Mid-western United States	The intervention group changed their formulary from 2-tier to 3-tier with increased co-payment from $7 for generic and $12 for brand medication to $8 for generic, $15 for formulary brand and $25 for nonformulary brand products with no further changes for 30 months; the control group had a stable 2-tier formulary	Number of claims; drug spending	24 months following the implementation of the three-tier structure the intervention group showed a reduction in utilization of third-tier medication (-0.02) compared with 0.23 increased claims in the control group ($p < 0.01$); net cost (drug cost minus copayment) changes in the intervention group were lower than control group ($58 v $118; $p < 0.001$)	4
Nair et al,[45] 2003	7 months before and 7 months after benefit change; with control group	8312 patients with chronic conditions in a managed care plan (pharmacy claims data, 2000 – 2001)	Western United States	Drug benefit plan of intervention group changed from 2-tier to 3 tier (formularies were varied); 2 control groups had stable 2- or 3-tier drug benefit	Discontinuation rates	Intervention group were 1.76 (95% CI, 1.19 to 2.60) times more likely to discontinue their nonformulary medication than those in the 2-tier comparison group and 1.49 (95% CI, 1.14 to 1.95) times more likely than those in the 3-tier group	4

Table 1.1 (cont) Studies examining the association between cost sharing policies and drug utilisation or prescribing

Source	Study design	Sample	Setting	Cost sharing variation	Unit of measure	Outcomes	Level of evidence
Huskamp et al,[46] 2003	More than 12 months before and more than 12 months after benefit change (exact implementation date was not revealed to protect employers' anonymity); with control group	151222 enrolees covered by 2 employers and were users of 1 of the following drugs: ACE inhibitors, PPIs, or statins (pharmacy claims data, 1999 – 2001)	US	Employer 1 changed formulary from 1-tier ($7) to 3-tier ($8 for generic, $15 for preferred branded, and $30 nonpreferred branded drugs); Employer 2 changed from 2-tier ($6/$12) to 3-tier (($6/$12/$24); The control group had stable 2-tier formulary $8/$15 (for Employer 1) and $6/$12 (for Employer 2)	Initiation of drug therapy; drug switching; discontinuation rate	Compared with the control group, Employer 1 showed higher rates of discontinuation of statins (11% v 21%; p = 0.04) and higher switching to lower cost medication (17% v 49%; p < 0.001); Employer 2 showed higher switching to drugs of a lower tier compared with the control group (48% v 8%; p < 0.001) but not higher discontinuation rates (9% v 4%; p = 0.45)	4
Kozyrskyj et al,[47] 2001	12 months before and 24 months after benefit change; with control group	10703 children who had asthma (administrative data, 1995 – 1998)	Manitoba, Canada	Before April 1996, a fixed deductible payment of $237 per family plus 40% copayment on prescription costs above $237 was used; since April 1996 the policy was replaced by income-based deductibles; exemption for household receiving income assistance remain unchanged	Initiation of drug therapy; number of prescription filled	Compared with the likelihood of children who received inhaled corticosteroid at no charge (0.87), those with mild to moderate asthma covered by the deductible program were less likely to receive a prescription (0.68; p < 0.05 in both higher and low income groups)	4

Table 1.1 (cont) Studies examining the association between cost sharing policies and drug utilisation or prescribing

Source	Study design	Sample	Setting	Cost sharing variation	Unit of measure	Outcomes	Level of evidence
Motheral et al,[48] 2001	12 months before and 12 months after benefit change; with control group	20160 employees whose employers were clients of the preferred provider organisation (medical and pharmacy claims data, 1997 – 1999)	Mid-western United States	The intervention group changed formulary from 2-tier to 3-tier with increased co-payments of $7 for generic and $12 for brand medication to $8 for generic, $15 for formulary brand and $25 for nonformulary brand products; the control group had a stable 2-tier formulary	Number of claims; drug spending	Compared with the control group, the intervention group experienced lower prescription utilisation with minimal change in the total number of claims (1.28 v 0.76; $p < 0.001$) and smaller change in prescription costs ($61 v $41; $p < 0.001$) following the implementation of the three-tier structure	4
Holloway et al,[49] 2001	6 to 12 months interval before (1992) and after (1995) new fee systems; with control group	33 government primary health care facilities (other survey study, 1992 and 1995)	Three rural districts in Nepal	In 1995 one intervention district changed user fee to 1-band item fee of NR3(Nepali Rupees) per item; another intervention district changed user fee to 2-band item fee with NR2 per cheap item and NR5 per expensive item; the control district had a stable NR5 per prescription	Number of item and cost per prescription	Compared with a fee per prescription, a fee per drug item showed fewer drug items prescribed per prescription (95% CI, -1.1 to -0.6 for 1-band item fee, and -0.9 to -0.4 for 2-band item fee) and lower drug costs per prescription (95% CI, -10.5 to -1.0 for 1-band item fee, and -13.8 to -4.8 for 2-band item fee)	4

Table 1.1 (cont) Studies examining the association between cost sharing policies and drug utilisation or prescribing

Source	Study design	Sample	Setting	Cost sharing variation	Unit of measure	Outcomes	Level of evidence
Motheral et al,[50] 1999	6 months before and 6 months after benefit change; with control group	3184 enrolees in commercial plans (pharmacy claims data 1996 – 1997)	US	Copayment level in 2 commercial plans increased from $10 to $15 for brand drugs (generic drugs changed from $4 to $5 for Plan A and from $5 to $7 for Plan B); copayment in control group had a stable $5 for generic and $10 for brand drugs	Number of filled prescription; discontinuation rate	Total brand claims decreased by 0.15 for the intervention group and increased by 0.70 for the control group ($p = 0.0001$); overall use or discontinuation rates for long term medication were not different	4

The majority of the articles reviewed looked at relatively large sample sizes. The study period varied from 6 months before and 6 months after to 28 months before and 36 months after the change in the cost sharing policy of interest. Eight studies were conducted in the United States (US) where most patients (or beneficiaries) are covered by incentive-based formularies in which drugs are assigned to one of several tiers based on their cost to the health plan, the number of close substitutes, and other factors. Cost sharing in those 8 US studies were generally changed from beneficiaries' copayment of 1-tier (generic drugs) or 2-tier (generic and preferred brand drugs) to 3-tier (generic, preferred brand, and nonpreferred brand drugs). Changes in cost sharing in other studies varied and were based on cost sharing policies used in each of the countries studied.

Only one study[50] showed that neither total use nor discontinuation rates changed following an increase in cost sharing, although the use of brand drugs did significantly reduce. This was probably due to the relatively short period studied after the change in cost sharing (6 months) and a higher switch to generic drugs to overcome the increase in the copayment charge for brand medicines. In addition, the results on discontinuation rates were not supported by statistical evidence. At least 90% of subjects in both control and intervention groups were still continuing with their medication at the end of the study.

Overall, results from the literature reviewed were consistent and showed that an increase in cost sharing was associated with a decrease in the use of prescription medicines or drug expenditure. However, it should be noted that cost sharing schemes in all the studies reviewed were different from the prescription charge, a flat

rate charge per item, used in the UK. In addition, the impact of the reduction of cost sharing on pattern of prescribing, as proposed in the present study, were not examined in any of the studies reviewed.

1.2 Reclassification of medicines

In the UK the primary purpose of classifying drugs into three categories (POM, P and GSL) is to promote the safe use of medicines and protect public health. New medicines are normally first registered as POMs and remain in this status until their safety is proven.

Medicines can subsequently be switched from POM to P if they no longer meet any of the following criteria:[51] (a) dangerous when not used under medical supervision; (b) frequently used incorrectly; (c) new and require further investigation; and (d) not normally given parenterally. For a switch from P to GSL the criteria is that the medicine can with reasonable safety be sold or supplied otherwise than by or under the supervision of a pharmacist.

There are many reasons why medicines are reclassified and these include the need of the Government to find new ways of addressing the ever increasing NHS drugs bill;[52-54] the wish of the pharmaceutical industry to extend the commercial life of products whose patent has expired and which may be prescribed on NHS prescriptions in diminishing amounts;[52-54] the rise of consumerism, patient empowerment and demand for self-medication;[55, 56] and the desire to strengthen the role of community pharmacists.[52-54]

1.2.1 Impact of reclassification of medicines

It has been suggested that medicines reclassification will widen patient choice, increase their access to medicines, increase patient independence, decrease doctor visits and in some instance decrease costs.[57, 58] However, many concerns associated with increasing access to OTC medicines have been raised. These relate to effectiveness, safety, drug interactions and delays in diagnosis.

Whilst safety and the potential for misuse are important factors taken into account at the time of reclassification, the decisions made are generally based on data from clinical trials and adverse events reported in clinical practice that may not reflect the diverse circumstances in which the medicine will be used when purchased. Likewise, the efficacy of medicines reclassified from prescription only status should be questioned more closely because they have rarely been evaluated in clinical trials at the dose recommended in packs that can be purchased, or have been shown to be of limited efficacy when subjected to systematic review.[59]

Perhaps the lack of efficacy of purchased medicines should not be a surprise given that the dose regimens recommended for purchased medicines are generally lower than their prescription counterparts. Whether the informed patient may choose to ignore this and use the higher dose that would normally be prescribed is unknown, although there is a single anecdotal case that suggests professionals themselves encourage patients to use OTC medicines at doses greater than those indicated on the pack.[60] This then raises the question of whether it may be potentially hazardous to assume patients use OTC medicines within the licensed dose and regimen.

Reduced efficacy and emerging resistance is of particular concern with purchased medicines such as antiviral, antifungal, parasiticidal and bacterial agents. In the US, for example, the Food and Drug Administration (FDA)[61] did not approve the reclassification of the antiviral agent aciclovir from a prescription only to OTC category because of fears of emerging resistance. In the UK, resistance to headlice preparations is recognised[62] but whether prescribing or purchasing for self care has contributed to this is unclear.

Problems with safety may also arise if the purchased medicine interacts with prescribed medicines taken concurrently,[63] if the purchased medicine is taken in overdose,[64] where there is the potential for an adverse reaction when used by the elderly[65, 66] or patients with pre-existing conditions,[67] where overuse or misuse can result in addiction,[68] or where the purchased medicine can be used as the starting point to synthesise a substance of misuse.[69] The dangers associated with incorrect self diagnosis and treatment have been highlighted in research focussing on the inappropriate use of OTC eye drop preparations[70] and OTC antifungals.[71, 72]

Responses and attitudes towards the reclassification of medicines from prescription only to OTC status varies and depends on the medicine being reclassified. For example, a large number of general practitioners (GPs) supported the reclassification of H_2 antagonists,[73] but were worried about the availability of over the counter emergency hormonal contraceptive (EHC).[74] Their concerns with the reclassification of EHC were the potential for abuse by some women and the characteristics of community pharmacy premise which might make it an unsuitable setting for the provision of EHC. In addition, it has been suggested that access to over the counter

EHC will encourage sexual promiscuity and thereby increase the incidence of sexually transmitted infections, especially adolescents, and discourage responsible behaviour among current contraceptive users.[75] In contrast, positive attitudes were received from pharmacists and nurse-midwives.[76] Most women surveyed supported the reclassification of EHC[77] and expressed a preference to purchase it from a pharmacy.[78]

The increasing number of OTC medicines made available following reclassification has improved access to a wide range of effective therapies. How this access should be monitored is unclear. It has been suggested that sales volume can be used as a surrogate to estimate patient access to medicines.[57] However, there are few robust studies examining the association between medicine reclassification and the sale of OTC medicines or prescription medicines.

1.2.2 Review of relevant literature

During the period January 1996 to September 2007, 82 English language articles were identified in Medline database search (via Ovid) which used the following keywords and standard medical subject headings (MeSH): "reclassification or deregulation or switch" and "over the counter or OTC (keyword) or drug, nonprescription or prescriptions, drug or pharmaceutical preparations".

After screening titles and/or abstracts, 4 out of 82 articles that examined the association of medicine reclassification and access to medicine or medication utilization were selected for review and are presented in Table 1.2.

Table 1.2 Studies examining the association between medicine reclassification and sale of over the counter medicine or prescribing

Source	Study design	Sample	Setting	Medicine reclassified	Unit of measure	Outcomes	Level of evidence
Sullivan et al,[79] 2005	12 months before and 12 months after the index date formulary changed following reclassification	58329 patients with allergic rhinitis (national pharmacy benefit management organization database, 2002 – 2003)	US	Loratadine (2002)	Number of prescriptions filled per member per month (PMPM)	Annual utilisation PMPM of prescription second generation antihistamines (SGAs) decreased by 66% ($p < 0.001$) in plan where sponsor made no change to the formulary status of SGA, 65% ($p < 0.001$) in plan where sponsor moved all SGA to the third tier, and 88% ($p < 0.001$) in plan where sponsor imposed a prior authorization restriction for SGA	4
Lundberg et al,[80] 1999	1 year before and 6 years after reclassification	20000 inhabitants (the National Corporation of Swedish Pharmacies and Centre for Primary Care Research at Uppsala University, 1988 – 1995)	Tierp, Sweden	All nasal sprays containing oxymetazoline or xylometazoline (1989)	Number of packages sold per 1000 inhabitants; number of dispensed prescriptions per 1000 inhabitants	Sales of nasal drop decreased from 408 packages per 1000 inhabitants in 1988 to 30 packages per 1000 inhabitants in 1995; sale of nasal spray package per 1000 inhabitants increased from 152 packages in 1988 to 669 packages in 1995; prescriptions per 1000 inhabitants decreased from 143 prescriptions in 1988 to 37 prescriptions in 1992	4

Table 1.2 (cont) Studies examining the association between medicine reclassification and sale of over the counter medicine or prescribing

Source	Study design	Sample	Setting	Medicine reclassified	Unit of measure	Outcomes	Level of evidence
Andrade et al,[81] 1999	12 months before and 12 months after reclassification	2028 chronic users of H_2 antagonists (Fallon Community Health Plan database, 1994 – 1996)	Central and Eastern Massachusetts, US	Famotidine, cimetidine, and ranitidine (1995)	Mean absolute difference in frequency of drug dispensed	One year after the availability of OTC H_2 antagonists the mean absolute number of prescriptions dispensed for H_2 antagonists and all gastrointestinal agents was reduced by 1.5 ($p < 0.001$) and 1.3 prescriptions ($p < 0.001$), respectively	4
Carlsten et al,[82] 1997	2 year before and 2 years and 4 years after reclassification (interval depends on medicine studied)	Invoices for drug delivered to pharmacies; 1 in 288 (1 in 25 from 1988) stratified random sample drawn from all prescriptions dispensed in Sweden (National Prescription Survey, 1980 – 1994)	Sweden	16 drugs* (1980 – 1992)	The 12 month average number of defined daily doses (DDD)	Except for oxymetazoline spray and sodium cromoglycate a medicine reclassification led to an increase in overall sales. The increase 2 years after reclassification for individual medicines ranged from 12% to 309%; 4 years after the reclassification the changes in overall sales of the individual drugs ranged from -54% to 52%	

*Oxymetazoline (1981), hydrocortisone (1983), clotrimazole (1983), Econazole (1983), miconazole (1983), lignocaine (1987), ibuprofen (1988), oxymetazoline (1989), xylometazoline (1989), loperamide (1989), nicotine (1990), sodium fluoride (1991), oestriol (1991), hydrocortisone-miconazole (1992), loratadine (1992), sodium cromoglycate (1992)

Medicines in different therapeutic classes were studied over different time periods and in different countries. Two of the studies that were reviewed[79, 81] only examined the impact of medicines reclassification on prescription medicine utilisation whilst the remaining two[80, 82] measured both prescription utilisation and sales of OTC medicines. Of particular interest was the study by Sullivan et al,[79] which examined the effect of loratadine reclassification on prescription drug utilisation in different cost sharing (pharmacy benefit) structures. The results suggested there was a substantial decrease in utilisation and cost for prescription of second generation antihistamines after the reclassification regardless of the status changes in pharmacy benefits. However, due to the lack of data on sales of OTC medicines, this study failed to identify if patients who decreased their utilisation of prescription second generation antihistamines had switched to use OTC loratadine or a first generation antihistamine. Similarly, the inability to determine the actual use of OTC H_2 receptor antagonists limited the findings of a study by Andrade et al,[81] which showed that the reclassification of H_2 receptor antagonists reduced the number of prescriptions for those agents dispensed among a population of chronic users.

Carlsten et al,[82] studied a large number of medicines reclassified in Sweden over 12 years. However, the source of the sales data was not well defined and the sampling ratio of prescription data collected was not consistent during the study period. In addition, the results were only presented with descriptive figures and no statistical analysis.

Lundberg et al[80] studied the impact of the availability of OTC oxymetazoline nasal spray on several parameters, including the prescription of oxymetazoline nasal spray

over a 6-year period following reclassification. By measuring both prescribing and OTC sales, the authors suggested the decrease in prescribing and increase in sales after reclassification indicated an extended use of OTC medicine. This may reflect an increase in consumer interest in self medication.

In summary, the studies reviewed consistently showed that medicines reclassification was associated with increased sales of medicines and reduced prescription drug utilisation. Whether this relationship extends to recently reclassified medicines in the UK needs to be explored.

1.3 Deprivation

Several different measures of socioeconomic status or deprivation have been, and continue to be used in health research.[83] These range from individual measures based on income, education and occupation to area based measures. Examples of area based measured are the Jarman index which uses unemployment, number of persons that are unskilled, overcrowding in households, single parent families, population under the age of 5, lone pensioners, 1-year immigrants and ethnic minorities);[84] the Townsend index which uses unemployment, number of households that do not own a car, overcrowding in households, and the number of households that are non-owner occupied;[85] and the Index of Multiple Deprivation (IMD) which uses income, employment, health and disability, education, skills and training, barriers to housing and services, living environment, and crime.[86]

1.3.1 Impact of deprivation

Socioeconomic status or deprivation are recognized as major factors affecting health and healthcare utilisation. This has arisen because of the association between morbidity, poor socioeconomic status and deprivation.[87-90] Patients with lower education tend to live in poorer areas, suffer more ill health, and have higher GP consultation rates than those from a higher socioeconomic group.[91-93] The association between socioeconomic status, deprivation and access to medicines or medication utilisation will be reviewed in the following section.

1.3.2 Review of relevant literature

Two hundred and forty one English language articles were identified in Medline database search (via Ovid) and covered the period January 1996 to September 2007. The following standard medical subject headings (MeSH) were used in the search: "social class or income or education or occupations or socioeconomic factors or poverty or deprivation" and "primary health care or physician's practice pattern, or drug utilization or prescription, drug or drugs, non-prescription"

Abstracts and, in some cases, the full text of the 64 articles that passed the screening of the titles of the articles were examined. Of the 64 articles, 11 reported on the association of socioeconomic status or deprivation with access to medicines or medication utilisation and these were selected for review in the present study (Table 1.3). Five studies examined individual level of socioeconomic status and six examined area based level of deprivation. Different socioeconomic/deprivation indicators were used in the 11 studies reviewed.

Table 1.3 Studies examining the association between socioeconomic/deprivation and drug utilisation or prescribing

Source	Study design	Sample	Setting	Socioeconomic/ deprivation parameter	Unit of measure	Outcomes	Level of evidence
Mortensen et al,[94] 2007	Cross sectional (pharmacoepide-miological prescription database, 1999)	385879 patients (aged 18 years or older)	North Jutland County, Denmark	Socioeconomic status based on income/social benefits, employer, occupation and education	Number of redeemed prescriptions	People in the upper half of the socioeconomic scale (self employed, top manager, upper and intermediate level salaried employees) were less likely than those with basic level employees to redeem prescriptions for treating muscle, joints and bone (e.g. 95% CI, 0.71 to 0.84 for male top managers), and central nervous system (e.g. 95% CI, 0.78 to 0.90 for male upper level salaried employees)	6
Blais et al,[95] 2006	Cohort (administrative health database, 1997 – 1999)	21564 children (5 – 12 years) and 7454 adolescent (13 – 17 years) with asthma	Quebec, Canada	Family's socioeconomic status was measured by dichotomous variable: families receiving social assistance (low-income) or families with working parents (higher-income)	Adherence to Canadian Asthma Guidelines	Low-income children had lower rates of adherence than higher-income children (76% v 80%; $p < 0.001$); low-income adolescents had similar rates of adherence as higher income adolescents (67% v 68%; $p = 0.4$)	4

Table 1.3 (cont) Studies examining the association between socioeconomic/deprivation and drug utilisation or prescribing

Source	Study design	Sample	Setting	Socioeconomic/ deprivation parameter	Unit of measure	Outcomes	Level of evidence
Ashworth et al,[96] 2006	Cross sectional (Prescribing Analyses and Cost database, 2004 – 2005)	8430 general practices	England	Index of Multiple Deprivation (IMD) 2004 which is described according to: income, employment, health and disability, education skills, barriers to housing and services, crime and living environment	Cost (net ingredient cost) and volume (average daily quantity) of statins prescribing	After adjustment for increased disease prevalence and practice variables, social deprivation scores (IMD score) was significantly ($p < 0.001$) correlated with the volume of statins prescribing (standardized adjusted regression coefficient = 0.24)	6
Williams et al,[97] 2003	Cross sectional (Pharmacy claims data, 1999 – 2000)	181647 patients that eligible for free health service (General Medical Services scheme)	Eastern Regional Health Authority, Ireland	Material deprivation derived from five indicators from the 1996 Irish census, which include unemployment, low social class, car ownership, rented accommodation and overcrowding	Prescribing rate presented as age-sex standardised prescription ratios (SPRs) for each District Electoral Division (DED)	Prescribing rates increased with increasing material deprivation for anti-asthma preparations, insulin, oral hypoglycaemic agents, nitrate therapy, antiulcer preparations and benzodiazepines whilst prescribing rates fell with increasing material deprivation for antipsychotic agents, antiparkinsonian drugs, antiepileptic agents and antidepressive agents (all $p < 0.01$)	6

Table 1.3 (cont) Studies examining the association between socioeconomic/deprivation and drug utilisation or prescribing

Source	Study design	Sample	Setting	Socioeconomic/ deprivation parameter	Unit of measure	Outcomes	Level of evidence
Senior et al,[98] 2003	Cross sectional (the prescribing support unit, 1997)	131 general practices	Bro-Taf Health Authority, Wales	Deprivation was measured by Townsend score	Cost and number of items	Material deprivation showed a consistent, positive influence on prescribing costs and items for the prescribing of antidepressants, bronchodilators, inhaled corticosteroids and oral antidiabetics, with the exception of items (but not cost) of insulin	6
Nielsen et al,[99] 2003	Cross sectional (the Danish Health and Morbidity Survey, 2000)	16690 adult population aged 16 years and above	14 Danish counties, Denmark	Socioeconomic position was measured by occupation, education and personal income	Use of prescription medicine or OTC medicine within 14 days	After adjusting for age and gender, occupation showed a significant correlation with prescription medicine ($p < 0.0001$) and OTC medicine use ($p = 0.004$); income was associated with prescription medicine use ($p < 0.0001$), but not with the use of OTC medicine ($p = 0.49$); use of prescription medicine was associated with education among men ($p = 0.004$) but not women ($p = 0.31$); use of OTC medicine and education were not associated	6

Table 1.3 (cont) Studies examining the association between socioeconomic/deprivation and drug utilisation or prescribing

Source	Study design	Sample	Setting	Socioeconomic/ deprivation parameter	Unit of measure	Outcomes	Level of evidence
Finley et al,[100] 2001	Cross sectional (mailed questionnaire)	469 women (61% response rate) aged 50 – 70 years	Vermont or New York, US	Socioeconomic status was presented as household income and education level	Reported taking hormone replacement therapy (HRT) in the past 30 days	After adjustment for age, women with annual household income of $35000 or more were 2.7 times (95% CI, 1.3 to 5.6) more likely to use HRT than women with the lowest income group (< $15000); women with advanced education degree were more likely to be on HRT than those with a high school education or less (95% CI, 0.9 to 3.5)	6
Kozyrskyj et al,[101] 2001	Cohort (prescription and health care data, 1995 – 1996)	12481 children (5 – 15 years)	Manitoba, Canada	Socioeconomic status was categorized by neighbourhood income quintiles (aggregated household income data within the enumeration area from the Statistics Canada Census 1996)	The receipt of a new prescription for an inhaled corticosteroid following 6 months of no use	In comparison with higher-income children, the adjusted likelihood ratio for a new inhaled corticosteroid prescription was 0.88 (95% CI, 0.80 to 0.97) in low-income children insured through the same cost sharing drug plan	4

Table 1.3 (cont) Studies examining the association between socioeconomic/deprivation and drug utilisation or prescribing

Source	Study design	Sample	Setting	Socioeconomic/ deprivation parameter	Unit of measure	Outcomes	Level of evidence
Packham et al,[102] 1999	Cross sectional (Prescribing Analyses and Cost database, 1996)	114 general practices	Nottingham, England	Deprivation measured by Townsend and Jarman UPA(8) score derived from the 1991 Census	Average daily quantity	Practices with higher level of deprivation, according to Townsend and UPA(8) score, had significantly lower levels of statin prescribing per 1000 population aged 35 – 69 (both $p < 0.0001$)	6
Majeed et al,[103] 1999	Cohort (Prescribing Analyses and Cost database, 1992 – 1998)	100 health authorities	England	Jarman deprivation score obtained from Department of Health (1997)	Number of prescribed items per specific therapeutic group age-sex related prescribing units (STAR-PUs); ratio of inhaled steroids to beta-2 agonists	At health authority level, the number of items of inhaled beta-2 agonists was associated with deprivation ($r = 0.33$; $p = 0.001$); there were significant negative correlations between the ratio of inhaled steroids to beta-2 agonists and Jarman deprivation scores ($r = -0.51$; $p < 0.0001$)	4
Hawkey et al,[104] 1997	Cohort (Prescribing Analyses and Cost database, 1986 – 1991)	103 general practices	Nottingham, England	Deprivation index according to York Health Consortium Criteria (1 – 7 grade)	Prescribing rates in November in consecutive years	Higher index of deprivation was associated with lower NSAIDs prescribing rates (95% CI, 0.96 to 0.97; $p < 0.001$)	4

Mixed results were found from the studies reviewed. A small survey[100] showed that women with lower income were less likely to use hormone replacement therapy (HRT) than women with higher income. Similar findings were reported by two publications from Canada,[95, 101] which showed low usage of inhaled medication, specifically inhaled corticosteroids, in children with asthma from families with low socioeconomic status. The socioeconomic indicators used in these studies were income related and likely to be associated with different social issues that might influence access to medical care, such as the educational attainment of the parents and the understanding of the disease.

However, it was found in another study[99] that neither income nor education showed consistent associations with the use of medicines. When occupation or income were used as indicators of socioeconomic status they showed that groups with lower socioeconomic status had the highest use of prescription medicines. Using education as the indicator of socioeconomic status no gradient of association was demonstrated for women, although the association for men was stronger in those who had undergone further education. It is possible that education may capture aspects of social status to a greater extent than occupation or income.

A combination of individual level indicators such as income/social benefits, employer, occupation and education were studied in one paper reviewed.[94] This showed that individuals with high socioeconomic status were less likely than those with lower socioeconomic scores to have their prescription dispensed if it was for medicines to treat musculoskeletal or central nervous system disorders.

In the remaining six papers reviewed, different indicators of socioeconomic status were grouped to represent area based deprivation. Again, wide variations in outcomes were observed as deprivation showed a positive correlation with the prescribing of some medicines and a negative correlation with others. Of interest are contradictory results from two studies[96, 102] which evaluated the association of deprivation with the prescribing of statins.

Ashworth et al[96] found that those general medical practices serving more deprived communities prescribe higher volumes of statins. In contrast, others[102] have shown that practices in areas with higher deprivation indices prescribed fewer statins than less deprived practices. Major differences between the two studies including the deprivation indices used (Index of Multiple Deprivation 2004 v Townsend and Jarman UPA [Under-privileged area] score), sample size (8430 v 114 general practices), and year of data collection (2004 to 2005 v 1996), all of which could have contributed to the different outcomes observed.

Overall, variations in association between socioeconomic status/deprivation and either access to medicines or medication utilisation may be real or influenced by the different indicators used, the status of the medication (prescription or OTC), the therapeutic class of the medicine, and the organisation of the healthcare structure. However, none of the studies reviewed have examined the association between social deprivation and changes in the prescribing rate or sale of recent reclassified medicines. This will form the basis of the present study which will focus on the impact of the reduction of the prescription charge in Wales and the sales of a number of reclassified medicines.

1.4 Study Aims

The aims of the present study were to explore the impact of changes in prescription charge policy and medicines reclassification on the volume of selected medicines prescribed in primary care and the sale of over the counter medicines from community pharmacy.

CHAPTER 2

REDUCTION OF THE PRESCRIPTION CHARGE IN WALES

Our pledge to provide free prescriptions for everyone in Wales will benefit the whole population and will help improve health in Wales (Jane Hutt, 1949 –; Minister for Health and Social Services, Wales).

2.1 Introduction

The imposition of a prescription charge in the UK is arguably incompatible with the principles of the NHS.[105, 106] Whatever the rights and wrongs of this statement it is evident the system used in recent years across the UK to determine those patients who pay for their prescription and those who are exempt is unfair.[107] This may, of course, be simply due to the fact that the exemption criteria were set out in 1968 and have remained relatively unchanged since.[105] Updating these criteria may not, however, resolve the inequity the current system has produced nor address the concerns of those who perceive the prescription charge as an indirect tax. It has also been questioned whether the prescription charge generates much income for the Government considering the associated administration and transaction costs such as the cost of handling the pre-payment certificate, and the hidden legal costs of prosecuting those who try to avoid charge evasion.[108]

2.1.1 Abolition of the prescription charge

The unified approach to the prescription charge started to come to an end in 1998 following the devolution of power from the UK central government to each of the

constituent countries.[109] In the case of Wales the responsibility for the provision of health services was transferred to the National Assembly for Wales.[110] Initially it was uncertain whether the right to abolish the prescription charge in Wales was within the power of the Assembly.[111] However, in 2000, the National Assembly for Wales took its first step and announced the prescription charge in Wales was to be held at £6 per item. In the following year, in April 2001, the prescription charge for all Welsh residents aged less than 25 years was abolished.

In the run up to the National Assembly for Wales elections in 2003 the Labour party in Wales announced it would abolish the prescription charge if it was returned to power. After winning that election the Labour party duly announced prescription charges in Wales would be abolished by the year 2007 and this was to be introduced in phases. In October 2004, the prescription charge was reduced from £6 to £5. There were further reductions to £4 in April 2005 and £3 in April 2006 prior to abolition in April 2007. Wales was the first, and remains the only country in the UK to take this step although Scotland has recently announced a similar intent. [112]

2.1.2 Impact of the abolition of prescription charge

The prescription charge was first introduced in 1952, four years after the founding of the NHS in 1948.[113] Across the UK the prescription charge has been in place since that date with the exception of a brief period when it was abolished in 1965. This abolition of the prescription charge in 1965 coincided with a sharp rise in the number of prescriptions dispensed and this continued unabated until the prescription charge was re-instated in 1968 (Figure 2.1).

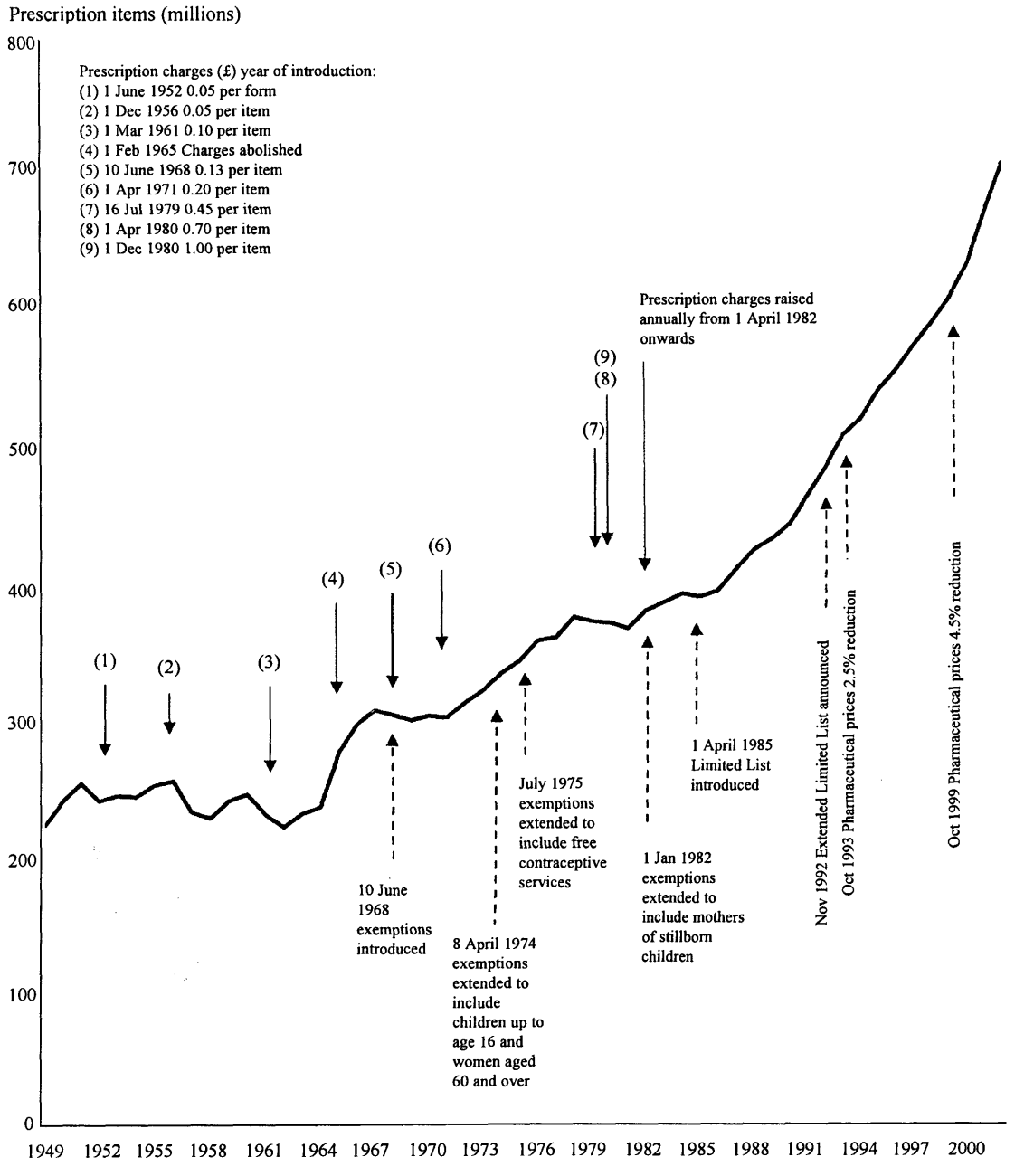


Figure 2.1 NHS prescription charges and items dispensed by chemists and appliance contractors, UK, 1949 – 2002[114]

2.1.2.1 Government perspective

The decision to abolish the prescription charge in Wales was calculated to benefit around 11% those receiving a prescription who would have previously had to pay the prescription charge. It would also result in the loss of more than £30 million in prescription charge revenue each year to the health service in Wales.[115] However, the cost of abolishing the prescription charge was probably much less than the associated administration costs of collecting the charge and checking for fraudulent claims. It could also be argued that getting rid of the prescription charge would remove the financial barrier that was thought to prevent some patients obtaining the medicines they had been prescribed. As a consequence this could improve health, reduce hospital admissions and thereby generate a net saving for the health service. The Welsh Assembly Government also gained some credit as the abolition of prescription charge got rid of an inequity in the health care system.[106]

2.1.2.2 Healthcare professional perspective

On the announcement of the abolition of the prescription charge there was concern that this could perversely increase the workload of GPs.[116] It was also assumed that their prescribing pattern would change with the removal of any concern the prescriber may have previously had regarding the financial strain imposed on their patients.[117] From the community pharmacy perspective there were additional concerns that the abolition of the prescription charge would discourage individuals from purchasing OTC medicines and thereby impact on their non-NHS income.[106]

2.1.2.3 Individual perspective

It was anticipated that the introduction of free prescriptions would remove a barrier for some patients to have their prescription dispensed. A survey[118] of 1,085 patients who had paid a prescription charge in the previous 12 months revealed that up to half of the respondents found it difficult to afford the prescription charge. In addition, 28% did not have all their prescribed medicine dispensed due to the cost of the prescription charge, and, importantly, this figure increased to 37% for people with a long term health problem. It was therefore expected that the abolition of the prescription charge would increase the uptake of prescriptions, and allow all patients to receive the medication intended.[106]

There were also concerns that not having to pay the prescription charge would encourage patients to visit their GP to obtain the item on a free prescription rather than purchase a non-prescription medicine for self care. If such an approach was adopted it would be contrary to the wishes of the UK Government[4, 6] in their endeavours to promote self care and shift some of the burden of the NHS bill for prescribing medicines onto the patient.[52-54]

Overall, it was anticipated that the reduction and subsequent abolition of the prescription charge in Wales would remove a deterrent for some to obtain their prescribed medicines. In addition, it was also predicted it would change health seeking behaviour by encouraging individuals to request a prescription for an item they may otherwise have purchased.

Although the Welsh Assembly Government would have a monitoring system in place to observe any change in prescribing patterns after the reduction and subsequent abolition of the prescription charge, there was no proposed study in place to monitor and compare prescribing in Wales with that in England. The present study therefore was established to carry out a comparative analysis of prescribing patterns in Wales and England.

2.2 Aims

The aims of this study were to determine i) the impact on the pattern of prescribing in primary care on the phased reduction of the prescription charge in Wales; and ii) the additional influence, if any, deprivation may have on this.

2.3 Method

2.3.1 Design

A cross-sectional study was undertaken that involved a retrospective analysis of prescriptions dispensed in primary care over the period October 2001 to September 2006, i.e. three years before and two years after the first reduction of the prescription charge. There were two main study designs to achieve the aims of the study and these are detailed below.

2.3.1.1 Changes in prescribing pattern

To identify the impact of the phased reduction of the prescription charge in Wales on the pattern of prescribing in primary care the percent change in the number of dispensed prescription items for each medicine studied were compared before and after the reduction of the prescription charge in three settings: (1) groups of Primary Care Organisations (PCOs; known as Local Health Boards [LHBs] in Wales and Primary Care Trusts [PCTs] in England) with a comparable population size to that of Wales but drawn from the North East of England and the South East of England; (2) groups of PCOs in Wales and England with similar rank of deprivation; and (3) groups of LHBs in Wales with contrasting levels of deprivation.

PCOs with comparable population size

Dispensed prescription data for all 22 LHBs in Wales (2.9 million population) were compared with groups of PCTs in the South East and the North East region of England. PCTs in the South East of England were selected by random number generation using SPSS version 14 to represent a population of between 2.5 to 3.0

million and be comparable in size to that of Wales. Fifteen PCTs in the South East of England (2.5 million population) and all 16 PCTs in the North East of England (2.5 million population) were included in the study. Below are the LHBs in Wales and PCTs in the South East and the North East of England used in the study:

Wales: Anglesey (Ynys Mon), Blaenau Gwent, Bridgend, Caerphilly, Cardiff, Carmarthenshire, Ceredigion, Conwy, Denbighshire, Flintshire, Gwynedd, Merthyr Tydfil, Monmouthshire, Neath Port Talbot, Newport, Pembrokeshire, Powys, Rhondda Cynon Taff, Swansea, Torfaen, Vale of Glamorgan, and Wrexham

South East of England: Adur Arun & Worthing Teaching, Bexhill & Rother, Brighton & Hove City, Crawley, Eastbourne Downs, Elmbridge East & Mid Surrey, Guildford & Waverley, Hastings & St Leonards, Horsham & Chanctonbury, Mid Sussex, Surrey East, Surrey North, Surrey Heath & Woking, Sussex Downs & Weald, and Sussex West

North East of England: Darlington, Derwentside, Durham and Chester-le-Street, Durham Dales, Easington, Gateshead, Hartlepool, Langbaurgh, Middlesbrough, Newcastle, North Tees, North Tyneside, Northumberland Care Trust, Sedgefield, South Tyneside, and Sunderland Teaching

PCOs with similar deprivation rank

Data for limiting long term illness (LLTI) in local authorities in Wales and England were extracted from Census 2001 and used as a proxy marker for deprivation. In Wales, boundaries of local authorities are coterminous with those of their LHB and the five local authorities/LHBs in Wales with the highest scores for LLTI were

selected and included: Blaenau Gwent, Caerphilly, Merthyr Tydfil, Neath Port Talbot, and Rhondda Cynon Taff. In England, the five local authorities with the highest reported LLTI and with boundaries coterminous with those of their PCT were chosen and included: Barnsley, Derwentside, Easington, Knowsley, and Sedgefield.

LHBs in Wales with contrasting levels of deprivation

The five most deprived LHBs in Wales and the five least deprived LHBs were selected based on the percentage of their Lower Super Output Areas (LSOAs) that fell into the most deprived 20% in Wales for all deprivation measures according to the Welsh Index of Multiple Deprivation (WIMD) 2005. Consequently the five most deprived LHBs were Blaenau Gwent, Caerphilly, Merthyr Tydfil, Neath Port Talbot, and Rhondda Cynon Taff, and the five least deprived LHBs included Ceredigion, Gwynedd, Monmouthshire, Powys and Vale of Glamorgan.

The terms "LLTI" and "WIMD" were used to distinguish deprivation measured by different indicators in comparative groups of PCOs stated above.

2.3.1.2 Influence of deprivation

The association of deprivation, using WIMD 2005 as an indicator, with any change in the pattern of prescribing after the first reduction of the prescription charge was explored for the 22 LHBs in Wales.

2.3.2 Unit of measure

The primary measure for the prescribing of medicines utilized in this study was dispensed prescription items per 1000 population. Population size was used as the denominator for all calculations.

2.3.3 Medicines studied

The following criteria were used to select the medicines studied:

- Classified as P or GSL;
- Widely used for self-management of disorders; and
- Widely prescribed in primary care practice

The medicines subsequently selected included loperamide, laxatives, non-sedating antihistamines and fluconazole (see section 4.4.3 for explanation of exclusion criteria).

2.3.4 Data

Data for the variables studied were obtained from different sources and these are detailed below.

2.3.4.1 Dispensed prescription data

Wales

Dispensed prescription data for Wales from October 2001 to September 2006 were obtained from the CASPA (Comparative Analysis System for Prescribing Audit) database maintained and updated by Health Solutions Wales. This database includes details of all NHS prescriptions in Wales issued by GPs and dispensed by community pharmacists, dispensing GPs or appliance contractors.

England

Dispensed prescription data for selected PCTs in England were obtained in a quarterly format supplied in Microsoft Excel by the Prescription Pricing Division (PPD). Data were not obtained on the same occasion and consequently the timescales for the datasets varied due to PPD data storage issues. The timescales over which prescription data for medicines were studied included:

- October 2001 to September 2006: non-sedating antihistamines (obtained in October 2006)
- April 2002 to September 2006: loperamide (obtained in March 2007), laxatives (obtained in May 2007), and fluconazole (obtained in March 2007)

2.3.4.2 Population data

Population data for each Welsh LHB were extracted from the Census 2001 (Appendix 1). Population data for PCTs in England were obtained directly from the PCT website.

2.3.4.3 Deprivation data for Wales

Although, there are no official deprivation scores at local authority/LHB level in Wales, this study derived deprivation scores from the percent LSOAs in each LHB amongst the most deprived 20% in Wales (Appendix 2).

2.3.5 Data organisation

Data organisation was the process of changing the original dispensed prescription data into a format that allowed statistical analysis over a specific period. The analysis was set out to identify the difference in the percent change in the number of prescription items dispensed in the 24 months before and 24 months after the first reduction of the prescription charge in Wales in October 2004. To minimise the impact of seasonal trends prescription data for non-sedating antihistamines were aggregated into 12 month blocks (Figure 2.2).

Data for PCTs in England for loperamide, laxatives and fluconazole were supplied from April 2002 to September 2006. Aggregation of these data into 12 month blocks would therefore overlap with October 2004, the month when the prescription charge was first reduced. Therefore, to maximise use of the data supplied medicines data were aggregated into 6 month blocks (Figure 2.3).

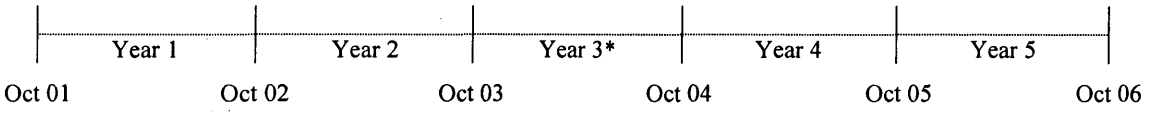


Figure 2.2 Organisation of data into 12 month blocks. *Period immediately prior to the reduction of the prescription in October 2004

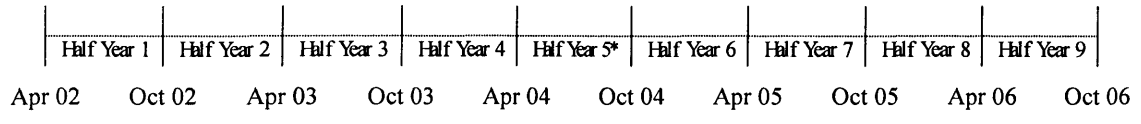


Figure 2.3 Organisation of data into 6 month blocks. *Period immediately prior to the reduction of the prescription in October 2004

Dispensed prescription data for Wales in appropriate time blocks were extracted from the CASPA database and transferred into a Microsoft Excel spreadsheet (Appendix 3). Quarterly data for PCTs in England supplied in Microsoft Excel format were combined into appropriate time blocks.

Codes for each medicine, PCO, and time block were allocated to the organised data. Prescription data for PCTs in England were combined with the organised data for Wales and presented in one Excel spreadsheet for each of the following medicines:

- Loperamide: oral solid dosage forms at strengths indicated for administration to adults (British National Formulary: BNF section 1.4.2)
- Laxatives: all preparations (BNF section 1.6)
- Non-sedating antihistamines: oral solid dosage forms at strengths indicated for administration to adults (BNF section 3.4.1)
- Fluconazole: oral solid dosage forms at strength of 150 mg (BNF section 5.2)

Data were transferred from Excel to Statistical Package for the Social Sciences (SPSS) version 14 for analysis. Prior to analysis, data in SPSS were screened for errors that may have occurred during organisation and coding.

2.3.6 Analysis

Data were analysed by non-parametric statistical tests using SPSS version 14. To determine the effect of the phased reduction of the prescription charge in Wales the percent change in the number of prescription items dispensed before and after the first reduction of the prescription charge were compared. Percent changes were identified by two different approaches depending on the data used i.e. 12 month or 6 month blocks (see section 2.3.5).

2.3.6.1 Data in 12 month blocks

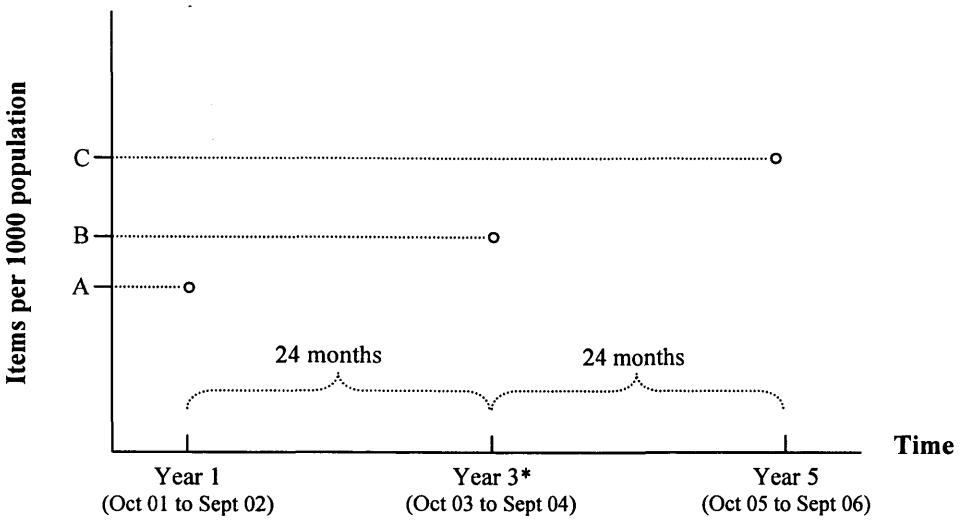
For non-sedating antihistamines, the number of prescription items per 1000 population dispensed in the 12 month periods of October 2001 to September 2002 (Year 1), October 2003 to September 2004 (Year 3) i.e. the 12 months immediately prior to the first reduction of the prescription charge in Wales in October 2004, and the 12 months from October 2005 to September 2006 (Year 5) were determined.

The percent change in the number of prescription items dispensed from Year 1 to Year 3 (24 months before the first reduction of the prescription charge: X) and from Year 3 to Year 5 (24 months after the first reduction of the prescription: Y) were determined (Figure 2.4).

2.3.6.2 Data in 6 month blocks

For loperamide, laxatives, and fluconazole, the number of prescription items per 1000 population dispensed in the 6 month periods of April 2002 to September 2002 (Half Year 1), April 2004 to September 2004 (Half Year 5) i.e. the 6 months immediately prior to the reduction of the prescription charge in Wales in October 2004, and the 6 months from April 2006 to September 2006 (Half Year 9) were determined.

The percent change in the number of prescription items dispensed from Half Year 1 to Half Year 5 (24 months before the first reduction of the prescription charge: X) and from Half Year 5 to Half Year 9 (24 months after the first reduction of the prescription: Y) were determined (Figure 2.5).



* Period immediately prior to the first reduction of the prescription charge

A = number of dispensed prescription items per 1000 population in Year 1

B = number of dispensed prescription items per 1000 population in Year 3

C = number of dispensed prescription items per 1000 population in Year 5

$$X = \frac{(B - A)}{A} \times 100$$

$$Y = \frac{(C - B)}{B} \times 100$$

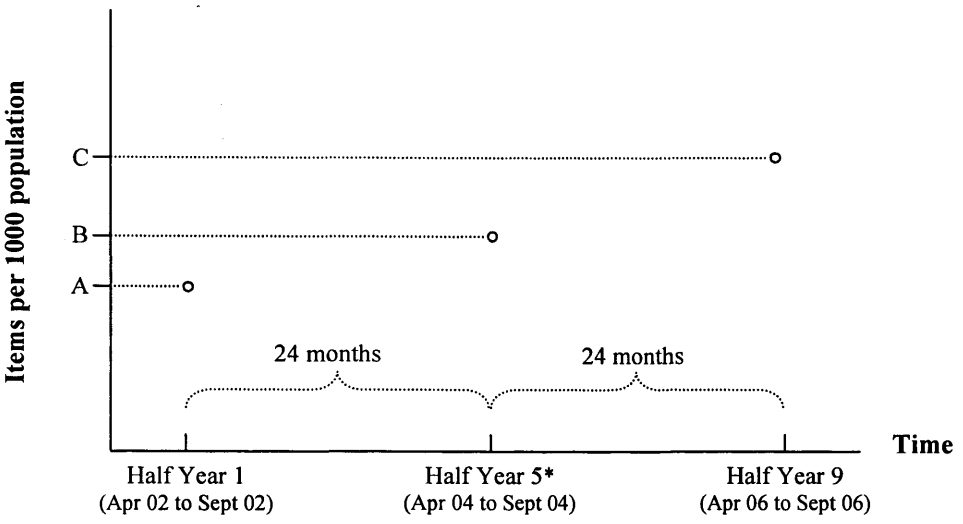
$$Z = Y - X$$

X = percent change in the number of prescription items dispensed 24 months before the first reduction of the prescription charge

Y = percent change in the number of prescription items dispensed 24 months after the first reduction of the prescription charge

Z = difference in the percent change

Figure 2.4 Model to illustrate the calculation of the percent change in the number of dispensed prescription items relative to the first reduction of the prescription charge in Wales for data in 12 month blocks



* Period immediately prior to the first reduction of the prescription charge

A = number of dispensed prescription items per 1000 population in Half Year 1

B = number of dispensed prescription items per 1000 population in Half Year 5

C = number of dispensed prescription items per 1000 population in Half Year 9

$$X = \frac{(B - A)}{A} \times 100$$

$$Y = \frac{(C - B)}{B} \times 100$$

$$Z = Y - X$$

X = percent change in the number of prescription items dispensed 24 months before the first reduction of the prescription charge

Y = percent change in the number of prescription items dispensed 24 months after the first reduction of the prescription charge

Z = difference in the percent change

Figure 2.5 Model to illustrate the calculation of the percent change in the number of dispensed prescription items relative to the first reduction of the prescription charge in Wales for data in 6 month blocks

2.3.6.3 Statistical analysis

The Wilcoxon Signed Rank test was used to determine the difference between percent change in the number of dispensed prescription items in the 24 months before (X%) and 24 months after (Y%) the first reduction of the prescription charge in each setting studied, i.e. the 22 LHBs in Wales, 15 PCTs in the South East of England, 16 PCTs in the North East of England, the five most deprived (LLTI) LHBs in Wales, the five most deprived (LLTI) PCTs in England, the five most deprived (WIMD) LHBs in Wales, and the five least deprived (WIMD) LHBs in Wales.

Differences in the percent change (Z) in the 24 months before and 24 months after the first reduction of the prescription charge between the following groups were compared using the Mann-Whitney U test:

- 22 LHBs in Wales and 15 PCTs in the South East of England
- 22 LHBs in Wales and 16 PCTs in the North East of England
- The five most deprived (LLTI) LHBs in Wales and the five most deprived (LLTI) PCTs in England
- The five most deprived (WIMD) LHBs in Wales and the five least deprived (WIMD) LHBs in Wales

The association between the deprivation score (WIMD 2005) of the 22 LHBs in Wales and the difference in percent change (Z) was investigated using Spearman's rank order correlation coefficient.

The volumes of prescriptions dispensed were expressed as items per 1000 population and presented as median (interquartile range [IQR]). Descriptive results are

presented as tables and boxplots. In each boxplot the line across the inside of the box represents the median value. The length of the box is the interquartile range. The whiskers protruding from the box go out to the smallest and largest values. Results for statistical analysis were presented as p-values and correlation coefficients (r) where appropriate. A p-value of less than 0.05 was considered to be statistically significant.

2.4 Results

The present study involved the analysis of four medicines/groups of medicines from different therapeutic categories. For ease the results are presented according to these four categories:

2.4.1 Non-sedating antihistamines

The number of dispensed prescription items for non-sedating antihistamines across groups of PCOs with comparable population size in Wales, the South East of England and the North East of England are shown for each year of the study in Figure 2.6. Figure 2.7 provides the number of prescription items dispensed in groups of PCOs with similar rank of deprivation in Wales and England, and Figure 2.8 shows the number of prescription items dispensed in groups of LHBs in Wales with contrasting levels of deprivation.

As shown in Table 2.1, the numbers of dispensed prescription items (median [interquartile range]) for non-sedating antihistamines in Wales appeared higher than those in the South East of England and the North East of England at Years 1, 3 and 5. In the five deprived (LLTI & WIMD) LHBs in Wales 133.3 [126.2 – 140.7], 147.1 [133.8 – 150.2] and 168.5 [153.1 – 170.1] prescription items per 1000 population were dispensed at Year 1, 3 and 5 compared to 132.6 [125.8 – 137.9], 137.6 [124.6 – 148.0] and 152.6 [134.0 – 160.7] items per 1000 population in the five deprived (LLTI) PCTs in England, and 115.9 [104.9 – 136.2], 122.5 [114.8 – 150.4] and 141.8 [134.9 – 169.1] items per 1000 population in the five least deprived (WIMD) LHBs in Wales.

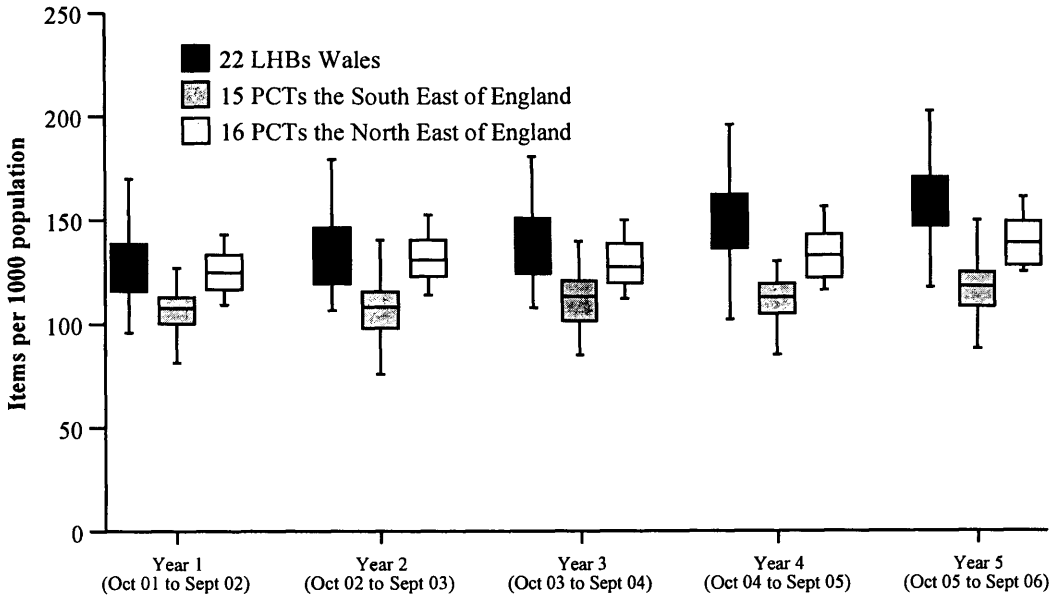


Figure 2.6 Dispensed prescription items for non-sedating antihistamines in Wales, selected PCTs in the South East and the North East of England in five consecutive 12 month periods

Figure 2.7 Dispensed prescription items for non-sedating antihistamines in the five deprived (LLTI) LHBs in Wales and the five deprived (LLTI) PCTs in England in five consecutive 12 month periods

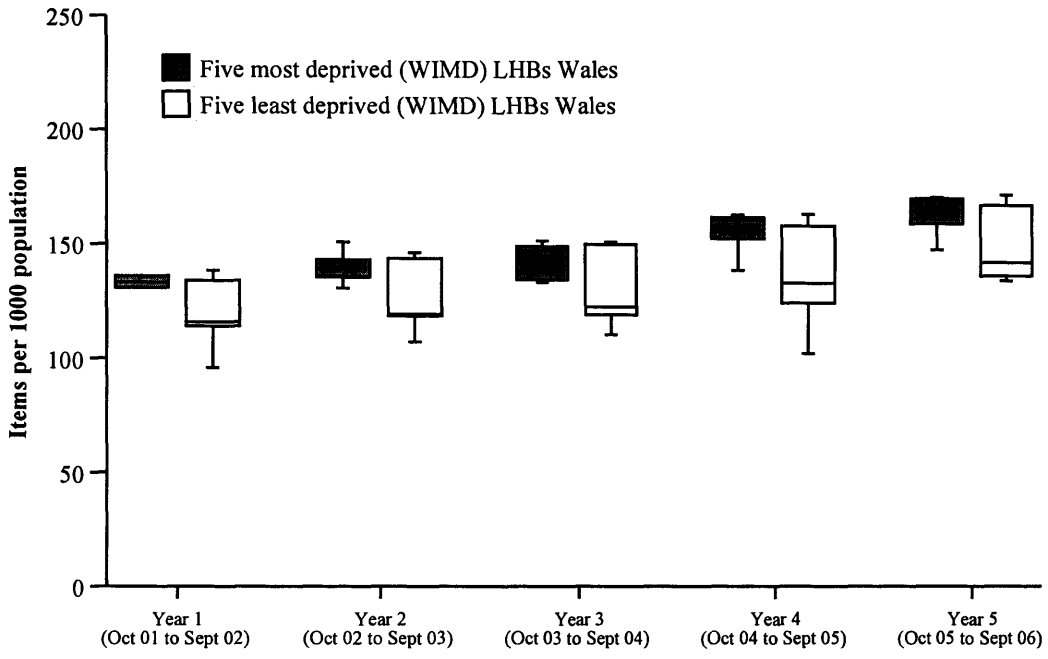


Figure 2.8 Dispensed prescription items for non-sedating antihistamines in the five most deprived (WIMD) and the five least deprived (WIMD) LHBs in Wales in five consecutive 12 month periods

In Wales, the percent change (median [IQR]) in the number of prescription items for non-sedating antihistamines dispensed in the 24 months before (X) the first reduction of the prescription charge was significantly lower than the percent change in the 24 months after (Y) the first reduction of the prescription charge (7.3 [5.0 – 10.7] v 13.7 [10.9 – 17.1], $p < 0.001$) (Table 2.2). In contrast, there was no difference in percent change in the number of prescription items dispensed in the PCTs in the South East of England in the 24 months before and 24 months after the reduction of the prescription charge in Wales (4.5 [0.8 – 7.9] v 4.4 [3.4 – 7.5], $p = 0.73$).

When the difference in percent change (Z; where $Z = X - Y$) between the number of prescription items dispensed for non-sedating antihistamines in the 24 months before and 24 months after the first reduction of the prescription charge in Wales were

Table 2.1 Number of dispensed prescription items per 1000 population for non-sedating antihistamines in three 12 month periods in different settings

	Year 1 (Oct 01 to Sept 02)	Year 3 (Oct 03 to Sept 04)	Year 5 (Oct 05 to Sept 06)
PCOs with comparable populations			
Wales (22 LHBs)	132.1 [115.4 – 139.7]	139.4 [123.9 – 151.0]	158.8 [145.7 – 170.7]
South East of England (15 PCTs)	107.6 [98.0 – 113.1]	113.3 [100.0 – 121.4]	118.0 [105.5 – 128.6]
North East of England (16 PCTs)	124.8 [116.5 – 133.6]	127.4 [119.6 – 141.0]	138.9 [127.7 – 149.8]
PCOs with similar rank of deprivation			
Five deprived (LLTI) LHBs Wales	133.3 [126.2 – 140.7]	147.1 [133.8 – 150.2]	168.5 [153.1 – 170.1]
Five deprived (LLTI) PCTs England	132.6 [125.8 – 137.9]	137.6 [124.6 – 148.0]	152.6 [134.0 – 160.7]
LHBs in Wales with contrasting levels of deprivation			
Five most deprived (WIMD) LHBs	133.3 [126.2 – 140.7]	147.1 [133.8 – 150.2]	168.5 [153.1 – 170.1]
Five least deprived (WIMD) LHBs	115.9 [104.9 – 136.2]	122.5 [114.8 – 150.4]	141.8 [134.9 – 169.1]

Results presented as median [interquartile range] of the dispensed prescription items per 1000 population. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

Table 2.2 Comparison of the percent change in the number of prescription items for non-sedating antihistamines dispensed in the 24 months before and the 24 months after the first reduction of the prescription charge in different settings

	Before	After	p-value[†]
PCOs with comparable populations			
Wales (22 LHBs)	7.3 [5.0 – 10.7]	13.7 [10.9 – 17.1]	< 0.001*
South East of England (15 PCTs)	4.5 [0.8 – 7.9]	4.4 [3.4 – 7.5]	0.73
North East of England (16 PCTs)	2.8 [-1.4 – 6.8]	8.5 [7.1 – 12.2]	0.005*
PCOs with similar rank of deprivation			
Five deprived (LLTI) LHBs Wales	9.5 [2.9 – 10.4]	13.1 [10.9 – 17.5]	0.08
Five deprived (LLTI) PCTs England	3.8 [-1.3 – 7.9]	8.6 [0.7 – 8.8]	0.08
LHBs in Wales with contrasting levels of deprivation			
Five most deprived (WIMD) LHBs	9.5 [2.9 – 10.4]	13.1 [10.9 – 17.5]	0.08
Five least deprived (WIMD) LHBs	9.0 [5.1 – 13.5]	14.3 [11.5 – 19.4]	0.04*

Results presented as median [interquartile range] of the percent change in the number of dispensed prescription items for non-sedating antihistamines. *Statistically significant; [†]Wilcoxon Signed Rank test. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

compared to the South East of England, the change was significantly greater in Wales than in the South East of England (5.6 [2.4 – 8.4] v 0.2 [-3.4 – 2.0], $p < 0.001$) (Table 2.3).

A similar pattern to Wales was found in the North East of England as the percent change in the number of prescription items for non-sedating antihistamines dispensed in the 24 months before the first reduction of the prescription charge was significantly lower than the percent change 24 months following this period (2.8 [-1.4 – 6.8] v 8.5 [7.1 – 12.2], $p = 0.005$).

The percent change in the number of prescription items for non-sedating antihistamines dispensed in the 24 months before and the 24 months after the first reduction of the prescription charge were not different in the five deprived (LLTI) LHBs Wales (9.5 [2.9 – 10.4] v 13.1 [10.9 – 17.5], $p = 0.08$) when compared to the five deprived (LLTI) PCTs England (3.8 [-1.3 – 7.9] v 8.6 [0.7 – 8.8], $p = 0.08$).

No association was found between the difference in percent change (Z) of items dispensed for non-sedating antihistamines in each LHB calculated from the two 24 month periods and the deprivation score (WIMD) of each LHB ($r = -0.14$, $p = 0.54$). However, comparison of the percent change of items dispensed for non-sedating antihistamines in the five least deprived (WIMD) LHBs with the five most deprived (WIMD) LHBs did reveal a difference. The percent change in the number of prescription items for non-sedating antihistamines dispensed in the five least deprived (WIMD) LHBs increased significantly from 9.0 [9.1 – 13.5] in the 24 months before the first reduction of the prescription charge to 14.3 [11.5 – 19.4]; p =

Table 2.3 Comparison of the difference in percent change (Z) in the number of prescription items for non-sedating antihistamines from the 24 months before and the 24 months after the first reduction of the prescription charge between each of the two settings

	Difference percent change (Z)	p-value†
PCOs with comparable populations		
Wales (22 LHBs)	5.6 [2.4 – 8.4]	< 0.001*
South East of England (15 PCTs)	0.2 [-3.4 – 2.0]	
Wales (22 LHBs)	5.6 [2.4 – 8.4]	0.94
North East of England (16 PCTs)	6.8 [2.5 – 9.6]	
PCOs with similar rank of deprivation		
Five deprived (LLTI) LHBs Wales	5.6 [1.4 – 12.7]	1.00
Five deprived (LLTI) PCTs England	7.1 [0.7 – 8.8]	
LHBs in Wales with contrasting levels of deprivation		
Five most deprived (WIMD)LHBs	5.6 [1.4 – 12.7]	1.00
Five least deprived (WIMD) LHBs	7.8 [2.0 – 8.9]	

Results presented as median [interquartile range] of the difference in percent change (Z). *Statistically significant; †Mann-Whitney U test. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

0.04, in the 24 months after the first reduction of the prescription charge. In contrast, the percent change in the number of prescription items dispensed in the five most deprived (WIMD) LHBs 24 months before and 24 months after the first reduction of the prescription charge were not different (9.5 [2.9 – 10.4] v 13.1 [10.9 – 17.5], p = 0.08).

2.4.2 Loperamide

The number of prescription items for loperamide dispensed in each six month block of the study (Half Year 1 to Half Year 9) for groups of PCOs with comparable populations, groups of PCOs with similar rank of deprivation and groups of LHBs in Wales with contrasting levels of deprivation are illustrated in Figures 2.9, 2.10, and Figure 2.11, respectively.

In Wales, the number of dispensed prescription items per 1000 population for loperamide were 16.8 [14.7 – 19.6] in April to September 2002 (Half Year 1), 17.1 [15.2 – 19.2] in April to September 2004 (Half Year 5), and 17.0 [15.8 – 19.4] in April to September 2006 (Half Year 9) (Table 2.4). Over the same period, the number of dispensed prescription items in the selected PCTs in the South East of England were 10.0 [7.9 – 12.4], 11.2 [8.8 – 12.7] and 11.5 [9.9 – 14.7], and in the North East of England were 14.6 [11.9 – 16.1], 15.2 [12.5 – 16.8], and 16.2 [14.0 – 17.9], respectively. It appeared that the number of dispensed prescription items for loperamide in the five deprived (LLTI) LHBs in Wales were higher than those in the five deprived (LLTI) PCTs in England.

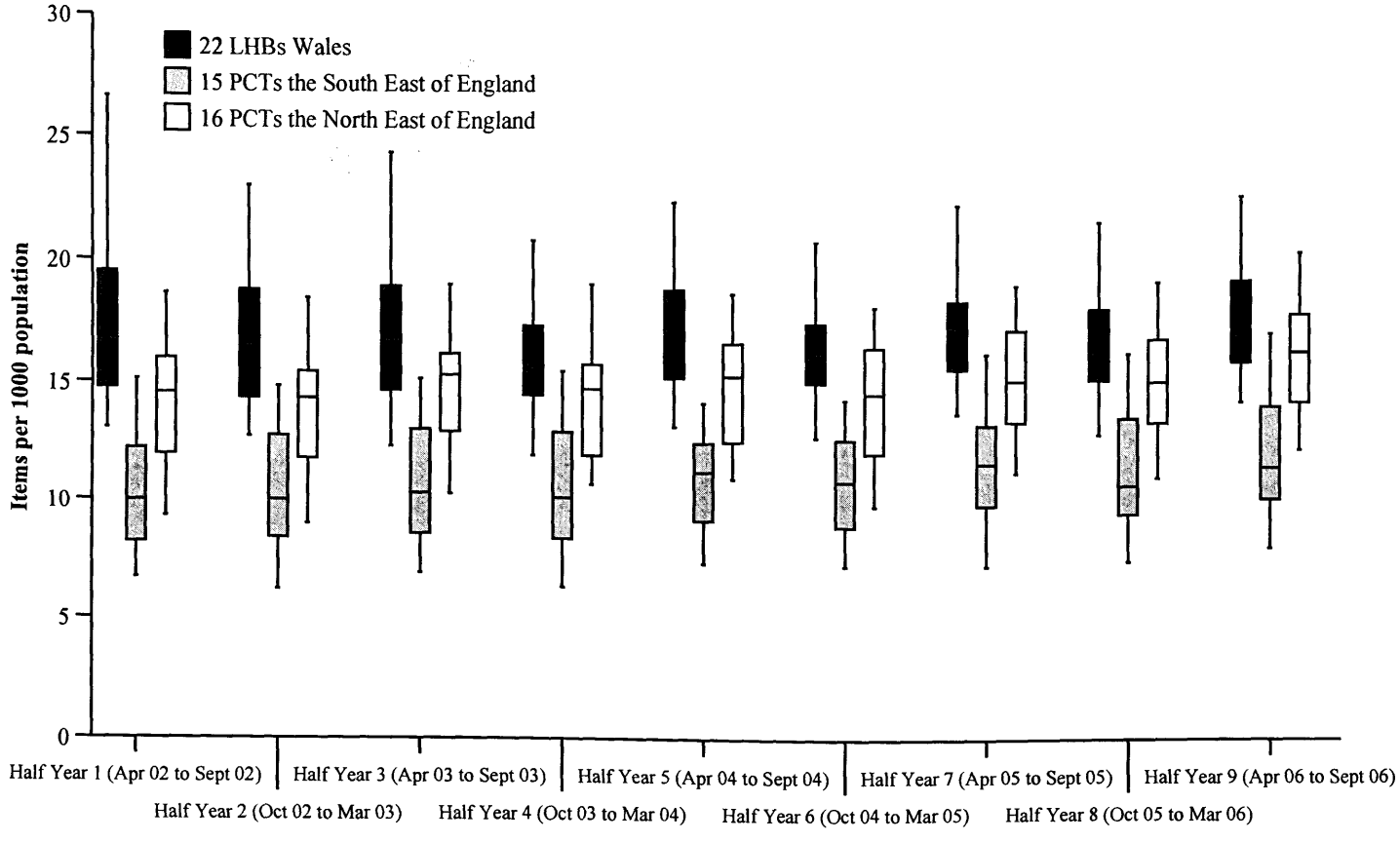


Figure 2.9 Dispensed prescription items for loperamide in Wales, selected PCTs in the South East and the North East of England in nine consecutive 6 month periods

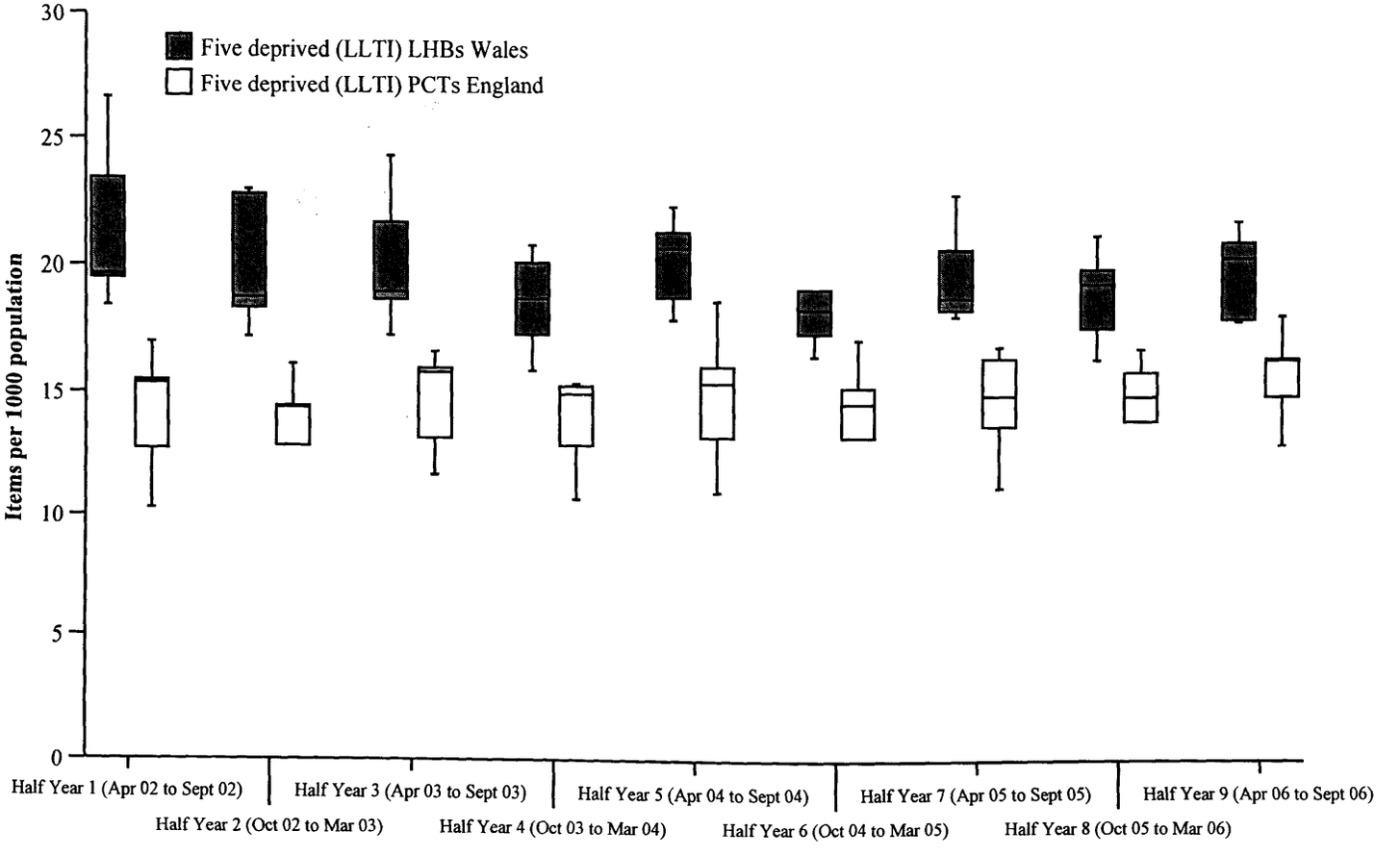


Figure 2.10 Dispensed prescription items for loperamide in the five deprived (LLTI) LHBs in Wales and the five deprived (LLTI) PCTs in England in nine consecutive 6 month periods

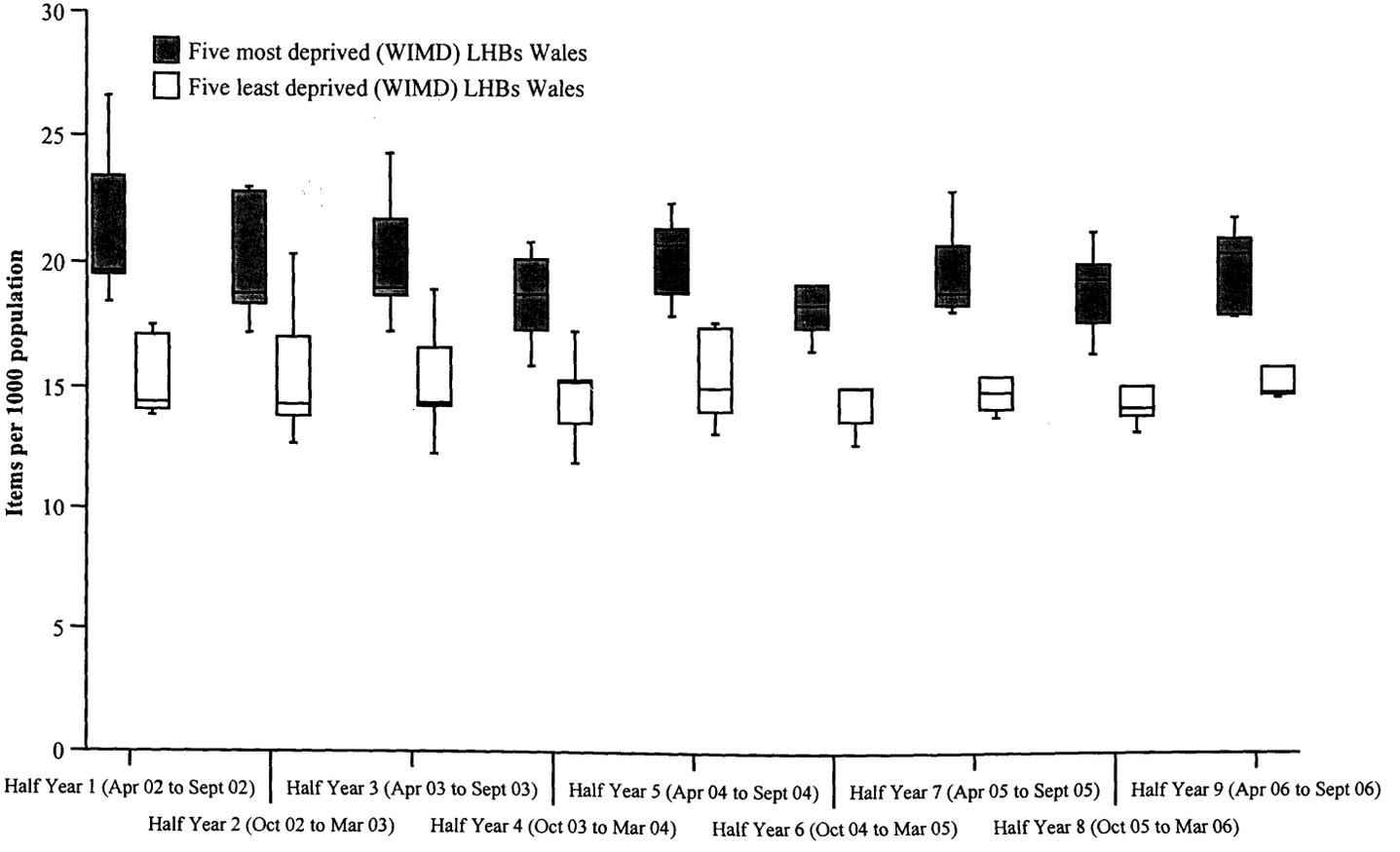


Figure 2.11 Dispensed prescription items for loperamide in the five most deprived (WIMD) and the five least deprived (WIMD) LHBs in Wales in nine consecutive 6 month periods

Table 2.4 Number of dispensed prescription items for loperamide in three 6 month periods in different settings

	Half Year 1 (Apr 02 to Sept 02)	Half Year 5 (Apr 04 to Sept 04)	Half Year 9 (Apr 06 to Sept 06)
PCOs with comparable populations			
Wales (22 LHBs)	16.8 [14.7 – 19.6]	17.1 [15.2 – 19.2]	17.0 [15.8 – 19.4]
South East of England (15 PCTs)	10.0 [7.9 – 12.4]	11.2 [8.8 – 12.7]	11.5 [9.9 – 14.7]
North East of England (16 PCTs)	14.6 [11.9 – 16.1]	15.2 [12.5 – 16.8]	16.2 [14.0 – 17.9]
PCOs with similar rank of deprivation			
Five deprived (LLTI) LHBs Wales	19.7 [19.0 – 25.0]	20.7 [18.3 – 21.8]	20.3 [17.9 – 21.4]
Five deprived (LLTI) PCTs England	15.4 [11.5 – 16.3]	15.4 [12.1 – 17.3]	16.3 [13.9 – 17.2]
LHBs in Wales with contrasting levels of deprivation			
Five most deprived (WIMD) LHBs	19.7 [19.0 – 25.0]	20.7 [18.3 – 21.8]	20.3 [17.9 – 21.4]
Five least deprived (WIMD) LHBs	14.4 [14.0 – 17.3]	15.0 [13.6 – 17.5]	14.8 [14.7 – 17.0]

Results presented as median [interquartile range] of the dispensed prescription items per 1000 population. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

There was no difference (all $p > 0.05$) in percent change in the number of prescription items for loperamide dispensed in the 24 months before and the 24 months after the first reduction of the prescription charge in any of the settings studied (Table 2.5).

Comparison of the difference in percent change in the number of prescription items for loperamide over the two 24 month periods revealed no change (all $p > 0.05$) in the group of LHBs in Wales and the PCTs in the South East of England, the group of LHBs in Wales and the PCTs in the North East of England, the five deprived (LLTI) LHBs Wales and the five deprived (LLTI) PCTs England, the five most deprived (WIMD) LHBs Wales and the five least deprived (WIMD) LHBs Wales (Table 2.6).

There was no association between deprivation score (WIMD) of each of the 22 LHBs in Wales and the difference in percent change (Z) in the number of prescription items for loperamide in the 24 months before and 24 months after the first reduction of the prescription charge ($r = 0.15$, $p = 0.50$).

2.4.3 Laxatives

The number of prescription items for laxatives dispensed in each six month block from Half Year 1 (April to September 2002) to Half Year 9 (April to September 2006) are presented in Figures 2.12, 2.13 and 2.14 for the three setting groups studied.

Table 2.5 Comparison of the percent change in the number of prescription items for loperamide dispensed in the 24 months before and the 24 months after the first reduction of the prescription charge in different settings

	Before	After	p-value[†]
PCOs with comparable populations			
Wales (22 LHBs)	-1.2 [-3.3 – 3.2]	2.6 [-0.9 – 5.2]	0.11
South East of England (15 PCTs)	3.6 [-0.4 – 12.3]	6.3 [3.2 – 13.0]	0.57
North East of England (16 PCTs)	6.7 [-0.8 – 11.8]	8.7 [4.5 – 13.4]	0.23
PCOs with similar rank of deprivation			
Five deprived (LLTI) LHBs Wales	-3.8 [-12.2 – 1.1]	-2.5 [-4.6 – 0.4]	0.50
Five deprived (LLTI) PCTs England	3.9 [-3.2 – 14.0]	6.6 [-0.7 – 15.0]	0.50
LHBs in Wales with contrasting levels of deprivation			
Five most deprived (WIMD) LHBs	-3.8 [-12.2 – 1.1]	-2.5 [-4.6 – 0.4]	0.50
Five least deprived (WIMD) LHBs	1.3 [-3.7 – 3.4]	4.0 [-5.9 – 8.8]	0.34

Results presented as median [interquartile range] of the percent change in the number of dispensed prescription items for loperamide. [†]Wilcoxon Signed Rank test. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

Table 2.6 Comparison of the difference in percent change (Z) in the number of prescription items for loperamide from the 24 months before and the 24 months after the first reduction of the prescription charge between each of the two settings

	Difference percent change (Z)	p-value[†]
PCOs with comparable populations		
Wales (22 LHBs)	1.8 [-1.8 – 7.0]	0.75
South East of England (15 PCTs)	1.3 [-8.2 – 10.0]	
Wales (22 LHBs)	1.8 [-1.8 – 7.0]	0.85
North East of England (16 PCTs)	5.9 [-5.9 – 9.6]	
PCOs with similar rank of deprivation		
Five deprived (LLTI) LHBs Wales	2.0 [-2.4 – 8.9]	0.55
Five deprived (LLTI) PCTs England	7.4 [-8.5 – 9.6]	
LHBs in Wales with contrasting levels of deprivation		
Five most deprived (WIMD) LHBs	2.0 [-2.4 – 8.9]	1.00
Five least deprived (WIMD) LHBs	1.5 [-6.9 – 10.7]	

Results presented as median [interquartile range] of the difference in percent change (Z). [†]Mann-Whitney U test. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

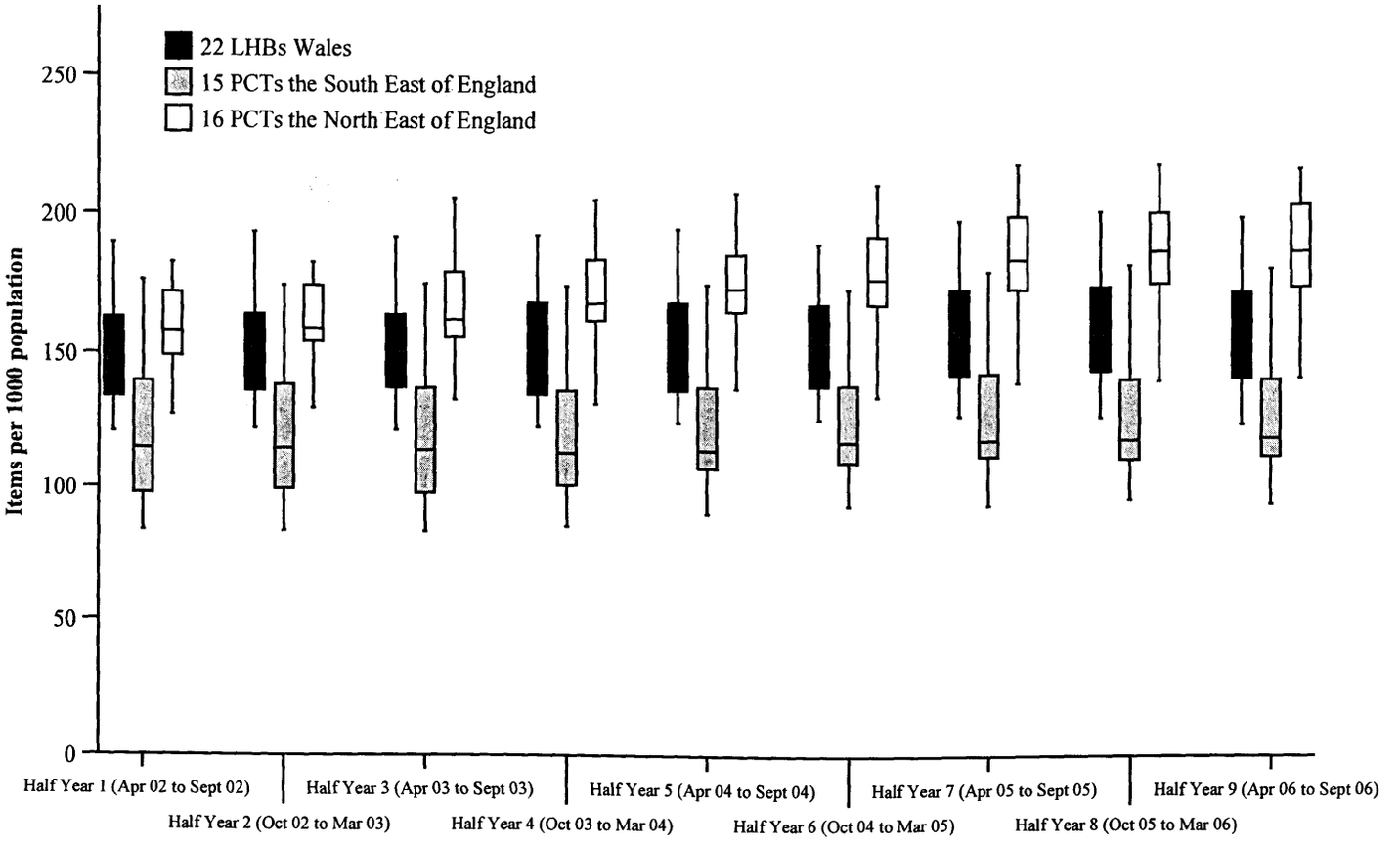


Figure 2.12 Dispensed prescription items for laxatives in Wales, selected PCTs in the South East and the North East of England in nine consecutive 6 month periods

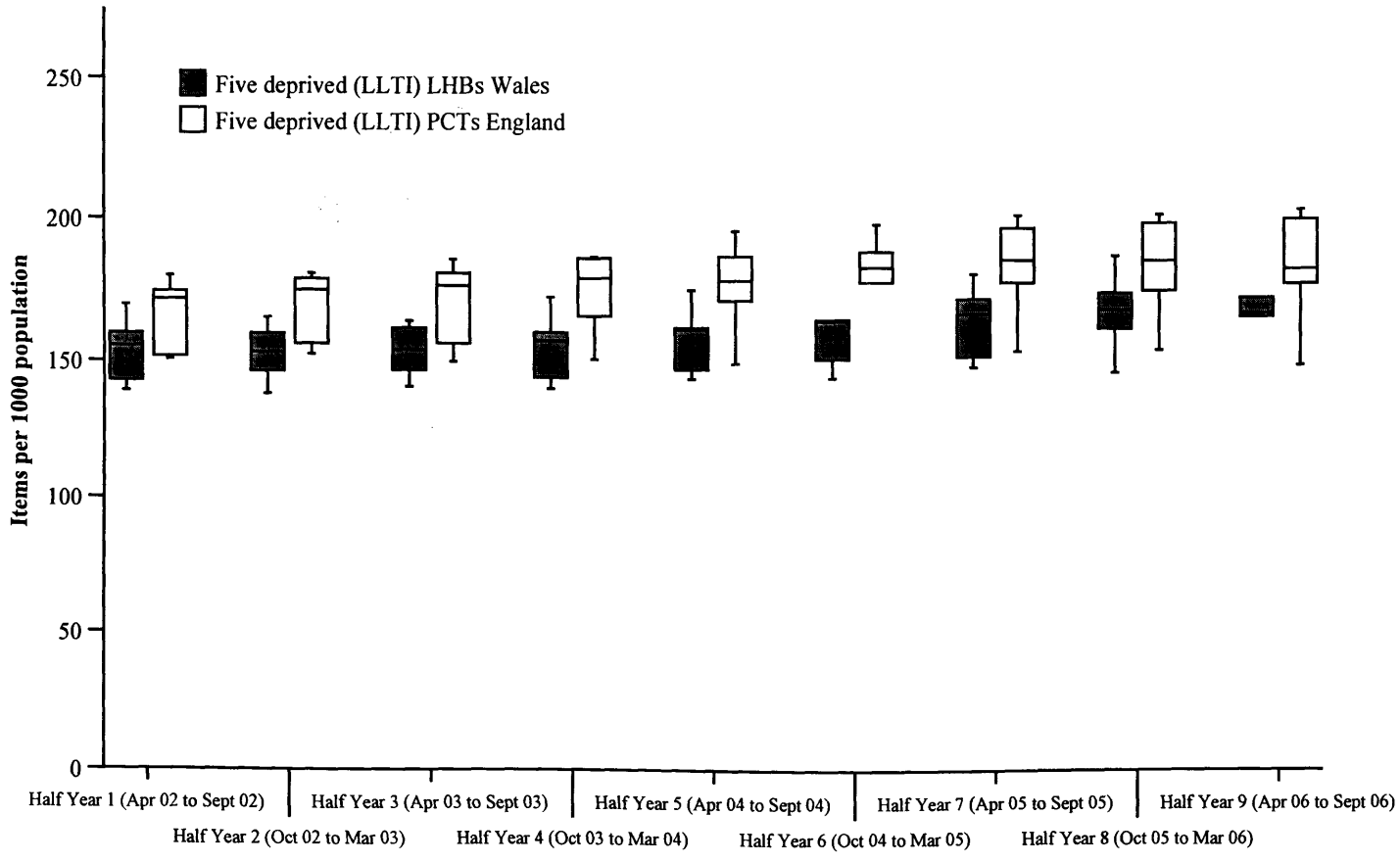


Figure 2.13 Dispensed prescription items for laxatives in the five deprived (LLTI) LHBs in Wales and the five deprived (LLTI) PCTs in England in nine consecutive 6 month periods

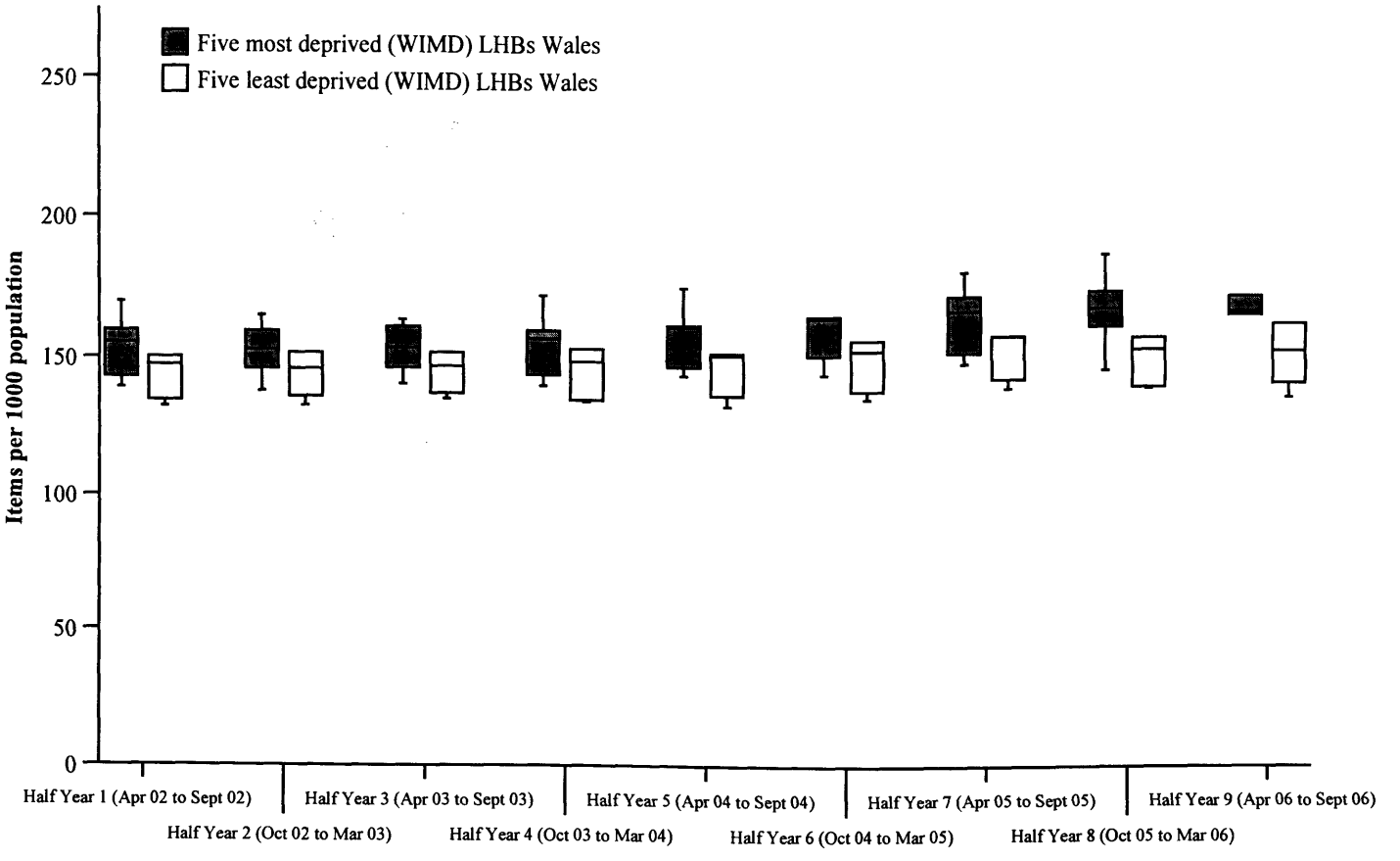


Figure 2.14 Dispensed prescription items for laxatives in the five most deprived (WIMD) and the five least deprived (WIMD) LHBs in Wales in nine consecutive 6 month periods

The number of dispensed prescription items for laxatives in the North East of England appeared higher than those in Wales and selected PCTs in the South East of England (Table 2.7). In the five deprived (LLTI) PCTs in England the number of dispensed prescription items per 1000 population for laxatives in April to September 2002, April to September 2004, and April to September 2006 were 171.7 [151.1 – 177.2], 178.0 [159.9 – 190.9] and 182.1 [162.3 – 201.4] compared to 155.3 [141.1 – 164.7], 161.1 [145.2 – 168.3] and 166.4 [158.6 – 177.8] in the five deprived (LLTI & WIMD) LHBs in Wales. Over the same period the number of dispensed prescription items per 1000 population for laxatives in the five least deprived (WIMD) LHBs in Wales were 147.5 [133.6 – 170.0], 150.8 [134.4 – 172.8], and 152.3 [138.3 – 180.3].

The percent change in the number of prescription items for laxatives dispensed in Wales in the 24 months before the first reduction of the prescription charge was significantly lower than the percent change in the following 24 months (2.2 [0.8 – 3.1] v 3.7 [1.4 – 6.4], p = 0.04) (Table 2.8). In contrast, there were no differences in the percent change in the number of prescription items dispensed in the 24 months before and 24 months after the reduction of the prescription charge in the South East of England (2.0 [-1.0 – 3.3] v 3.3 [1.8 – 4.8, p = 0.23) and the North East of England (8.2 [6.7 – 11.2 v 6.4 [4.2 – 10.8], p = 0.88).

When the difference in percent change between the number of prescription items dispensed for laxatives in the 24 months before and 24 months after the first reduction of the prescription charge were compared (Table 2.9), the value in Wales (2.1 [-0.7 – 4.2]) was not different from that in the South East of England (1.0 [-0.5 – 4.9]; p=0.84), or the North East of England (-0.2 [-4.7 – 4.8]; p = 0.30).

Table 2.7 Number of dispensed prescription items for laxatives in three 6 month periods in different settings

	Half Year 1 (Apr 02 to Sept 02)	Half Year 5 (Apr 04 to Sept 04)	Half Year 9 (Apr 06 to Sept 06)
PCOs with comparable populations			
Wales (22 LHBs)	149.3 [133.6 – 164.4]	151.2 [136.0 – 168.7]	157.6 [140.8 – 171.7]
South East of England (15 PCTs)	114.7 [92.7 – 155.6]	114.1 [106.2 – 154.0]	119.1 [110.8 – 155.6]
North East of England (16 PCTs)	158.1 [148.3 – 173.2]	173.0 [164.6 – 185.8]	186.4 [173.0 – 203.4]
PCOs with similar rank of deprivation			
Five deprived (LLTI) LHBs Wales	155.3 [141.1 – 164.7]	161.1 [145.2 – 168.3]	166.4 [158.6 – 177.8]
Five deprived (LLTI) PCTs England	171.7 [151.1 – 177.2]	178.0 [159.9 – 190.9]	182.1 [162.3 – 201.4]
LHBs in Wales with contrasting levels of deprivation			
Five most deprived (WIMD) LHBs	155.3 [141.1 – 164.7]	161.1 [145.2 – 168.3]	166.4 [158.6 – 177.8]
Five least deprived (WIMD) LHBs	147.5 [133.6 – 170.0]	150.8 [134.4 – 172.8]	152.3 [138.3 – 180.3]

Results presented as median [interquartile range] of the dispensed prescription items per 1000 population. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

Table 2.8 Comparison of the percent change in the number of prescription items for laxatives dispensed in the 24 months before and the 24 months after the first reduction of the prescription charge in different settings

	Before	After	p-value†
PCOs with comparable populations			
Wales (22 LHBs)	2.2 [0.8 – 3.1]	3.7 [1.4 – 6.4]	0.04*
South East of England (15 PCTs)	2.0 [-1.0 – 3.3]	3.3 [1.8 – 4.8]	0.23
North East of England (16 PCTs)	8.2 [6.7 – 11.2]	6.4 [4.2 – 10.8]	0.88
PCOs with similar rank of deprivation			
Five most deprived (LLTI) LHBs Wales	3.0 [1.9 – 3.4]	5.8 [4.1 – 9.5]	0.04*
Five most deprived (LLTI) PCTs England	3.7 [0.9 – 12.8]	2.3 [-0.7 – 7.7]	0.34
LHBs in Wales with contrasting levels of deprivation			
Five most deprived (WIMD) LHBs	3.0 [1.9 – 3.4]	5.8 [4.1 – 9.5]	0.04*
Five least deprived (WIMD) LHBs	1.2 [0.1 – 2.5]	2.3 [0.3 – 6.6]	0.34

Results presented as median [interquartile range] of the percent change in the number of dispensed prescription items for laxatives. †Wilcoxon Signed Rank test. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

Table 2.9 Comparison of the difference in percent change (Z) in the number of prescription items for laxatives from the 24 months before and the 24 months after the first reduction of the prescription charge between each of the two settings

	Difference percent change (Z)	p-value†
PCOs with comparable populations		
Wales (22 LHBs)	2.1 [-0.7 – 4.2]	0.84
South East of England (15 PCTs)	1.0 [-0.5 – 4.9]	
Wales (22 LHBs)	2.1 [-0.7 – 4.2]	0.30
North East of England (16 PCTs)	-0.2 [-4.7 – 4.8]	
PCOs with similar rank of deprivation		
Five deprived (LLTI) LHBs Wales	2.7 [1.9 – 6.3]	0.10
Five deprived (LLTI) PCTs England	-4.4 [-8.4 – 3.2]	
LHBs in Wales with contrasting levels of deprivation		
Five most deprived (WIMD) LHBs	2.7 [1.9 – 6.3]	0.42
Five least deprived (WIMD) LHBs	0.7 [-0.9 – 5.3]	

Results presented as median [interquartile range] of the difference in percent change (Z). †Mann-Whitney U test. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

The percent change in the number of prescription items for laxatives dispensed in the five deprived (LLTI) LHBs in Wales increased from 3.0 [19.4 – 3.4] in the 24 months before the first reduction of the prescription charge to 5.8 [4.1 – 9.5]; p = 0.04, in the following 24 months. In contrast the percent change in the number of prescription items dispensed in the five deprived (LLTI) PCTs in England 24 months before and 24 months after the first reduction of the prescription charge revealed no difference (3.7 [0.9 – 12.8] v 2.3 [-0.7 – 7.7], p = 0.34). However, when comparing deprived PCOs in Wales and England there was no difference in percent change in the number of prescription items for laxatives between the two 24 month periods in the five deprived (LLTI) LHBs in Wales and the five deprived (LLTI) PCTs in England (2.7 [1.9 – 6.3] v -4.4[-8.4 – 3.2], p = 0.10).

The difference in percent change of items dispensed for laxatives in each of the 22 LHBs in Wales over the two 24 month periods before and after the first reduction of the prescription charge was not associated with the deprivation score (WIMD) of each LHB (r = 0.22, p = 0.34). However, comparison of the percent change in the number of items dispensed for laxatives 24 months before and 24 months after the first reduction of the prescription charge revealed a significant difference in the five most deprived (WIMD) LHBs (3.0 [1.9 – 3.4] v 5.8 [4.1 – 9.5], p = 0.04), but not in the five least deprived (WIMD) LHBs (1.2 [0.1 – 2.5] v 2.3 [0.3 – 6.6], p = 0.34).

2.4.4 Fluconazole

The number of prescription items for fluconazole 150 mg dispensed in each six month block from Half Year 1 (April to September 2002) to Half Year 9 (April to

September 2006) are presented for groups of PCOs with comparable populations, PCOs with similar rank of deprivation and groups of LHBs in Wales with contrasting levels of deprivation (Figures 2.15, 2.16 and Figure 2.17).

Table 2.10 shows the number of prescription items for fluconazole 150 mg dispensed in the different settings studied. It appeared that a higher number of prescription items per 1000 population for fluconazole 150 mg were dispensed in Wales than in selected PCTs in the South East and the North East of England at Half Years 1, 5, and 9.

The percent change in the number of prescription items for fluconazole 150 mg dispensed in the 24 months before and the 24 months after the first reduction of the prescription charge showed no difference in any of the settings studied (Table 2.11).

Comparison of the difference in percent change in the number of prescription items for fluconazole 150 mg dispensed over the two 24 month periods showed no difference in the following comparisons (Table 2.12): LHBs in Wales and PCTs in the South East of England ($p = 0.09$), LHBs in Wales and PCTs in the North East of England ($p = 0.11$), five deprived (LLTI) LHBs in Wales and five deprived (LLTI) PCTs in England ($p = 0.55$), and five most deprived (WIMD) LHBs in Wales and five least deprived (WIMD) LHBs in Wales ($p = 0.55$).

The level of deprivation (WIMD) in each of the 22 LHBs in Wales was not associated with the difference in percent change in the number of prescription items for fluconazole 150 mg dispensed over the two 24 month periods ($r= -0.14$, $p = 0.54$).

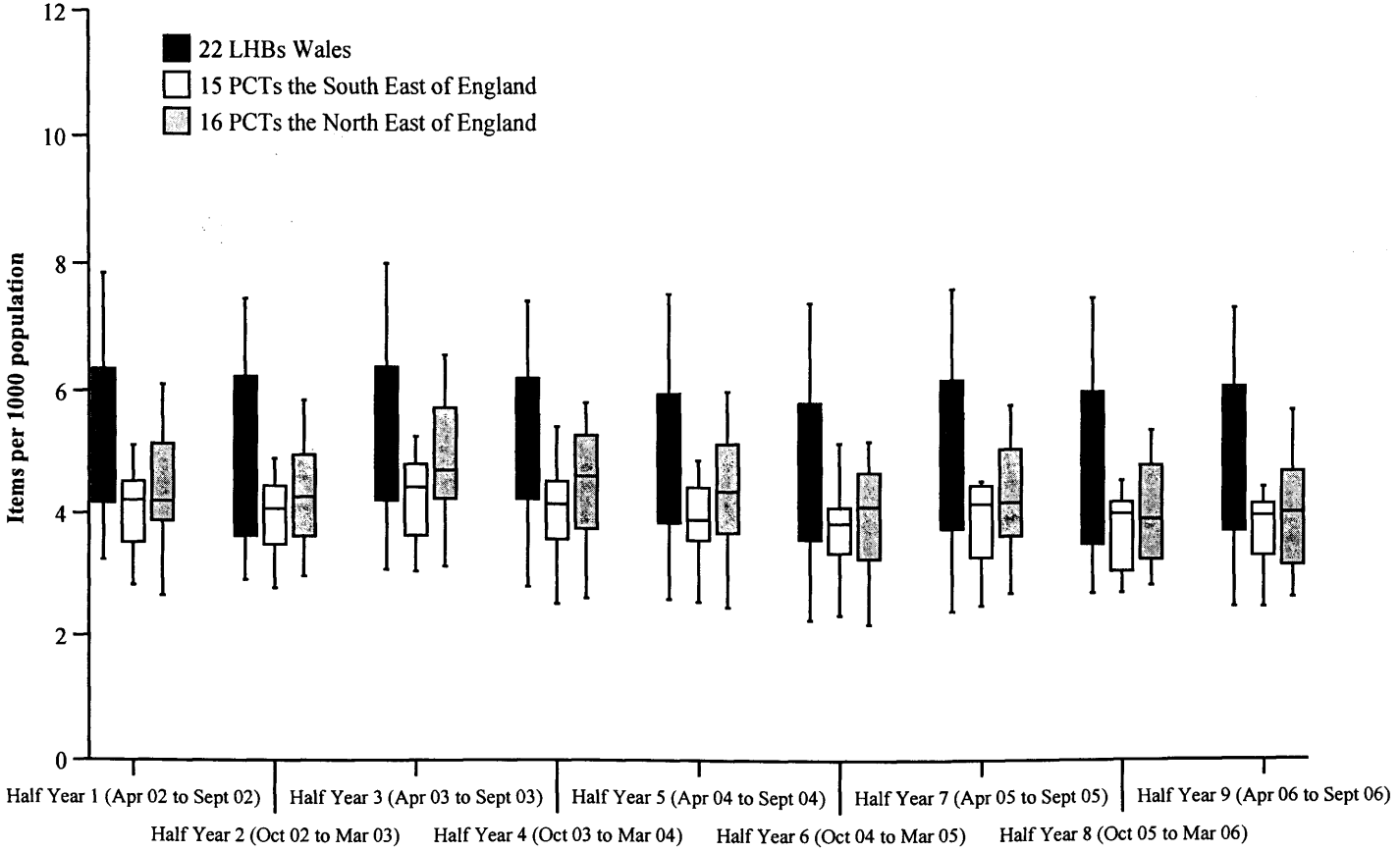


Figure 2.15 Dispensed prescription items for fluconazole 150 mg in Wales, selected PCTs in the South East and the North East of England in nine consecutive 6 month periods

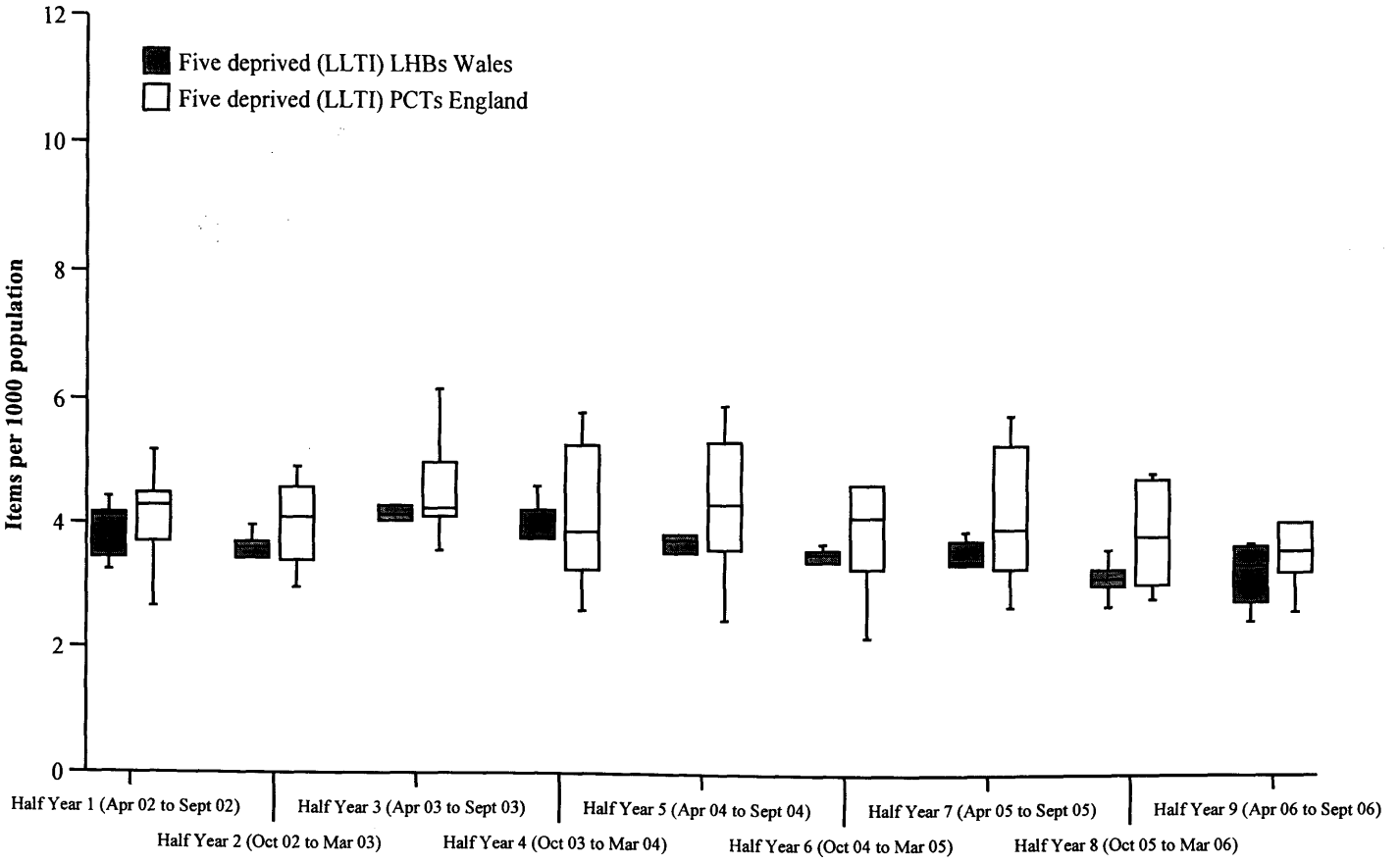


Figure 2.16 Dispensed prescription items for fluconazole 150 mg in the five deprived (LLTI) LHBs in Wales and the five deprived (LLTI) PCTs in England in nine consecutive 6 month periods

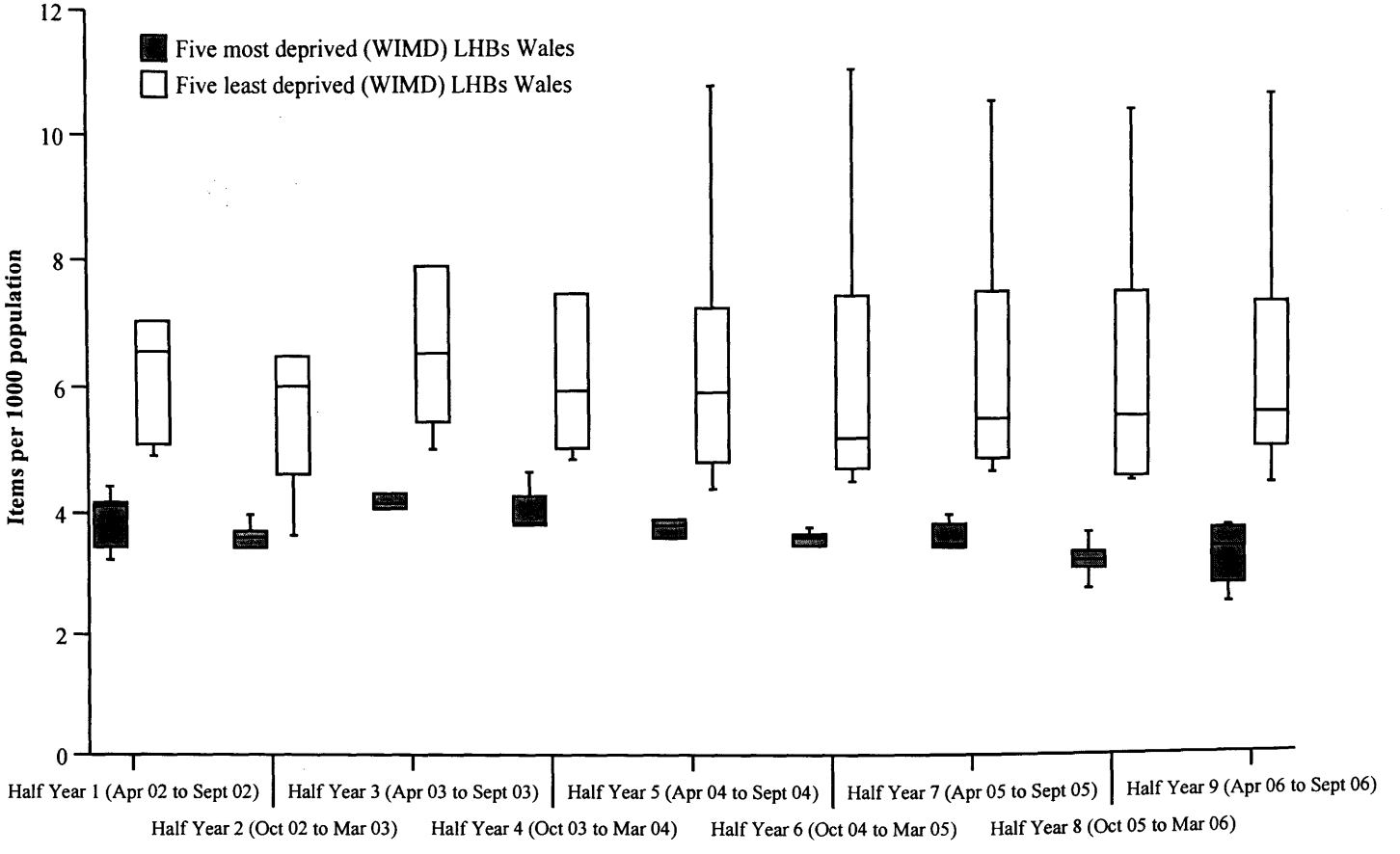


Figure 2.17 Dispensed prescription items for fluconazole 150 mg in the five most deprived (WIMD) and the five least deprived (WIMD) LHBs in Wales in nine consecutive 6 month periods

Table 2.10 Number of dispensed prescription items for fluconazole 150 mg in three 6 month periods in different settings

	Half Year 1 (Apr 02 to Sept 02)	Half Year 5 (Apr 04 to Sept 04)	Half Year 9 (Apr 06 to Sept 06)
PCOs with comparable populations			
Wales (22 LHBs)	5.4 [4.2 – 6.4]	5.3 [3.8 – 6.1]	5.2 [3.7 – 6.0]
South East of England (15 PCTs)	4.2 [3.4 – 4.6]	3.9 [3.4 – 4.5]	4.0 [3.3 – 4.2]
North East of England (16 PCTs)	4.2 [3.9 – 5.2]	4.4 [3.7 – 5.2]	4.0 [3.1 – 4.7]
PCOs with similar rank of deprivation			
Five deprived (LLTI) LHBs Wales	4.1 [3.3 – 4.3]	3.8 [3.1 – 4.1]	3.4 [2.6 – 3.7]
Five deprived (LLTI) PCTs England	4.3 [3.2 – 4.8]	4.3 [3.0 – 5.6]	3.6 [2.9 – 4.9]
LHBs in Wales with contrasting levels of deprivation			
Five most deprived (WIMD) LHBs	4.1 [3.3 – 4.3]	3.8 [3.1 – 4.1]	3.4 [2.6 – 3.7]
Five least deprived (WIMD) LHBs	6.5 [5.0 – 9.4]	5.8 [4.6 – 9.0]	5.5 [4.7 – 8.9]

Results presented as median [interquartile range] of the dispensed prescription items per 1000 population. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

Table 2.11 Comparison of the percent change in the number of prescription items for fluconazole 150 mg dispensed in the 24 months before and the 24 months after the first reduction of the prescription charge in different settings

	Before	After	p-value†
PCOs with comparable populations			
Wales (22 LHBs)	-7.4 [-14.4 – 2.1]	-3.7 [-10.9 – 1.4]	0.52
South East of England (15 PCTs)	-1.2 [-7.9 – 7.7]	-5.8 [-14.4 – -2.5]	0.36
North East of England (16 PCTs)	2.9 [-10.7 – 10.2]	-10.0 [-15.8 – -1.7]	0.08
PCOs with similar rank of deprivation			
Five deprived (LLTI) LHBs Wales	-7.5 [-19.4 – 8.5]	-12.1 [-20.5 – -0.5]	0.69
Five deprived (LLTI) PCTs England	1.3 [-4.2 – 16.5]	-9.6 [-20.1 – 1.0]	0.14
LHBs in Wales with contrasting levels of deprivation			
Five most deprived (WIMD) LHBs	-7.5 [-19.4 – 8.5]	-12.1 [-20.5 – -0.5]	0.69
Five least deprived (WIMD) LHBs	-8.6 [-12.6 – -0.3]	1.1 [-3.6 – 3.2]	0.08

Results presented as median [interquartile range] of the percent change in the number of dispensed prescription items for fluconazole 150 mg. †Wilcoxon Signed Rank test. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

Table 2.12 Comparison of the difference in percent change (Z) in the number of prescription items for fluconazole 150 mg from the 24 months before and the 24 months after the first reduction of the prescription charge between each of the two settings

	Difference percent change (Z)	p-value[†]
PCOs with comparable populations		
Wales (22 LHBs)	2.8 [-6.2 – 12.4]	0.09
South East of England (15 PCTs)	-6.6 [-11.0 – 2.9]	
Wales (22 LHBs)	2.8 [-6.2 – 12.4]	0.11
North East of England (16 PCTs)	-10.7 [-18.9 – 8.2]	
PCOs with similar rank of deprivation		
Five deprived (LLTI) LHBs Wales	-4.6 [-29.0 – 19.0]	0.55
Five deprived (LLTI) PCTs England	-17.9 [-30.4 – 2.6]	
LHBs in Wales with contrasting levels of deprivation		
Five most deprived (WIMD) LHBs	-4.6 [-29.0 – 19.0]	0.55
Five least deprived (WIMD) LHBs	7.1 [1.8 – 12.0]	

Results presented as median [interquartile range] of the difference in percent change (Z). [†]Mann-Whitney U test. PCO = Primary Care Organisation, LHB = Local Health Board, PCT = Primary Care Trust, LLTI = Limiting Long Term Illness, WIMD = Welsh Index of Multiple Deprivation

2.5 Discussion

2.5.1 Methodology

2.5.1.1 Study design

One of the aims of this study was to identify the impact of the phased reduction of the prescription charge in Wales on the pattern of prescribing in primary care. To evaluate this, prescribing patterns in Wales both before and after the first reduction of the prescription charge in October 2004 were compared. To determine whether any of the changes observed were unique to Wales the prescribing patterns were compared to settings in England.

2.5.1.2 PCOs with comparable population size

Primary Care Trusts from the South East and the North East regions of England were selected as comparators to Wales because they had not, and were not, in the process of experiencing the changes in the prescription charge comparable to that seen in Wales. Outside London, the South East has the highest average gross weekly household income at £658 compared to Wales which has the joint lowest at £461.[119] Similarly, outside London the South East accounted for the lowest number of prescription items per person at 12.2 in 2004 whilst Wales recorded the highest at 18.4 prescription items per person. Because the total population of all 49 PCTs in the South East of England (8.1 million) was nearly three times greater than that of Wales (2.9 million) it was necessary to select a number of these PCTs to give a comparable population size to that of Wales. Fifteen PCTs in the South East of England (2.5 million) were therefore randomly selected for this comparative study.

In contrast to the South East, the North East of England has the joint lowest average gross weekly household income at £458 in 2004.[119] The North East of England also has a similar economic history to Wales with coal mining dominating the recent-past economy of both areas. The North East is the smallest region in England and the total population of 16 PCTs (2.5 million) was comparable to that of Wales.

2.5.1.3 PCOs with similar deprivation rank

An additional component of the present study was to compare groups of PCOs in Wales and England that had similar levels of deprivation and monitor if there were changes in prescribing patterns between the two settings. Selection of the PCOs was relatively straight forward but identifying areas of comparative deprivation was more problematic. There are no comparative equivalent measurements for deprivation in use in both countries. Although the index of multiple deprivation (IMD) is used in England it cannot be compared to the WIMD[120] as the integrated domains measured in England and Wales are different. For example, the crime domain included in the IMD 2004 in England was not included in WIMD 2005.

Given that there was no tool readily available to compare deprivation in England and Wales it was necessary to utilise a proxy marker of deprivation. Limiting long term illness (LLTI) is one of few proxy markers readily available in both countries, which is calculated from a 'Yes' response to the question in the 2001 Census: 'Do you have any long term illness, health problem or disability which limits your activities or the work you can do?'. Others[121, 122] have indicated the validity of this approach and this was substantiated in the present study when it was noted that the five most deprived

LHBs in Wales ranked by LLTI score, based on the Census 2001, were identical to the five most deprived LHBs ranked by WIMD 2005.

Unfortunately even the use of LLTI to indicate deprivation was not as straightforward as it first appeared because although local authorities in Wales have boundaries coterminous with those of their LHB, not all the local authorities in England (the unit of measure for LLTI) were coterminous with those of their PCTs. As a consequence, only local authorities in England with boundaries coterminous with those of their PCT were included in this study.

LLTI scores for the five highest ranked LHBs (most deprived) in Wales (26.3 to 30.0) were of similar magnitude to those of the five highest ranked PCTs in England (24.7 to 30.8) (Appendix 4). In contrast the least deprived LHB in Wales had a score of 18.8 and was ranked 147th out of 376 in the combined England and Wales ranking. As a consequence of this disparity it was not feasible to compare the five least deprived LHBs in Wales with the five least deprived PCTs in England, and therefore only the most deprived PCOs in Wales and England were compared.

2.5.1.4 LHBs in Wales with contrasting levels of deprivation

To compare LHBs in Wales with contrasting levels of deprivation five LHBs were allocated to each of the most and least deprived groups to produce intuitively appropriate sample sizes.

2.5.1.5 Unit of measure

Unlike the problem of comparing deprivation in Wales and England the comparison of prescription data was relatively straightforward. Both Wales and England used the same therapeutic classification for dispensed prescription data based on the British National Formulary. It was therefore possible to directly compare prescription data between the two countries.

Dispensed prescription items were used and reported as the unit of measure for the volume of prescribing in both Wales and England. It was assumed that an item, which could indicate a single dose or six months supply or longer, was the same in all settings throughout the period studied.

2.5.1.6 Population data

Resident population was used as the denominator for all calculations to standardize the number of dispensed prescription items and facilitate direct comparison between settings. Although population data for LHBs in Wales were obtained from Census 2001, data for PCTs in England were obtained directly from their websites. This was necessary because boundaries of some PCTs were not coterminous with their local authority boundaries and thus their population data were not available in the Census 2001.

Although the estimated populations reflect the dynamics of inflation over the period studied, a preliminary analysis comparing outcomes when results using estimated populations were compared to those obtained using fixed population figures of Census data, revealed no significant difference in results. For ease, fixed population

data obtained from the sources mentioned above were used during the five years period studied.

2.5.1.7 Deprivation data for Wales

Multiple deprivation cannot be measured directly as it reflects a composite score derived from multiple indicators of deprivation. The WIMD 2005 was developed by allocating scores to lower super output areas (LSOAs) based on weightings of income (25%), employment (25%), health (15%), education, skills and training (15%), housing (5%), physical environment (5%), and geographical access to services (10%).[120]

Although there are no official deprivation scores for local authorities they can be worked out in several ways and there is no single obviously correct way to do it. In a preliminary analysis the proportion of LSOAs in each local authority that fell into the most deprived 10% and the most deprived 20% in Wales were identified and the 22 local authorities ranked accordingly. As mentioned earlier, the five most deprived local authorities ranked by the proportion of LSOAs in the most deprived 20% in Wales was identical to the five local authorities with highest LLTI scores. Therefore, it was logical to use the same five deprived local authorities/LHBs regardless of whether WIMD or LLTI were used as indicators for deprivation. Consequently, the percent LSOAs in each LHB amongst the most deprived 20% in Wales were used throughout this study to represent LHB deprivation (WIMD).

2.5.1.8 Analysis

Non-parametric statistics were used for the analysis in this study because the test for normality, the Kolmogorov-Smirnov test, failed to show normality of distribution in all settings studied.

Given the general year on year growth in prescription items, absolute differences in the number of prescription items dispensed before and after the reduction of the prescription charge may not identify an actual change in prescribing rates. For example, a pilot model of 20 PCOs has showed that if the number of prescription items dispensed per 1000 population (median [interquartile range]) for one of the medicines studied was 120.5 [115.3 – 124.8] items in Year 1, 132.5 [127.8 – 139] items in Year 3, and 151.0 [146.2 – 153.0] items in Year 5. It would demonstrate the difference between the number of item dispensed before (13.5 [12.0 – 15.0] items per 1000 population) and after (15.5 [14.0 – 20.5] items per 1000 population; $p = 0.002$) the reduction of the prescription charge, whilst the percent change before (11.4 [10.0 – 12.2]) and after (12.2 [10.3 – 16.1]) the reduction of the prescription charge actually revealed no significant difference ($p = 0.25$).

Therefore, to determine the effect of the phased reduction of the prescription charge in Wales it was more sensible to use the percent change in the number of dispensed prescription items and not the actual number of prescription items. This manipulation was necessary to minimise false positive results.

2.5.2 Changes in prescribing patterns

After the phased reduction of the prescription charge changes in the pattern of prescribing were identified for two out of four medicines studied and will be discussed in detail below.

2.5.2.1 Non-sedating antihistamines

The percent change in the number of prescription items for non-sedating antihistamines dispensed in Wales after the reduction of the prescription charge was greater than that seen over the same duration in the period before the reduction of the prescription charge. Although factors such as an outbreak of allergic disorders, a health promotion campaign to support the use of non-sedating antihistamines, or a related promotional campaign could have created an increase in the prescribing, no evidence for such interventions could be identified during the study period. Moreover, it would be anticipated any major confounding factor would be present in all comparator settings. As a consequence, it was assumed the phased reduction of the prescription charge was the only major factor that may have contributed to the observed increase in the prescribing of non-sedating antihistamines in Wales.

Allergic disorders, and allergic rhinitis (hay fever) in particular, are long term conditions that may be either intermittent or persistent and for which patients may need to take medicines regularly at least during the period of exacerbation.[123] Perhaps patients with allergic rhinitis were very aware of the product cost and the personal savings that would accrue because of the reduced prescription charge. Given the typical cost of purchasing a pack of a brand leader non-sedating antihistamine was £7.55 for Benadryl (acrivastine: 24 capsules per pack), £8.95 for

Zirtek (cetirizine: 21 tablets per pack), and £8.99 for Clarityn (loratadine: 21 tablets per pack), the reduction of the prescription charge from £6 to £3 over the study period may have acted as an incentive for some to obtain their non-sedating antihistamine on prescription. It is anticipated any such impact would be considerably less where branded generics were normally used.

The prescribing pattern of non-sedating antihistamines seen in the South East of England serves as a model to illustrate the steady increase in the prescribing of non-sedating antihistamines over the same period. However, whilst the prescribing pattern in the North East of England appeared similar to that in Wales it was different to that observed in the South East of England. There was no major national public policy to account for the increase in prescribing of non-sedating antihistamines in the North East of England. Other confounding factors such as local policies and clinical guidelines, health promotion campaigns, or outbreak of allergic rhinitis could have influenced the results although there is no evidence of any of these factors actually influencing the outcome.

At the outset of the study it was speculated that in the most deprived populations there would be more likelihood of an individual obtaining a prescription rather than purchasing the same medicine over the counter should price exceed the prescription charge. In addition, it was anticipated that a large number of patients in deprived areas were already exempt the prescription charge and thereby unlikely to purchase an OTC medicine. This was indirectly supported by the proportionally higher number of prescription items for non-sedating antihistamine dispensed in the most deprived LHBs.

Although it was impractical to identify the sale of OTC non-sedating antihistamines in this study (see Chapter 4), the high number of prescription items dispensed in the most deprived LHBs implied that sales of OTC non-sedating antihistamines would be expected to be low compared with sales in the least deprived area. Based on this assumption, it was not surprising that a change, and probably a small change in acquisition of non-sedating antihistamines, from OTC purchase to obtaining on prescription, could not be detected because of the small number who previously purchased OTC non-sedating antihistamines. This was different from that seen in the least deprived LHBs where it was speculated that the higher proportion of patients who had formerly purchased OTC medicines subsequently obtained their non-sedating antihistamine on prescription following the reduction of the prescription charge.

2.5.2.2 Loperamide

There were no changes in the prescribing pattern of loperamide after the reduction of the prescription charge in each of the settings studied. This was probably due to: 1) the low usage of prescription loperamide, and 2) the need for prompt access to symptomatic treatment for acute diarrhoea.

The number of prescription items dispensed for loperamide was low compared to other medicines that did demonstrate a significant change after the reduction of the prescription charge. For example, the number of dispensed prescription items per 1000 population for loperamide in Wales was 16.4 [14.3 – 18.9] items in October 2002 to March 2003 and 16.7 [14.6 – 19.0] items in April to September 2003, compared with 137.2 [119.2 – 147.4] items per 1000 population for non-sedating

antihistamines dispensed during October 2002 to September 2003. As a consequence of this low usage of prescription loperamide any variation in prescribing following the reduction of the prescription charge would probably be small and not have sufficient power to be statistically detected.

In addition to the above explanation there is also a need to reflect on the indication for the use of loperamide. Loperamide is indicated for the symptomatic treatment of acute and chronic diarrhoea[124] at a recommended adult daily dose of 6-8 mg for a maximum of 5 days. The dose for chronic diarrhoea needs to be adjusted according to response with a maximum recommended daily dose of 16 mg. Analysis of prescription data for Wales showed high quantities of loperamide (tablet or capsule) were ordered per prescription item, i.e. 48.2 units (during October 2001 to September 2002), 50.0 (during October 2002 to September 2003), and 52.0 (during October 2005 to September 2006). It is therefore likely that the large amount prescribed shown above was for the treatment of chronic conditions rather than for acute episodes.

It is anticipated that those who suffered from acute diarrhoea would seek prompt symptomatic treatment available OTC rather than make an appointment to see their doctor with the associated delay this may involve. The retail price of a small pack of branded OTC loperamide was relatively low, i.e. £3.15 for Imodium [loperamide] 6 capsules per pack and only £1.99 for a pack of 10 branded generics. This, together with the high sales figure of OTC loperamide following its reclassification from POM to P,[125] suggested that prompt access to OTC loperamide was the favoured option and this was preferred to the delay in obtaining the prescription medicine.

Although the prescription charge in Wales reduced to £3 during the study period, there was little difference from the retail price of a small pack of OTC loperamide. Overall, it appeared that there was little financial incentive for those with acute diarrhoea to change their pattern of health seeking behaviour to obtain loperamide on prescription.

2.5.2.3 Laxatives

The prescribing of laxatives in Wales after the reduction of the prescription charge was higher than that seen over the same duration in the period before the reduction of the prescription charge. In contrast, there were no changes in the pattern of prescribing of laxatives in both the South East and the North East of England. This indicated that the change in the prescribing of laxatives observed in this study was unique to Wales. There were no known major confounding factors, apart from the reduction of the prescription charge in Wales that could have influenced the prescribing for laxatives in Wales. Other factors, if any, were considered to be equally applicable to Wales, the South East and the North East of England. Accordingly, the phased reduction of the prescription charge appeared the only major factor that may have contributed to an increasing in the prescribing of laxatives in Wales.

Laxatives are a group of medicines indicated for the treatment of constipation.[124] Although laxatives are widely used, non-drug treatment, including education and advice on diet and exercise remain first line therapy for uncomplicated constipation.[126] Costs of OTC laxatives varied greatly ranging from £1.13 for Dulco-Lax (bisacodyl: 10 tablets per pack) to £7.75 for Laxoberal (sodium picosulfate 300

ml). However, long term use of an OTC laxative would account for a cumulative higher cost than the prescription charge, especially when the prescription charge was reduced from £6 to £3. As a consequence this may have motivated people to obtain the medication on prescription and goes some way to explain why the results of the present study showed a significant increase in the prescribing for laxatives following the reduction of the prescription charge in Wales.

When comparing the two groups of LHBs in Wales with contrasting levels of deprivation, it was found that the prescribing of laxatives increased in the five most deprived (WIMD) LHBs whereas prescribing in the five least deprived (WIMD) LHBs showed no difference after the reduction of the prescription charge. This was in contrast to the prescribing pattern seen with non-sedating antihistamines where the five least deprived (WIMD) LHBs demonstrated an increase in prescribing following the reduction of the prescription charge compared to the five most deprived (WIMD) LHBs. This suggested that health seeking behaviour and the pattern of access to medication for the management of constipation and allergic rhinitis were different between geographical areas with contrasting levels of deprivation.

The number of dispensed prescription items for laxatives appeared relatively low in the least deprived LHBs compared to the most deprived LHBs (Figure 2.14). It has been suggested that constipation is more prevalent in the upper – middle social class population.[127] Whether this is true in Wales is unclear but certainly the results of the present study provide no evidence to support this. The results do, however, highlight our poor understanding of the relationship between deprivation, acute and long term conditions, the cost of OTC medicines and health seeking behaviour.

2.5.2.4 Fluconazole

Fluconazole is an imidazole antifungal with several indications including the treatment of vaginal candidiasis, mucosal candidiasis, tinea pedis, tinea corporis, tinea cruris, pityriasis versicolor and dermal candidiasis.[124] A single dose of fluconazole 150 mg is indicated for the treatment of vaginal candidiasis or candidal balanitis associated with vaginal thrush and, therefore, in dispensed prescription data could be differentiated from the use of fluconazole for other conditions.

The results of the present study revealed a downward trend in the prescribing of fluconazole 150 mg following the reduction of the prescription charge in Wales in all settings studied. The percent change in the number of dispensed prescription items for fluconazole after the reduction of the prescription charge was not different from the change prior to this period.

The number of dispensed prescription items per 1000 population for fluconazole 150 mg in Wales were low at 5.2 [3.6 – 6.2] items in October 2002 to March 2003 and 5.7 [4.6 – 6.4] items in April to September 2003, compared with 137.2 [119.2 – 147.4] items per 1000 population for non-sedating antihistamines dispensed during October 2002 to September 2003. Considering the relatively small number of prescriptions for fluconazole 150 mg, any changes may have been difficult to identify.

The retail cost of branded OTC fluconazole 150 mg single dose was higher than the prescription charge prior to its reduction, for example £12.50 for Diflucan One, £9.99 for Canesten Oral Capsule, and £6.99 for Care Fluconazole. However, an

analysis using the CASPA and IMS (Intercontinental Marketing Services) sell-in database (detailed in Chapter 3) showed that the combined sale volume of OTC fluconazole 150 mg (21,593 items) in Wales in 2005 was similar to the volume of prescribed fluconazole 150 mg (28,799 items). It is likely that prior knowledge and experience of vaginal candidiasis, its effective management, speed of access to treatment and the convenience of making a purchase could outweigh the delay in obtaining a prescription and the associated financial saving.

2.5.3 Influence of deprivation

When the difference in percent change of items dispensed for each of the four medicines studied was calculated over the two 24 month periods for the 22 LHBs in Wales there was no apparent association with deprivation. Others[97, 98, 128] have shown a correlation between deprivation and prescribing although no articles have demonstrated a link between deprivation and a change in prescribing rate, as was the object in this study. Perhaps the use of the WIMD to allocate deprivation scores, compared to the deprivation or socioeconomic parameters used by others, also countered observing any relationship with prescribing.

It should be noted that, in general, every area is a mix of those who are deprived and people who are more affluent. The indices used in the present study only quantified those deprived. Deprivation scores for each LSOA can be ranked to show that one area is more deprived than another. However, it is not possible to quantify differences between deprivation scores of two or more areas. For example, if area A has a score of 40 and area B has 20, it does not mean that A is twice as deprived as B. In the present study, deprivation scores of LSOAs were ranked and the proportion

of LSOAs in each local authority that fell into the most deprived 20% in Wales were used to represent LHB deprivation. This approach may not have been discriminating for those LHBs that comprised LSOAs with a mix of both high and low deprivation scores. These LHBs would typically be mid range when ranking the deprivation score of LHBs from 1 to 22.

By selecting the five most deprived and the five least deprived LHBs in Wales it was intended to overcome this problem although this approach clearly did not resolve all problems. Different prescribing patterns after the reduction of the prescription charge between groups of LHBs with contrasting levels of deprivation were identified for some medicines studied and have been discussed in the previous sections (sections 2.5.2.1 – 4).

2.6 Summary

In the first two years following the introduction of the phased reduction of the prescription charge in Wales it was found that:

- There was an increase in the prescribing of non-sedating antihistamines and laxatives in Wales.
- The prescribing of loperamide and fluconazole 150 mg in Wales did not change.
- There was no correlation between LHB deprivation and changes in prescribing for the drugs examined.
- Analysis of LHBs with contrasting levels of deprivation revealed that prescribing of selected drugs increased in less deprived LHBs compared to the more deprived LHBs.

CHAPTER 3

RECLASSIFICATION OF MEDICINES

When we truly care for ourselves, it becomes possible to care far more profoundly about other people (Eda LeShan, 1922 – 2002).

3.1 Introduction

Self medication, as part of self care management, can be undertaken if appropriate medicines are accessible to the general public and available for sale over the counter (OTC) without prescription. Policies as to which medicines are available OTC vary from country to country.[2] In many European countries, OTC medicines are available only through pharmacies whereas in the US all OTC medicines can be sold in general retail outlets. In the UK, OTC medicines may only be available from a pharmacy (P medicine) or available for self selection from general retail outlets if classified as a general sale list (GSL) medicine.

The number of medicines available OTC in the UK is on the increase. Between 1990 and 2005, 70 medicines were reclassified from POM to P,[129] and 78 medicines were reclassified from P to GSL[130] (Table 3.1). In accordance with the strategic intent of the NHS,[4] the UK Government has been striving to increase the number of medicines available without prescription by introducing a number of changes to ease the reclassification of medicines from POM to P and P to GSL.[131] Its aim is to enhance the rate of POM to P switches from 5 per year to 10 per year and expand the range of

medicines available for self medication to cover long term chronic conditions and preventative therapies[5].

Table 3.1 Number of medicines reclassified* from 1990 to 2005

Year	POM to P[129]	P to GSL[130]
1990	-	2
1991	2	-
1992	8	-
1993	5	-
1994	17	5†
1995	7	-
1996	3	9
1997	3	12
1998	5	5
1999	3	7
2000	4	1
2001	5	8
2002‡	2	7
2003	1	3
2004	3	12
2005	2	7

* Include reclassification for new indications, strength, dosage form, maximum single dose, maximum daily dose, and pack sizes

† Main reclassifications (190 substances, mostly herbals, were classified as GSL in 1994 but not considered as 'reclassifications')

‡ In 2002 the procedure for reclassification changed and reclassification by substance stopped. From 2002 only individual products could be reclassified[132]

In 2002, the Royal Pharmaceutical Society of Great Britain (RPSGB) published a strategy document to fit with the UK NHS plan. This document highlighted a number of potential candidates for POM to P reclassification.[133] The therapeutic classes considered were wide ranging and included antihypertensive agents, statins, inhaled $beta_2$-agonists, corticosteroids, oral contraceptives and hormone replacement therapy (Table 3.2). If all the drugs named in the document were reclassified, the implications for pharmacy would be significant. Availability of these drugs as P medicines would open the way for pharmacists, even without prescribing rights, to take on roles beyond a GP-directed supply function. However, it could rightly be assumed these medicines would not be reclassified without resistance. Every time a new therapeutic agent is proposed for deregulation there is opposition both from within and outside the profession and this will be discussed in more detail below.

It is not only the pharmacist who will benefit from the reclassification of medicines. The reclassification of medicines from P to GSL may also increase the profit of the pharmaceutical industry. Given that GSL medicines can be purchased from normal retail outlets means GSL medicines are widely promoted and more freely accessible thereby generating additional sales.

Between 2004 and 2005 five medicines were reclassified from POM to P and 19 were reclassified from P to GSL. Of these, the candidate medicines for the present study were the first in therapeutic class reclassifications which included omeprazole, simvastatin, hyoscine butylbromide, and chloramphenicol.

Table 3.2 List of possible candidates for POM to P switchs proposed by RPSGB in 2002

Therapeutic category	Examples of products
Gastrointestinal system	
Gastro-oesophogeal reflux disease	Proton pump inhibitors
Cardiovascular system	
Stable angina	Beta blockers Calcium channel blockers
Hypertension	Diuretics Drugs affecting the renin-angiotensin system
Cholesterol lowering therapy	Statins
Respiratory system	
Chronic stable asthma	Selective $beta_2$-agonists (inhaled) Corticosteroids (inhaled)
Influenza	Zanamivir Amantadine
Central nervous system	
Obesity	Orlistat Sibutramine
Migraine treatment	$5HT_1$ agonists
Anxiety	Beta blockers
Infections	
Malaria prophylaxis	Doxycycline Mefloquine Malarone
Endocrine system	
Postmenopausal osteoporosis	Bisphosphonates
Obstetrics, gynaecology and urinary-tract infections	
Contraception	Oral contraceptives
Menopause	Hormone replacement therapy
Urinary incontinence (female only)	Oxybutynin Tolterodine
Musculoskeletal and joint disease	
Rheumatic and arthritic pain	COX-2 specific NSAIDs
Skin	
Acne	Topical antibiotics
Impetigo	Topical antibiotics
Inflammatory skin disorders	Moderate/potent topical corticosteroids

3.1.1 Omeprazole

Omeprazole 10 mg was launched by GlaxoSmithKline Consumer Healthcare as a P medicine in March 2004 under the brand name Zanprol. The initial cost for one pack of Zanprol containing 14x10 mg omeprazole tablets was £9.49. The indication for OTC omeprazole was for the treatment of heartburn symptoms associated with acid reflux for a maximum period of 4 weeks. Given that omeprazole is indicated for symptomatic relief, dosage administration could be titrated according to symptoms, i.e. start with two 10 mg tablets once daily for three to four days and reduce to one 10 mg tablet daily as symptoms improve. According to the Zanprol algorithm and RPSGB practice guidance,[134] OTC omeprazole should be considered for patients with recurrent attacks of heartburn symptoms. Simple antacid preparations such as antacid/alginate combinations or H_2 antagonists should be recommended for a discrete one-off attack that requires rapid symptomatic relief.

Despite the fact that omeprazole is well tolerated and side effects are generally mild and reversible, several concerns have been raised regarding the availability of omeprazole to the public. Amongst these concerns are inaccurate self diagnosis and the possibility that the medicine will not be used as directed.[135]

Omeprazole first became available without prescription in Sweden in November 1999. Historically, Sweden has been reluctant to switch drugs and has the lowest number of switches among 15 European Union countries.[136] It is likely that the decision to switch omeprazole in Sweden was prompted by economic consideration in relation to the prescribing cost.[137] The reasons underlying the reclassification of omeprazole in the UK may not be much different from those in Sweden.

Nonetheless, it has been suggested that people with frequent gastro-oesophageal reflux disease (GORD) symptoms need more effective therapy than that of OTC antacids or H_2 antagonists,[135] and therefore the availability of OTC omeprazole was welcome. Whether this reclassification had any impact on the sale of H_2 antagonists was one of the issues investigated in this study.

3.1.2 Simvastatin

Simvastatin was launched as a P medicine in the UK in July 2004. The product, which contains 10 mg simvastatin, was marketed as Zocor Heart-Pro at the price of £12.99 per pack of 28 tablets. Zocor Heart-Pro was licensed for the prevention of a first major coronary event in people at moderate risk of coronary heart disease (CHD), defined as a 10 to 15% risk of an event in the next 10 years. Individuals who fall into this category will be men aged over 55 years, or men aged between 45 and 55 and women aged over 55 who have risk factor such as family history of CHD, smoking, being overweight, or being of South Asian ethnic origin.

When simvastatin was reclassified to a P medicine the NHS were offering lipid-lowering treatment for secondary prevention or primary prevention where the individual risk was much higher at 30% over 10 years. As a consequence of this treatment threshold it was estimated that 1.8 million patients in the UK were being prescribed statins at a cost to the NHS of £750m per year, and was the single largest contributor to the NHS drug bill.[138] The threshold for primary prevention with statins has been subsequently revised and sits at a 20% risk over 10 years. There may be benefit in targeting an even lower 10 year risk but this is probably not cost-effective for the NHS.[139]

The reclassification of simvastatin in the UK was the first occasion, anywhere in the world, that it was made available for OTC sale and marked a new phase in the role of pharmacists in managing chronic disease. It was the first time that a long term cardiovascular condition could be managed by self medication purchased OTC. It also created debate and raised concerns among health care professionals and the public regards as to the value of simvastatin being available without prescription. This continues to be a topical issue not only in the UK but also in other countries.[140-142] Some of these concerns will be discussed below and include the efficacy of low dose simvastatin, the risk of adverse effects, and whether serum cholesterol should be measured in a pharmacy setting.

There is strong evidence that the cardiovascular risk reduction seen with statins is a direct function of both the magnitude of the reduction in concentration of low density lipoprotein (LDL) cholesterol and the level of LDL cholesterol achieved by the treatment.[143] Therefore, it is necessary to use the highest doses of the most effective statin to achieve the recommended LDL cholesterol target.[144] It is unlikely these targets will be achieved using the 10 mg strength of simvastatin available OTC.[143]

Although the consultation document circulated prior to the reclassification of simvastatin stated that treatment with 10 mg simvastatin would produce a 27% reduction in LDL cholesterol,[145] there are no specific clinical trials of the 10 mg dose being used for primary prevention in patients at moderate risk.[145, 146] Such trials are unlikely ever to materialise and consequently the debate around the clinical efficacy of 10 mg simvastatin may never be resolved.

Simvastatin has a good safety profile although in rare cases serious side effects have been reported.[147] Perhaps the best known serious adverse effect involves liver function abnormalities and myopathy that may result in potentially fatal rhabdomyolysis. Myopathy is a dose dependent adverse effect and risk is increased when simvastatin is used in elderly patients or coadministered with other drugs such as fibrates, macrolide antibiotics and azole antifungals.[143, 146] These particular drug interactions are of concern, especially when the use of simvastatin purchased over the counter is unlikely to be documented in patient records. However, the consultation document stated that the contraindications and cautions listed in the product labelling addressed the concerns about myopathy.[145] It stated that modest elevations of liver enzymes were common with statin use and did not reflect hepatotoxicity. In addition, the Medicines and Healthcare products Regulatory Agency (MHRA) at the time stated that the decision to reclassify simvastatin was only made following advice from the Committee on Safety of Medicines (CSM) having duly considered all responses to the consultation.[148]

Before OTC simvastatin can be sold, the pharmacist must undertake a risk assessment, using a tick-box questionnaire which covers the relevant medical and medication history. A cholesterol test is not necessary for risk assessment before treatment or for subsequent monitoring. The reason for this, according to the MHRA, is that the current evidence suggests that it can be beneficial to reduce cholesterol levels whatever the starting point. In addition, the manufacturer of the OTC product has made it clear that OTC simvastatin is focused on risk reduction not cholesterol reduction.[147]

It has, however, been suggested that not to measure cholesterol in those taking cholesterol-lowering medication is illogical.[149] It may lead to undertreatment of high risk individuals and unnecessary treatment for those at low risk.[150, 151] Although the RPSGB guidelines recommend that blood pressure and cholesterol should be checked to identify people at high risk and those who may benefit from referral to their GP, these tests are not available in every pharmacy. A survey[152] of 200 community pharmacies found that around two thirds of the respondents said they would be willing to carry out cholesterol testing in the pharmacy, but only one third had a private consultation area at the time.

Other concerns associated with the reclassification of simvastatin are that it may create health inequalities with many unable to afford the likely £10 to £15 per month it would cost long term. In addition, some individuals may substitute OTC medicine use in preference to lifestyle modification.[146] With respect to appropriate lifestyle modification, it is the responsibility of the pharmacist to inform and educate the patient on the importance of required lifestyle changes in addition to counselling on the appropriate use of the medication.

Given that the cost of treatment is constantly growing and the NHS is under pressure to fund statin therapy for an ever larger patient pool,[138] it is not surprising that the UK Government endorsed the reclassification of simvastatin in the hope it would offset some of the cost to the NHS.

3.1.3 Hyoscine butylbromide

Abdominal cramping and pain are common symptoms of irritable bowel syndrome (IBS) and have a significant impact on patients' quality of life and socioeconomic consequences.[153, 154] A recent survey showed that the prevalence of IBS varied between countries with an estimate of 31% in the adult population in the UK.[155]

Recommendations about diet, lifestyle and behavioural changes, and pharmacological therapy are integral parts of the treatment of IBS with their focus on relieving symptoms. The current therapeutic management of pain in IBS includes use of antispasmodics, analgesics, antacids, antidarrhoeals, laxatives, and anti-gas products.[155, 156] Antispasmodics are more frequently used than any of the other products.[157]

Hyoscine butylbromide (also known as scopolamine butylbromide) is an antispasmodic that is indicated for the treatment of abdominal cramps associated with IBS. Several studies[157-159] have shown that hyoscine butylbromide is effective in the treatment of abdominal cramping and pain/IBS. It is generally well tolerated as it is poorly absorbed and does not cross the blood-brain barrier. The incidence of typical systemic anticholinergic adverse events is very low and similar to that of placebo.

Hyoscine butylbromide was first registered in 1951 and has become available worldwide both as a prescription drug and as an OTC medicine in many countries including the UK, Belgium, Germany, Italy, Netherlands, Spain, Switzerland, Japan, South Korea, and Australia. In the UK, hyoscine butylbromide 10 mg has been

available as a P medicine since 1991.[129] It was reclassified from P to GSL in January 2005 and marketed as Buscopan IBS Relief at a retail price of £4.39 for a pack of 20 tablets. Apart from peppermint oil, hyoscine butylbromide is the only antispasmodic available as a GSL medicine indicated for symptomatic relief of gastrointestinal tract spasm associated with IBS.

3.1.4 Chloramphenicol eye drops

Chloramphenicol 0.5% eye drops were reclassified from POM to P in June 2005 and initially marketed as Optrex Infected Eyes at a retail price of £4.79 for 10 mL product. OTC chloramphenicol eye drops subsequently became available in other brands including Boots Pharmacy Antibiotic Eye Drops (June 2005), Brochlor eye drops (June 2006), Tubilux Infected Eyes (September 2006). Chloramphenicol eye drops are indicated for the treatment of bacterial conjunctivitis in adults and children aged two years old and over. This was the first reclassification of an antibiotic, albeit for ophthalmic use only, and marked a significant switch for pharmacy given the frequency the disorder presents but for which the pharmacist previously had no effective treatment in their armamentarium.[160]

The pending wider availability of chloramphenicol did raise the issue of resistance emerging. However, studies of the microbial flora in patients with eye infections have shown very low levels of resistance to chloramphenicol.[161, 162] Bone marrow toxicity following the use of chloramphenicol eye drops[163] also emerged as a concern prior to reclassification. However, results from international[164] and national[165] case control studies have demonstrated that the risk of serious haematological toxicity associated with chloramphenicol eye drops is small.

A recent randomized clinical trial has suggested that the outcome of delayed prescribing of chloramphenicol eye drops is similar, in terms of duration and severity of symptoms, to immediate prescribing.[166] However, the availability of OTC chloramphenicol provides patients the opportunity to obtain medication at their own discretion, avoids the need to obtain an appointment with their GP, and may reduce the risk of spreading an infection.[167]

3.1.5 Impact of reclassification of medicines

In general, increasing the range of medicines available for sale over the counter from community pharmacy allows individuals who may not previously have considered seeking treatment to do so, particularly when there are products or health service associated advertising campaigns. This could lead to increased sales for the manufacturer beyond that expected if the medicine had remained prescription only.[131]

The overall impact on the prescribing budget of increasing the availability of medicines for purchase by the public is unclear. In the UK early economic analyses have indicated significant savings to the NHS following the reclassification of hydrocortisone and loperamide,[125] although in practice savings appear to vary from drug to drug.[52] It should also be noted that the OTC versions of products are often only available at a lower dose than their POM counterpart. This means the stronger POM version may still be effective even when the OTC version has failed. Thus, the availability of OTC medicines may or may not impact on the use of POMs from the same therapeutic category. In addition, it has been suggested that even though there may be an increasing number of medicines available for purchase OTC from

community pharmacy, the workload of GPs may not change as those exempt the prescription charge are unlikely to want to pay for medicines at the pharmacy if they can get them free on prescription.[168] This is clearly a significant issue in Wales with the abolition of the prescription charge in April 2007.

3.2 Aims

The aims of this study were to determine i) the impact on prescribing and OTC sale of the reclassification of selected medicines, from POM to P or from P to GSL; and ii) any additional influence deprivation may have on this.

3.3 Method

3.3.1 Design

This was a cross-sectional study that involved a retrospective analysis of primary care dispensed prescription data and OTC sell-in data. Changes in the number of prescription items dispensed and OTC items sold for each medicine/group of medicines before and after reclassification from POM to P or from P to GSL were determined.

3.3.2 Setting

Dispensed prescription and OTC sell-in data were included for analysis from the following groups:

- Groups of primary care organisations (PCOs, known as local health board [LHB] in Wales and primary care trust [PCT] in England) with comparable population size
    - All 22 LHBs in Wales
    - 15 PCTs in the South East of England
    - 16 PCTs in the North East of England
- Groups of LHBs in Wales with contrasting levels of deprivation according to the Welsh Index of Multiple Deprivation (WIMD) 2005
    - 5 most deprived (WIMD) LHBs
    - 5 least deprived (WIMD) LHBs

3.3.3 Unit of measure

The primary measure for the prescribing of medicines was dispensed prescription item per 1000 population. Sale of OTC medicines were also presented as items per 1000 population but in this case an item was a retail pack sold. Population sizes were used as the denominator for all calculations.

3.3.4 Medicines studied

The following criteria were used to select the medicines studied:

- First in class to be reclassified to P or GSL;
- Reclassified between 2004 and 2005; and
- Name of reclassified preparation (brand name) different from POM preparation

The medicines subsequently selected included omeprazole, simvastatin, hyoscine butylbromide and chloramphenicol.

Prescription and sale of medicines/groups of medicines related to the medicines studied were also included and specific preparations selected are listed below:

Omeprazole

Prescription medicines

- All H_2 antagonists in oral solid dosage forms at strengths indicated for administration to adults (BNF section 1.3.1)
- All proton pump inhibitors in oral solid dosage forms at strengths indicated for administration to adults (BNF section 1.3.5)
- Omeprazole in oral solid dosage forms at a strength of 10 mg (BNF section 1.3.5)

OTC medicines

- H_2 antagonists available as P or GSL medicines:
  - Cimetidine 10 mg: Tagamet® 100 (12 tablets per pack)
  - Famotidine 10 mg: Pepcid AC® (6 and 12 tablets per pack), Pepcid Two® (6, 12 and 24 tablets per pack)
  - Ranitidine 75 mg: Gavilast® (6 and 12 tablets per pack), Gavilast-P® (24 and 48 tablets per pack), Ranzac® (6 tablets per pack), Zantac® 75 Dissolve (24 tablets per pack), Zantac® 75 Relief Dissolve (12 tablets per pack), Zantac® 75 Relief (6 and 12 tablets per pack), Zantac® 75 (6, 12, 24 and 48 tablets per pack)
- Omeprazole 10 mg: Zanprol® (14 tablets per pack), Galpharm® Heartburn Relief (14 tablets per pack)

Simvastatin

Prescription medicines

- All statins in oral solid dosage forms at strengths indicated for administration to adults (BNF section 2.12)
- All simvastatin in oral solid dosage forms at strengths indicated for administration to adults (BNF section 2.12)
- Simvastatin in oral solid dosage forms at strength of 10 mg (BNF section 2.12)

OTC medicines

- Simvastatin 10 mg: Zocor Heart-Pro® (28 tablets per pack)

Hyoscine butylbromide

Prescription medicines

- All preparations of antispasmodics and other drugs altering gut motility (BNF section 1.2)
- Hyoscine butylbromide in oral solid dosage forms at a strength of 10 mg (BNF section 1.2)

OTC medicines

- Hyoscine butylbromide 10 mg available as P medicine: Buscopan® (20 tablets per pack)
- Hyoscine butylbromide 10 mg available as GSL medicine: Buscopan® IBS Relief (20 tablets per pack)

Chloramphenicol

Prescription medicines

- Chloramphenicol ophthalmic preparations including eye drops and ointment (BNF section 11.3.1)
- Chloramphenicol 0.5% eye drops (BNF section 11.3.1)
- Chloramphenicol 1% eye ointment (BNF section 11.3.1)

OTC medicines

- Chloramphenicol 0.5% eye drops: Optrex® Infected Eyes (10 ml)

3.3.5 Data

3.3.5.1 Dispensed prescription data

Dispensed prescription data for Wales were obtained from the CASPA (Comparative Analysis System for Prescribing Audit) database. Dispensed prescription data for selected PCTs in England were supplied in Microsoft Excel by the Prescription

Pricing Division (PPD) and presented on a quarterly basis from October 2001 to September 2006.

3.3.5.2 Over the counter sell-in data

Over the counter sell-in data were supplied by IMS (Intercontinental Marketing Services) Health under an agreement with the Welsh Assembly Government. Data supplied included the sale of selected pharmaceutical preparations from main suppliers into retail pharmacies across the UK on a monthly basis for the following periods:

- August 2002 to July 2003;
- May 2003 to April 2006; and
- February 2005 to January 2007

3.3.5.3 Population data

Population data for LHBs in Wales and PCTs in England were obtained as described in the reduction of the prescription charge study (Section 2.3.4.2 and Appendix 1).

3.3.5.4 Deprivation data for Wales

Deprivation data were obtained from the Welsh Index of Multiple Deprivation 2005. Deprivation scores for each local authority/LHB were determined from the percent of Lower Layer Super Output Areas (LSOAs) in the LHB that fell into the most deprived 20% in Wales for all deprivation measures (Appendix 2).

3.3.6 Data organisation

Data organisation was the process of changing the original dispensed prescription and OTC sell-in data into a format that allowed statistical analysis over a specific period. The organisation of dispensed prescription data was similar to that used in the reduction of the prescription charge study (Appendix 3). Over the counter sell-in data for selected preparations for all settings were transferred from the IMS Health database into an Excel spreadsheet (Appendix 5).

Sell-in data for all medicines studied, except OTC H_2 antagonists and omeprazole, were aggregated into 12 month blocks. Due to the limited timescale of the available period (August 2002 to September 2006), a collective six month blocks analysis approach was applied to sell-in data for OTC H_2 antagonists and omeprazole (section 3.5.1.4).

3.3.6.1 Omeprazole

Dispensed prescription data for H_2 antagonists and proton pump inhibitors were organised into four 12 month blocks, Year 1 to Year 4, from April 2002 to March 2006 (Figure 3.1).

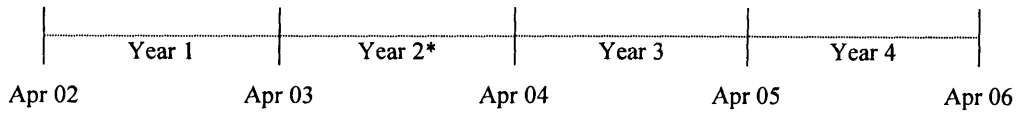


Figure 3.1 Organisation of dispensed prescription data for H_2 antagonists and proton pump inhibitors into 12 month blocks. *Period immediately prior to the reclassification of omeprazole (POM to P) in March 2004

In the period OTC Half Year 1 to OTC Half Year 3 (Figure 3.2) before the reclassification of omeprazole only OTC sell-in data for H_2 antagonists were available. OTC sell-in data for both H_2 antagonists and omeprazole were subsequently organised into three six month blocks (OTC Half Year 4 to OTC Half Year 6).

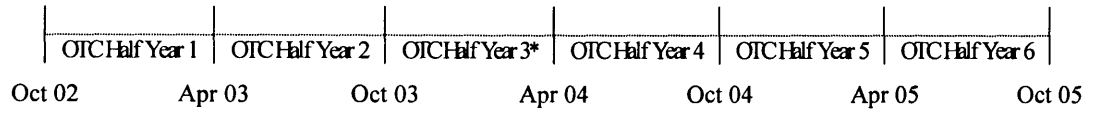


Figure 3.2 Organisation of OTC sell-in data for H_2 antagonists (OTC Half Year 1 to OTC Half Year 3), and both H_2 antagonists and omeprazole (OTC Half Year 4 to OTC Half Year 6) into 6 month blocks. OTC = over the counter sell-in data. *Period immediately prior to the reclassification of omeprazole (POM to P) in March 2004

3.3.6.2 Simvastatin

Dispensed prescription data for statins including simvastatin were organised into four 12 month blocks, Year 1 to Year 4, from July 2002 to June 2006 (Figure 3.3). Over the counter sell-in data for simvastatin were arranged into two 12 month blocks after reclassification from July 2004 to June 2006.

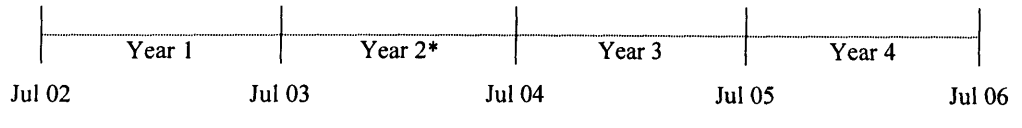


Figure 3.3 Organisation of dispensed prescription data for statins including simvastatin into 12 month blocks. *Period immediately prior to the reclassification of simvastatin (POM to P) in July 2004

3.3.6.3 Hyoscine butylbromide

Dispensed prescription data for antispasmodics including hyoscine butylbromide were organised into four 12 month blocks, Year 1 to Year 4, from January 2002 to December 2005 (Figure 3.4). Prior to the reclassification of hyoscine butylbromide from P to GSL in January 2005 OTC sell-in data for the P product were organized into two 12 months blocks (Figure 3.5). Both OTC sell-in data for the P and GSL hyoscine butylbromide products were included in 12 month blocks following reclassification (OTC Year 3).

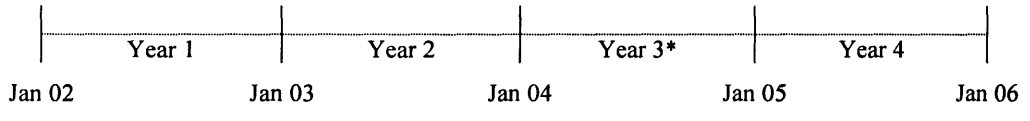


Figure 3.4 Organisation of dispensed prescription data for antispasmodics into 12 month blocks. *Period immediately prior to the reclassification of hyoscine butylbromide (P to GSL) in January 2005

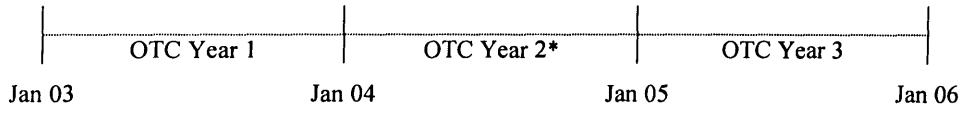


Figure 3.5 Organisation of OTC sell-in data for P hyoscine butylbromide (OTC Year 1 to OTC Year 2), and both P and GSL hyoscine butylbromide (OTC Year 3) into 12 month blocks. OTC = Over the counter sell-in data, *Period immediately prior to the reclassification of hyoscine butylbromide (P to GSL) in January 2005

3.3.6.4 Chloramphenicol eye drops

Dispensed prescription data for ophthalmic chloramphenicol, including chloramphenicol eye drops and ointment, were organised in four 12 month blocks, Year 1 to Year 4, from July 2002 to June 2006 (Figure 3.6). Over the counter sell-in data for chloramphenicol eye drops, reclassified from POM to P in 2005, were monitored for the first 12 months after reclassification.

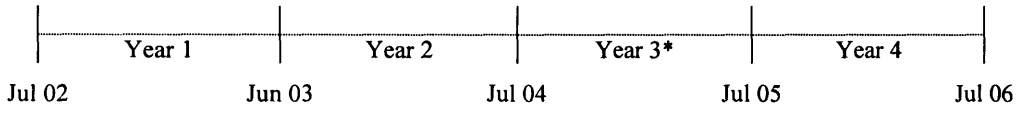


Figure 3.6 Organisation of dispensed prescription data for ophthalmic chloramphenicol into 12 month blocks. *Period immediately prior to the reclassification of chloramphenicol eye drops (POM to P) in June 2005

3.3.7 Arrangement of organised data

Dispensed prescription data for PCOs in Wales and England were combined and presented in one Excel spreadsheet. OTC sell-in data for PCOs in Wales and England were also combined and presented in the same Excel file with the dispensed prescription data but in another spreadsheet. Codes for each medicine, setting, and time block were allocated to the data accordingly. Data were then transferred from the Excel spreadsheet to SPSS version 14. Data in SPSS were screened for errors that may have occurred during data manipulation and coding.

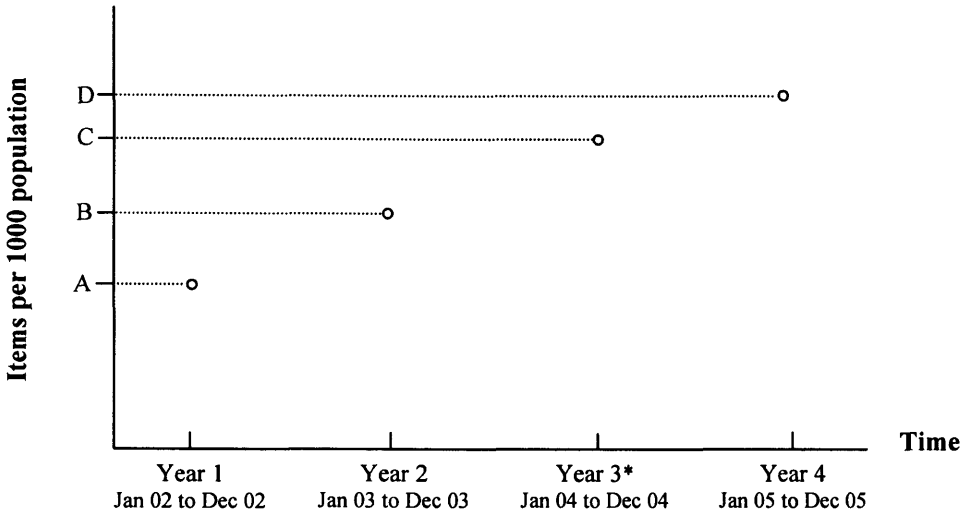
3.3.8 Analysis

Data were analysed by non-parametric statistical tests using SPSS version 14. According to the aims of the study, three different analyses were undertaken to identify the impact of reclassification on the pattern of prescribing and the sale of related OTC medicines, and to determine the impact of deprivation on the sale of reclassified medicines.

3.3.8.1 Impact of reclassification on the pattern of prescribing in primary care

The impact on the pattern of prescribing in primary care was only determined for the reclassification of hyoscine butylbromide and chloramphenicol eye drops. The percent change in the number of prescription items dispensed from Year 1 to Year 2 (Q), Year 2 to Year 3 (R), and Year 3 to Year 4 (S) were determined for both hyoscine butylbromide (Figure 3.7) and chloramphenicol eye drops (Figure 3.8).

The Wilcoxon Signed Rank test was used to determine the difference in the percent change before (between Q and R) and after (between R and S) the reclassification of hyoscine butylbromide and chloramphenicol eye drops in each setting, i.e. the 22 LHBs in Wales, 16 PCTs in the North East of England, 15 PCTs in the South East of England, the five most deprived (WIMD) LHBs in Wales, and the five least deprived (WIMD) LHBs in Wales.



*Period prior to the reclassification of hyoscine butylbromide (P to GSL) in January 2005

A = number dispensed prescription items per 1000 population for antispasmodics and hyoscine butylbromide in Year 1

B = number dispensed prescription items per 1000 population for antispasmodics and hyoscine butylbromide in Year 2

C = number dispensed prescription items per 1000 population for antispasmodics and hyoscine butylbromide in Year 3

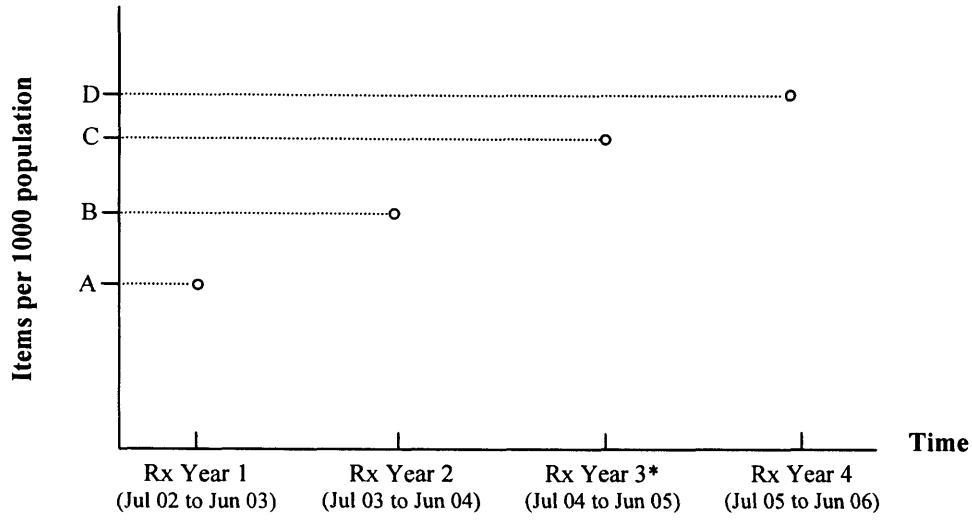
D = number dispensed prescription items per 1000 population for antispasmodics and hyoscine butylbromide in Year 4

$$Q = \frac{(B - A)}{A} \times 100$$

$$R = \frac{(C - B)}{B} \times 100$$

$$S = \frac{(D - C)}{C} \times 100$$

Figure 3.7 Model to illustrate the calculation of the percent change in the number of dispensed prescription items relative to the time of reclassification of hyoscine butylbromide



*Period prior to the reclassification of chloramphenicol eye drops (POM to P) in June 2005

A = number dispensed prescription items per 1000 population for chloramphenicol eye drops and ointment in Year 1

B = number dispensed prescription items per 1000 population for chloramphenicol eye drops and ointment in Year 2

C = number dispensed prescription items per 1000 population for chloramphenicol eye drops and ointment in Year 3

D = number dispensed prescription items per 1000 population for chloramphenicol eye drops and ointment in Year 4

$$Q = \frac{(B - A)}{A} \times 100$$

$$R = \frac{(C - B)}{B} \times 100$$

$$S = \frac{(D - C)}{C} \times 100$$

Figure 3.8 Model to illustrate the calculation of the percent change in the number of dispensed prescription items relative to the time of reclassification of chloramphenicol eye drops

3.3.8.2 Impact of reclassification on the pattern of sale of related OTC medicines

The impact of the reclassification of medicines on the pattern of sale of related OTC medicines were determined by descriptive statistics and presented as the total number of items sold per 1000 population in each study block (6 month or 12 month as appropriate) before and after the reclassification of the medicine under study.

3.3.8.3 Impact of deprivation on the sale of reclassified medicines

The study of the association between deprivation and the sale of reclassified medicines were restricted to Wales. Deprivation scores (WIMD 2005) for each of the 22 LHBs in Wales and the number of items of each selected product sold in the 12 month block post reclassification were investigated using Spearman's rank order correlation coefficient. The OTC sell-in periods for the correlation analysis with level of deprivation for each medicine studied are presented below:

- Omeprazole: months 13 to 24 after reclassification (April 2005 to March 2006)
- Simvastatin: months 13 to 24 after reclassification (July 2005 to June 2006)
- Hyoscine butylbromide: months 1 to 12 after reclassification (January 2005 to December 2005)
- Chloramphenicol eye drops: months 1 to 12 after reclassification (July 2005 to June 2006)

The number of items sold in the appropriate 12 month block as defined above for each reclassified medicine in the five most deprived (WIMD) LHBs and the five least deprived (WIMD) LHBs were compared using Mann-Whitney U test.

The volumes of prescriptions dispensed were expressed as items per 1000 population and presented as median (interquartile range [IQR]). Sales of OTC medicines were also expressed as items per 1000 population, but presented as total number of sales per 1000 population (section 3.5.1.5). Results for statistical analysis were presented as p-value and correlation coefficient (r) where appropriate. A p-value of less than 0.05 was considered to be statistically significant.

3.4 Results

The study involved the analysis of four different medicines following reclassification. The results are presented in the sequence the studies were undertaken.

3.4.1 Omeprazole

Declining trends in the number of dispensed prescriptions for H_2 antagonists were observed in Wales, the South East of England, and the North East of England over the four year study period from 2002 to 2006 (Table 3.3). In contrast, the number of dispensed prescription items for proton pump inhibitors in all settings appeared to increase over the same period.

Compared with the period October 2002 to March 2003 the number of items per 1000 population of OTC H_2 antagonists sold during the period October 2003 to March 2004 increased from 10.3 to 14.6 in Wales, 10.2 to 12.0 in the South East of England, and 10.3 to 14.2 in the North East of England (Table 3.4). The sale pattern of OTC H_2 antagonists subsequently decreased in all settings following the launch of OTC omeprazole in March 2004. During the period October 2004 to March 2005 the sale (items per 1000 population) of OTC H_2 antagonists decreased to 11.6 in Wales, 9.6 in the South East of England, and 10.9 in the North East of England. A decrease in the combined sales of H_2 antagonists and omeprazole were also noted over the period from April 2004 to September 2005 (Figures 3.9 and 3.10).

Table 3.3 Number of dispensed prescription items for proton pump inhibitors, H_2 antagonists, and omeprazole 10 mg in different settings

	H_2 antagonists				Proton pump inhibitors				Omeprazole 10 mg			
	Apr 02 to Mar 03 (Year 1)	Apr 03 to Mar 04* (Year 2)	Apr 04 to Mar 05 (Year 3)	Apr 05 to Mar 06 (Year 4)	Apr 02 to Mar 03 (Year 1)	Apr 03 to Mar 04* (Year 2)	Apr 04 to Mar 05 (Year 3)	Apr 05 to Mar 06 (Year 4)	Apr 02 to Mar 03 (Year 1)	Apr 03 to Mar 04* (Year 2)	Apr 04 to Mar 05 (Year 3)	Apr 05 to Mar 06 (Year 4)
22 LHBs Wales	147.8 [135.0 – 190.1]	140.7 [127.2 – 175.9]	130.7 [118.2 – 159.4]	116.8 [110.9 – 146.6]	496.9 [432.6 – 521.8]	559.5 [494.1 – 590.6]	635.7 [559.4 – 659.2]	723.3 [628.4 – 761.6]	46.3 [36.3 – 50.6]	47.6 [34.6 – 55.2]	51.7 [36.4 – 61.6]	54.8 [46.0 – 68.0]
15 PCTs South East of England	88.5 [70.7 – 99.3]	79.1 [65.0 – 95.6]	69.3 [61.9– 89.0]	62.2 [57.0 – 77.6]	263.6 [234.0 – 359.5]	305.3 [263.1 – 413.5]	383.2 [325.2 – 442.1]	442.6 [378.6 – 518.5]	19.3 [13.5 – 20.5]	18.7 [13.3 – 21.1]	19.9 [14.6– 24.7]	22.2 [20.7– 32.6]
16 PCTs North East of England	151.5 [129.4 – 158.8]	137.7 [119.2 – 151.5]	127.2 [108.8 – 140.4]	112.0 [97.1 – 123.1]	389.9 [343.7 – 422.9]	439.1 [397.4 – 473.7]	498.5 [463.9 – 537.5]	575.9 [539.8 – 614.6]	29.2 [23.7 – 39.1]	28.9 [23.5 – 37.6]	34.6 [25.9 –58.6]	50.7 [29.1 – 73.6]
Five most deprived (WIMD) LHBs Wales	171.7 [139.9 – 212.4]	164.8 [133.6 – 195.9]	155.8 [123.9 – 186.8]	142.0 [110.8 – 168.7]	492.5 [470.7 – 527.6]	554.5 [536.8 – 595.5]	635.8 [620.5 – 676.4]	727.1 [714.3 – 780.6]	40.9 [34.4 –59.6]	49.4 [38.2– 61.3]	55.0 [43.5 – 62.5]	62.6 [50.7 – 66.7]
Five least deprived (WIMD) LHB Wales	140.2 [108.6 – 154.8]	130.0 [100.3 – 139.2]	118.0 [93.4 – 128.2]	114.1 [85.5 – 117.3]	501.2 [440.1 – 553.0]	555.4 [502.1 – 631.4]	600.2 [562.5 – 705.5]	679.0 [627.4 – 801.8]	47.0 [39.6– 50.5]	44.2 [38.6 – 56.3]	43.1 [39.3 – 63.4]	54.4 [41.9 – 68.4]

Results presented as median [interquartile range] of the dispensed prescription items per 1000 population. LHB = Local Health Board, PCT = Primary Care Trust, WIMD = Welsh Index of Multiple Deprivation. *Period immediately prior to the reclassification of omeprazole (POM to P) in March 2004

Table 3.4 Items of OTC H_2 antagonists and omeprazole 10 mg sold in different settings

	22 LHBs Wales	15 PCTs South East of England	16 PCTs North East of England	Five most deprived (WIMD) LHBs Wales	Five least deprived (WIMD) LHBs Wales
H_2 antagonists					
Oct 02 to Mar 03 (OTC Half Year 1)	10.3	10.2	10.3	11.3	11.2
Apr 03 to Sep 03 (OTC Half Year 2)	12.4 (20.4%)	9.8 (-3.9%)	11.4 (10.7%)	12.5 (10.6%)	14.6 (30.4%)
Oct 03 to Mar 04* (OTC Half Year 3)	14.6 (17.7%)	12.0 (22.4%)	14.2 (24.6%)	15.0 (20.0%)	15.4 (5.5%)
Apr 04 to Sep 04 (OTC Half Year 4)	12.5 (-14.4%)	10.0 (-16.7%)	11.6 (-18.3%)	12.3 (-18.0%)	15.1 (-1.9%)
Oct 04 to Mar 05 (OTC Half Year 5)	11.6 (-7.2%)	9.6 (-4.0%)	10.9 (-6.0%)	11.1 (-9.8%)	12.6 (-16.6%)
Apr 05 to Sep 05 (OTC Half Year 6)	9.8 (-15.5%)	8.8 (-8.3%)	9.5 (-12.8%)	9.3 (-16.2%)	11.8 (-6.3%)
Omeprazole 10 mg					
Apr 04 to Sep 04 (OTC Half Year 4)	1.5	1.0	0.9	1.5	1.6
Oct 04 to Mar 05 (OTC Half Year 5)	0.5	0.6	0.3	0.5	0.5
Apr 05 to Sep 05 (OTC Half Year 6)	0.5	0.7	0.3	0.4	0.6

Results presented as total items per 1000 population (% change compared to the previous year). *Period immediately prior to the reclassification of omeprazole (POM to P) in March 2004

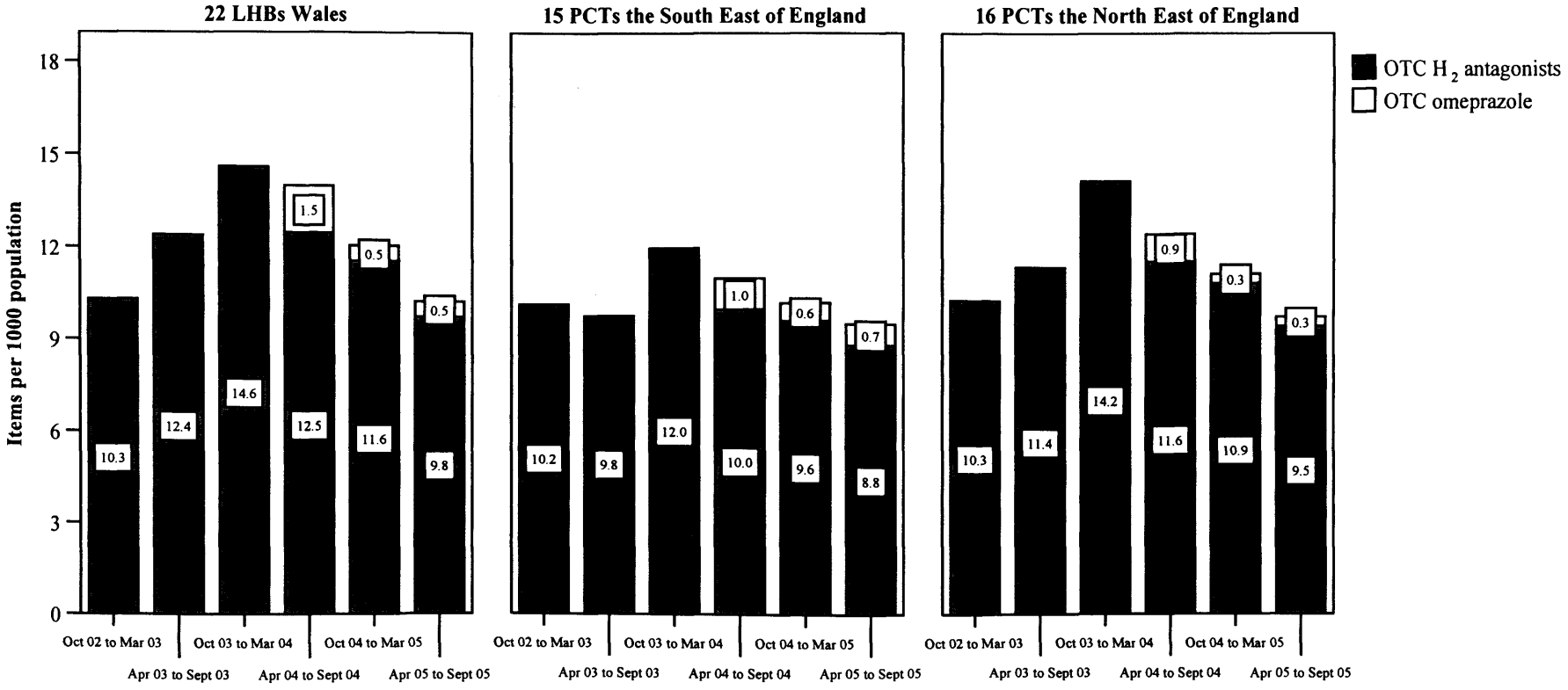


Figure 3.9 Sale (items per 1000 population) of OTC H_2 antagonists and omeprazole 10 mg in different settings

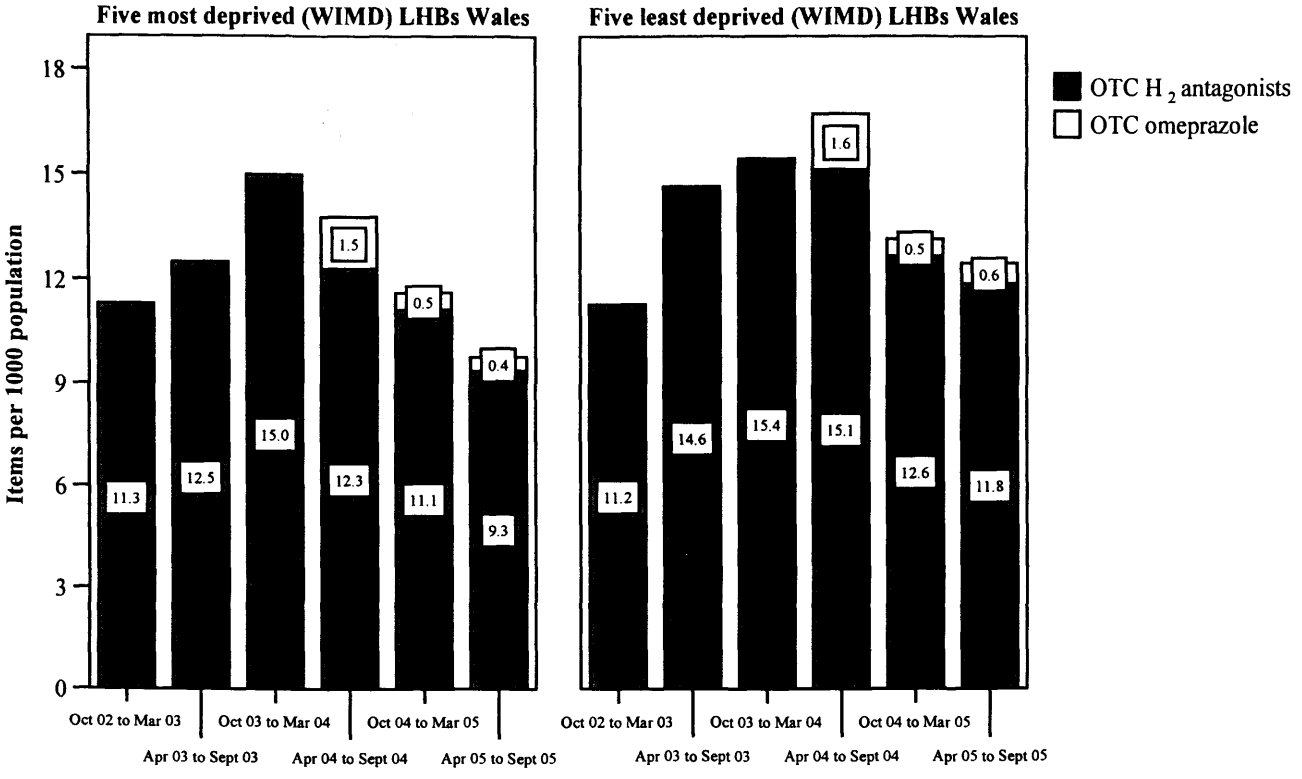


Figure 3.10 Sale (items per 1000 population) of OTC H_2 antagonists and omeprazole 10 mg in the five most deprived (WIMD) and the five least deprived (WIMD) LHBs in Wales

In the period April 2005 to September 2005, sales of OTC omeprazole accounted for 4.9% of the combined sales of omeprazole and H_2 antagonists in Wales, 7.4% in the South East of England, 3.1% in the North East of England, 4.1% in the five most deprived (WIMD) LHBs in Wales, and 4.8% in the five least deprived (WIMD) LHBs in Wales.

The deprivation scores (WIMD) of the 22 LHBs in Wales were not associated with the sale of OTC omeprazole in months 13 to 24 (April 2005 to March 2006) after reclassification (r = 0.09, p = 0.70) (Figure 3.11). Comparison of the number of items sold per 1000 population (median [IQR]) for OTC omeprazole in the five most deprived LHBs with the five least deprived LHBs also demonstrated no difference (1.4 [0.9 – 1.8]) v 1.6 [0.8 – 2.2], p = 0.6).

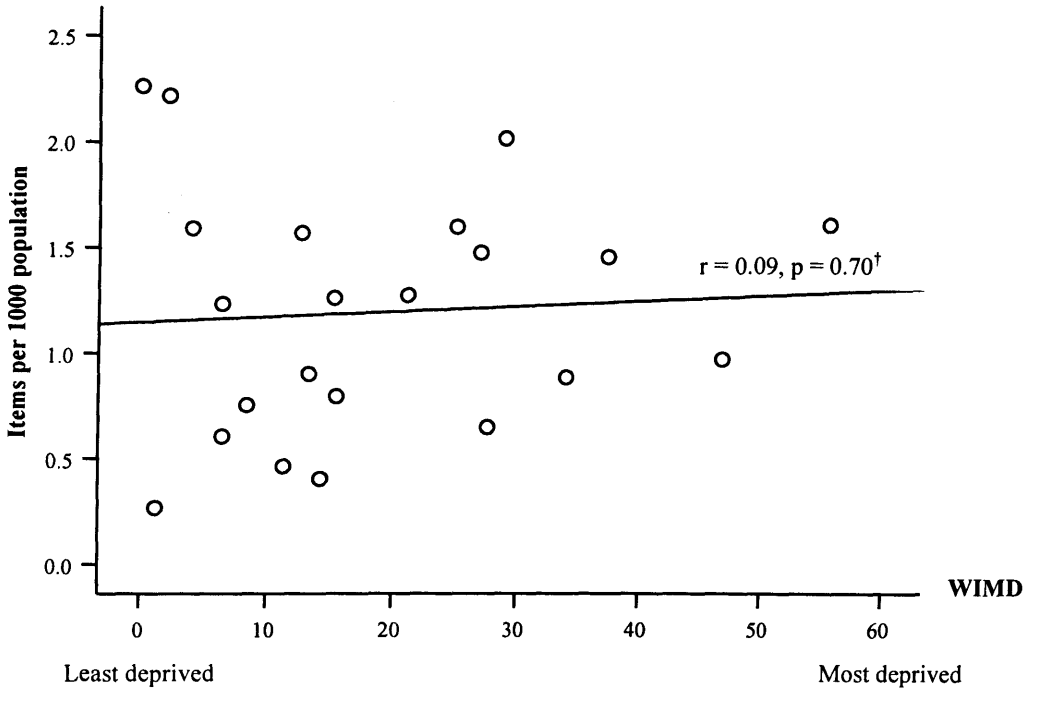


Figure 3.11 Deprivation score and sale of OTC omeprazole in the 22 LHBs in Wales in months 13-24 after reclassification (April 2005 to March 2006). †Spearman's rank order correlation coefficient

3.4.2 Simvastatin

An increasing trend in the number of dispensed prescription items for both statins as a group and simvastatin as an individual product were observed in all settings throughout the study (Table 3.5). In contrast, the number of dispensed prescription items for simvastatin 10 mg appeared to vary between settings.

Sales of OTC simvastatin in months 13 to 24 after reclassification (July 2005 to June 2006) appeared less than sales in the first 12 month in all settings (Table 3.6). During this period (month 13 to 24), sales of OTC simvastatin per 1000 population in Wales were 0.2 items, 0.6 items in the South East of England, 0.2 items in the North East of England, 0.1 items in the five most deprived (WIMD) LHBs in Wales, and 0.2 items in the five least deprived (WIMD) LHBs in Wales.

In Wales, the sale of OTC simvastatin 10 mg was 0.2% of the volume of simvastatin 10 mg prescribed during July 2005 to June 2006. Comparable values for OTC and prescribed volumes were 1.4% and 0.3% in the South East and the North East of England, respectively.

The sale of OTC simvastatin in Wales in months 13 to 24 after reclassification (July 2005 to June 2006) were not significantly associated with the deprivation score (WIMD) of each LHB ($r = -0.4$, $p = 0.07$) (Figure 3.12). The number of items per 1000 population (median [IQR]) for OTC simvastatin sold in the five least deprived LHBs and the five most deprived LHBs revealed no difference (0.26 [0.06 – 0.41] v 0.14 [0.06 – 0.15], $p = 0.35$).

Table 3.5 Number of dispensed prescription items for statins, simvastatin, and simvastatin 10 mg in different settings

	Statins				Simvastatin				Simvastatin 10 mg			
	Jul 02 to Jun 03 (Year 1)	**Jul 03 to Jun 04* (Year 2)**	**Jul 04 to Jun 05 (Year 3)**	**Jul 05 to Jun 06 (Year 4)**	**Jul 02 to Jun 03 (Year 1)**	**Jul 03 to Jun 04* (Year 2)**	**Jul 04 to Jun 05 (Year 3)**	**Jul 05 to Jun 06 (Year 4)**	**Jul 02 to Jun 03 (Year 1)**	**Jul 03 to Jun 04* (Year 2)**	**Jul 04 to Jun 05 (Year 3)**	**Jul 05 to Jun 06 (Year 4)**
22 LHBs Wales	557.7 [470.3 – 632.6]	731.2 [652.9 – 824.0]	946.5 [839.5 – 1066.3]	1109.8 [973.3 – 1258.2]	248.9 [224.2 – 289.4]	338.3 [301.3 – 391.5]	456.4 [391.2 – 539.3]	589.3 [492.2 – 673.5]	77.0 [65.1 – 102.5]	75.9 [64.8 – 104.0]	79.5 [63.2 – 97.4]	79.1 [67.1 – 100.7]
15 PCTs South East of England	309.2 [262.0 – 455.8]	396.3 [340.3 – 607.5]	543.8 [424.2 – 758.3]	638.2 [507.8 – 912.9]	159.8 [129.1 – 232.1]	217.3 [152.8 – 303.6]	271.2 [205.5 – 363.7]	327.8 [257.8 – 474.6]	44.0 [36.8 – 54.9]	37.8 [34.3 – 50.8]	39.5 [32.0 – 47.3]	42.1 [31.5 – 50.7]
16 PCTs North East of England	489.4 [430.3 – 524.5]	660.0 [549.9 – 703.9]	809.2 [681.9 – 852.5]	915.9 [802.8 – 986.4]	260.7 [238.1 – 317.6]	363.1 [319.6 – 466.1]	453.7 [402.9 – 579.9]	568.2 [501.8 – 691.1]	97.2 [77.4 – 119.2]	77.5 [65.8 – 89.2]	77.8 [54.8 – 92.2]	64.5 [49.3 – 98.8]
Five most deprived (WIMD) LHBs Wales	624.4 [594.6 – 638.5]	817.4 [803.8 – 854.2]	1066.8 [1021.2 – 1184.2]	1262.2 [1172.9 – 1351.8]	251.6 [226.6 – 286.7]	346.9 [335.5 – 387.1]	497.4 [461.4 – 521.3]	625.4 [615.9 – 712.9]	107.2 [67.7 – 115.7]	115.3 [74.3 – 116.6]	113.9 [84.3 – 126.5]	119.2 [82.5 – 134.3]
Five least deprived (WIMD) LHB Wales	552.3 [491.1 – 606.4]	702.7 [652.6 – 792.0]	867.7 [813.2 – 1000.9]	991.3 [944.3 – 1183.7]	270.4 [220.5 – 281.7]	340.1 [260.1 – 369.0]	443.1 [320.3 – 483.4]	525.2 [397.7 – 561.4]	77.9 [75.7 – 90.8]	79.9 [74.8 – 91.5]	79.5 [65.9 – 90.9]	80.0 [60.1 – 95.9]

Results presented as median [interquartile range] of the dispensed prescription items per 1000 population. LHB = Local Health Board, PCT = Primary Care Trust, WIMD = Welsh Index of Multiple Deprivation. *Period immediately prior to the reclassification of simvastatin (POM to P) in July 2004

Table 3.6 Items of OTC simvastatin 10 mg sold in different settings

	22 LHBs Wales	15 PCTs South East of England	16 PCTs North East of England	Five most deprived (WIMD) LHBs Wales	Five least deprived (WIMD) LHBs Wales
Jul 04 to Jun 05 (OTC Year 1)	0.7	1.1	0.6	0.6	0.6
Jul 05 to Jun 06 (OTC Year 2)	0.2	0.6	0.2	0.1	0.2

Results presented as total items per 1000 population

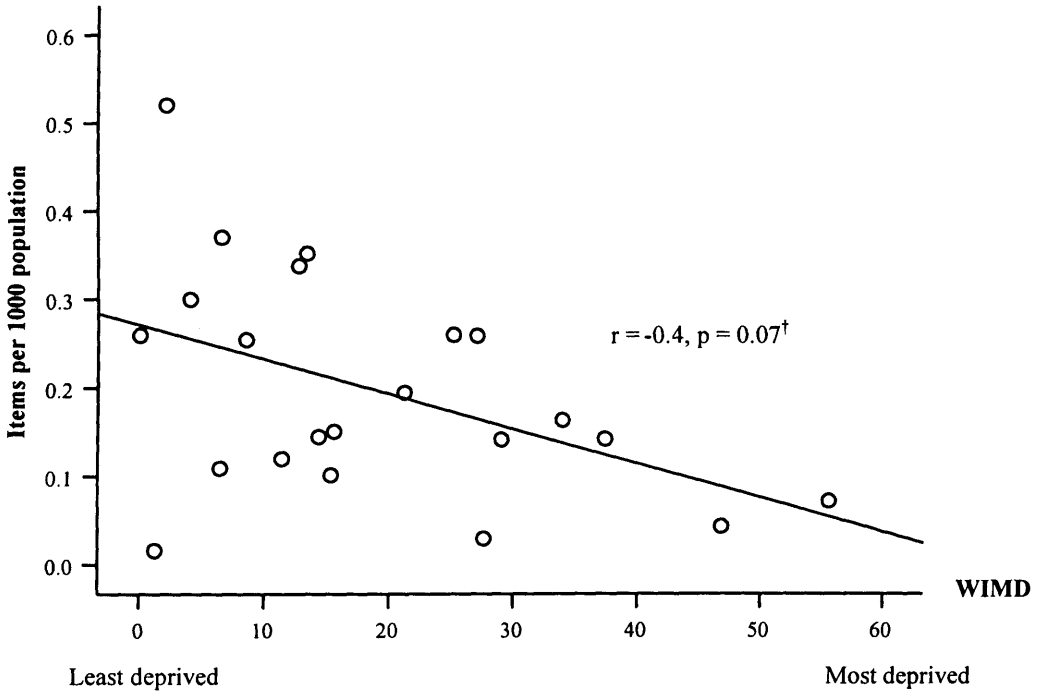


Figure 3.12 Deprivation score and sale of OTC simvastatin in the 22 LHBs in Wales in months 13-24 after reclassification (July 2005 to June 2006). †Spearman's rank order correlation coefficient

3.4.3 Hyoscine butylbromide

The number of dispensed prescription items for antispasmodics in all settings showed an upward trend over the four year study period (Table 3.7). It appeared, in the period January to December 2005 that relatively higher numbers of prescriptions for antispasmodics were dispensed in Wales (86.3 [72.4 – 95.0]) than in the South East (46.0 [39.0 – 58.9]) and the North East of England (63.9 [53.2 – 72.9]).

When the percent change in the number of prescription items were compared, it was found that there was no difference in the percent change in the number of prescription items for antispasmodics both before and after the reclassification of hyoscine butylbromide in any of the settings studied (Table 3.8). In the case of hyoscine butylbromide there was no significant difference in the percent change before its reclassification in the different settings studied. However, the percent change in the 12 months after the reclassification was significantly higher than in the previous 12 months in Wales (20.7 [4.4 – 25.6] v 5.8[0.2 – 12.6], $p < 0.01$) and in the South East of England (22.5 [10.4 – 27.8]) v 5.3[-0.9 – 14.8], $p = 0.02$), but not in the North East of England (16.0 [4.3 – 27.6] v 21.7 [8.2 – 26.7], $p = 0.30$).

Before hyoscine butylbromide became available as a GSL product the sale of P hyoscine butylbromide in Wales and England in the period January to December 2004 showed a growth of less than 10% compared with sales in the preceding year, i.e. 6.8% in Wales, 5.7% in the South East of England, and 6.7% in the North East of England (Table 3.9). The combined sales of OTC (P and GSL) hyoscine butylbromide in the 12 months after its reclassification increased by 31.1% in Wales, 37.5% in the South East of England, and 27.2% in the North East of England.

Table 3.7 Number of dispensed prescription items for antispasmodics collectively and hyoscine butylbromide individually in different settings

	Antispasmodics				Hyoscine butylbromide			
	Jan 02 to Dec 02 (Year 1)	**Jan 03 to Dec 03 (Year 2)**	**Jan 04 to Dec 04* (Year 3)**	**Jan 05 to Dec 05 (Year 4)**	**Jan 02 to Dec 02 (Year 1)**	**Jan 03 to Dec 03 (Year 2)**	**Jan 04 to Dec 04* (Year 3)**	**Jan 05 to Dec 05 (Year 4)**
22 LHBs Wales	76.0 [65.2 – 82.2]	79.8 [66.1 – 85.6]	83.0 [69.5 – 90.2]	86.3 [72.4 – 95.0]	5.7 [4.5 – 8.0]	6.4 [5.0 – 8.4]	6.8 [5.5 – 8.7]	8.3 [6.0 – 10.4]
15 PCTs South East of England	43.2 [38.5 – 54.5]	43.2 [38.2 – 56.0]	44.3 [37.7 – 54.9]	46.0 [39.0 – 58.9]	3.7 [3.4 – 4.7]	4.2 [3.5 – 5.2]	4.6 [4.0 – 5.5]	5.6 [4.9 – 6.9]
16 PCTs North East of England	56.6 [50.2 – 67.0]	62.2 [50.7 – 69.8]	63.5 [51.3 – 70.0]	63.9 [53.2 – 72.9]	5.7 [4.7 – 8.0]	5.7 [4.6 – 8.7]	6.5 [5.3 – 9.6]	8.5 [6.4 – 10.0]
Five most deprived (WIMD) LHBs Wales	75.9 [75.5 – 91.6]	81.0 [78.4 – 92.8]	84.2 [83.6 – 96.9]	89.6 [87.1 – 99.1]	7.7 [4.5 – 12.3]	7.1 [5.0 – 12.6]	9.0 [4.9 – 11.8]	8.9 [6.2 – 14.0]
Five least deprived (WIMD) LHB Wales	66.0 [54.1 – 84.6]	66.7 [58.6 – 86.8]	70.0 [63.3 – 93.4]	76.1 [68.9 – 96.2]	5.0 [3.8 – 7.7]	5.0 [4.7 – 8.3]	5.8 [4.9 – 8.5]	6.1 [5.6 – 9.8]

Results presented as median [interquartile range] of the dispensed prescription items per 1000 population. LHB = Local Health Board, PCT = Primary Care Trust, WIMD = Welsh Index of Multiple Deprivation. *Period immediately prior to the reclassification of hyoscine butylbromide (P to GSL) in January 2005

Table 3.8 Percent change in different settings in prescription items for antispasmodics and hyoscine butylbromide before and after the reclassification of hyoscine butylbromide

	Before			After		
	% change from Year1 to Year2	% change from Year 2 to Year 3	p value†	% change from Year 2 to Year 3	% change from Year 3 to Year 4	p value†
Antispasmodics						
22 LHBs Wales	4.7 [1.7 – 7.3]	5.2 [3.3 – 5.9]	0.57	5.2 [3.3 – 5.9]	4.1 [2.2 – 6.4]	0.20
15 PCTs South East of England	0.4 [-8.7 – 2.2]	1.2 [-1.8 – 4.7]	0.53	1.2 [-1.8 – 4.7]	3.2 [0.9 – 5.7]	0.33
16 PCTs North East of England	2.8 [0.5 – 6.4]	2.1 [1.2 – 3.0]	0.44	2.1 [1.2 – 3.0]	3.6 [1.3 – 6.1]	0.07
Five most deprived (WIMD) LHBs Wales	4.0 [0.9 – 5.9]	5.6 [3.2 – 7.2]	0.34	5.6 [3.2 – 7.2]	4.2 [1.2 – 6.6]	0.50
Five least deprived (WIMD) LHBs Wales	4.8 [0.6 – 8.5]	5.8 [2.0 – 12.6]	0.50	5.8 [2.0 – 12.6]	4.3 [3.1 – 6.9]	0.34
Hyoscine butylbromide						
22 LHBs Wales	6.3 [2.1 – 16.4]	5.8 [0.2 – 12.6]	0.22	5.8 [0.2 – 12.6]	20.7 [4.4 – 25.6]	0.007*
15 PCTs South East of England	11.6 [4.3 – 18.1]	5.3 [-0.9 – 14.8]	0.23	5.3 [-0.9 – 14.8]	22.5 [10.4 – 27.8]	0.02*
16 PCTs North East of England	2.2 [-4.2 – 18.0]	16.0 [4.3 – 27.6]	0.16	16.0 [4.3 – 27.6]	21.7 [8.2 – 26.7]	0.30
Five most deprived (WIMD) LHBs Wales	3.8 [-3.1 – 11.8]	5.2 [-11.5 – 20.6]	0.89	5.2 [-11.5 – 20.6]	20.6 [7.7 – 26.2]	0.22
Five least deprived (WIMD) LHBs Wales	9.2 [3.1 – 24.3]	1.6 [-0.4 – 15.2]	0.34	1.6 [-0.4 – 15.2]	20.7 [-1.1 – 32.2]	0.34

Results presented as median [interquartile range]. LHB = Local Health Board, PCT = Primary Care Trust, WIMD = Welsh Index of Multiple Deprivation. Year 1 = January 2002 to December 2002, Year 2 = January 2003 to December 2003, Year 3 = January 2004 to December 2004, Year 4 = January 2005 to December 2005. †Wilcoxon Signed Rank test. *Statistically significant

Table 3.9 Items of OTC hyoscine butylbromide sold in different settings

	22 LHBs Wales	15 PCTs South East of England	16 PCTs North East of England	Five most deprived (WIMD) LHBs Wales	Five least deprived (WIMD) LHBs Wales
Jan 03 to Dec 03 (OTC Year 1)	1.3	1.8	0.9	1.7	1.4
Jan 04 to Dec 04* (OTC Year 2)	1.4 (6.8%)	1.9 (5.7%)	1.0 (6.7%)	2.2 (30.1%)	1.3 (-6.8%)
Jan 05 to Dec 05 (OTC Year 3)	1.9 (31.1%)	2.6 (37.5%)	1.2 (27.2%)	2.4 (5.9%)	2.0 (56.0%)

Results presented as total items per 1000 population (% change compared to the previous year). *Period immediately prior to the reclassification of hyoscine butylbromide (P to GSL) in January 2005

In Wales, the sale of OTC hyoscine butylbromide in the first 12 months after reclassification (January 2005 to December 2005) in each LHB was not associated with the deprivation score (WIMD) of the LHB ($r = 0.18$, $p = 0.43$) (Figure 3.13). Comparison of the number of items sold per 1000 population (median [IQR]) for OTC hyoscine butylbromide in the five most deprived LHBs and the five least deprived LHBs also revealed no difference (1.4 [1.0 – 3.2]) v 1.4 [1.0 – 2.0], $p = 0.8$).

3.4.4 Chloramphenicol eye drops

The number of prescription items for chloramphenicol ophthalmic preparations dispensed in all settings in each year of the study are presented in Table 3.10. An increasing trend in the number of dispensed prescription items for chloramphenicol

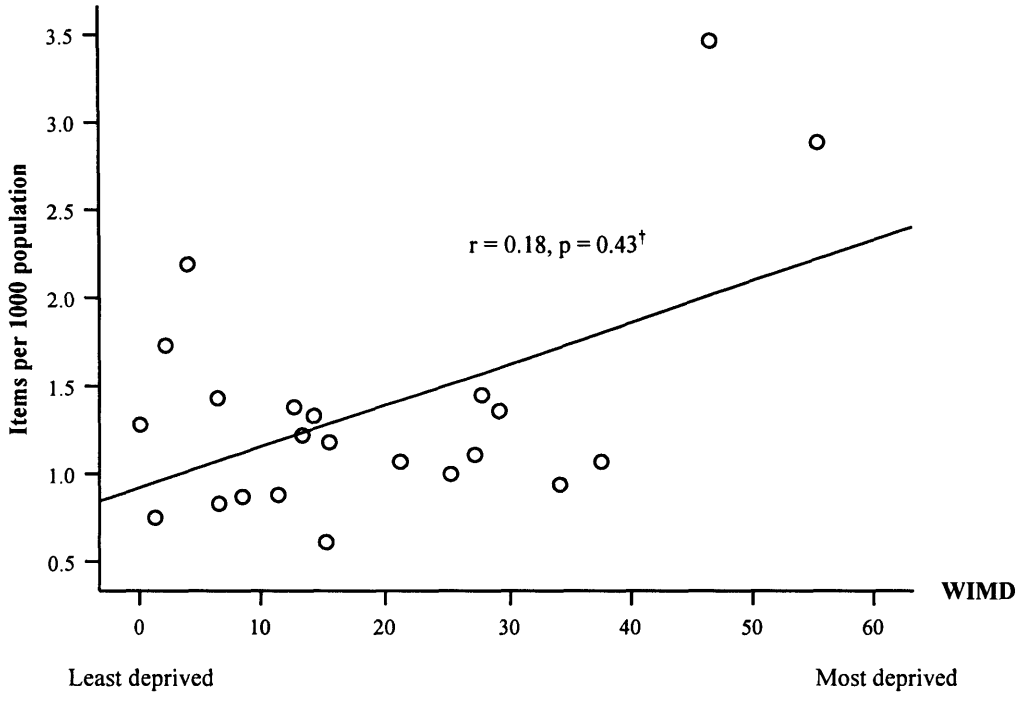


Figure 3.13 Deprivation score and sale of OTC hyoscine butylbromide in the 22 LHBs in Wales in months 1-12 after reclassification (January 2005 to December 2005). †Spearman's rank order correlation coefficient

eye drops was observed in all settings over the three 12 month periods before reclassification. In contrast there was no similar, consistent trend with prescription items for chloramphenicol eye ointment.

In the 12 months before reclassification there was a significant increase in prescription items for chloramphenicol eye drops in both Wales and the North East of England (Table 3.11). In comparison in the 12 months after reclassification there was a significant reduction in percent change in all settings.

Table 3.10 Number of dispensed prescription items for chloramphenicol ophthalmic preparations, chloramphenicol eye drops and chloramphenicol eye ointment in different settings

	Chloramphenicol ophthalmic preparations (eye drops and ointment)				Chloramphenicol eye drops				Chloramphenicol eye ointment			
	Jul 02 to Jun 03 (Year 1)	Jul 03 to Jun 04 (Year 2)	Jul 04 to Jun 05* (Year 3)	Jul 05 to Jun 06 (Year 4)	Jul 02 to Jun 03 (Year 1)	Jul 03 to Jun 04 (Year 2)	Jul 04 to Jun 05* (Year 3)	Jul 05 to Jun 06 (Year 4)	Jul 02 to Jun 03 (Year 1)	Jul 03 to Jun 04 (Year 2)	Jul 04 to Jun 05* (Year 3)	Jul 05 to Jun 06 (Year 4)
22 LHBs Wales	46.7 [43.4 – 51.2]	45.3 [43.6 – 53.1]	47.6 [45.0 – 55.2]	45.5 [41.6 – 50.9]	25.9 [22.5 – 30.5]	27.4 [23.4 – 29.8]	29.8 [25.5 – 32.3]	26.5 [23.7 – 30.1]	20.8 [19.3 – 24.0]	20.2 [17.4 – 23.3]	19.1 [16.0 – 22.4]	16.3 [14.7 – 19.0]
15 PCTs South East of England	42.0 [35.2 – 46.1]	44.2 [38.4 – 47.9]	48.7 [42.0 – 51.1]	39.3 [34.7 – 44.1]	25.2 [21.6 – 28.2]	27.6 [23.4 – 30.4]	29.1 [26.8 – 34.6]	23.4 [20.6 – 27.4]	16.3 [14.3 – 19.0]	16.3 [14.9 – 18.1]	16.1 [15.3 – 19.0]	15.4 [14.0 – 17.0]
16 PCTs North East of England	41.4 [37.7 – 44.5]	41.2 [39.7 – 44.4]	47.5 [46.5 – 49.5]	39.7 [37.6 – 43.2]	23.6 [21.8 – 27.1]	24.1 [20.9 – 26.8]	29.0 [26.8 – 31.0]	23.5 [22.0 – 26.2]	16.1 [14.3 – 20.7]	17.0 [14.2 – 19.9]	17.8 [14.8 – 21.0]	15.9 [13.5 – 18.2]
Five most deprived (WIMD) LHBs Wales	46.6 [44.0 – 47.5]	43.7 [42.7 – 45.0]	44.8 [40.3 – 46.0]	38.0 [35.8 – 42.8]	25.7 [23.4 – 27.7]	26.0 [22.9 – 27.5]	26.6 [23.3 – 28.9]	24.1 [20.9 – 25.9]	19.8 [19.1 – 21.8]	18.0 [16.4 – 20.8]	17.2 [15.8 – 18.8]	15.6 [13.4 – 17.6]
Five least deprived (WIMD) LHB Wales	45.7 [42.4 – 54.5]	46.4 [44.1 – 54.3]	49.0 [45.4 – 57.8]	50.8 [44.9 – 56.7]	25.6 [21.5 – 28.8]	27.3 [23.5 – 27.4]	30.2 [26.6 – 32.0]	27.9 [25.0 – 32.3]	24.3 [18.5 – 26.0]	23.8 [18.2 – 26.9]	20.4 [18.0 – 25.8]	22.3 [18.1 – 26.5]

Results presented as median [interquartile range] of the dispensed prescription items per 1000 population. LHB = Local Health Board, PCT = Primary Care Trust, WIMD = Welsh Index of Multiple Deprivation. *Period immediately prior to the reclassification of chloramphenicol eye drops (POM to P) in June 2005

Table 3.11 Percent change in different settings in the prescription items for chloramphenicol ophthalmic preparations, chloramphenicol eye drops and chloramphenicol eye ointment before and after the reclassification of chloramphenicol eye drops

	Before			After		
	% change from Year 1 to Year 2	% change from Year 2 to Year 3	p value†	% change from Year 2 to Year 3	% change from Year 3 to Year 4	p value†
Chloramphenicol ophthalmic preparations (eye drops and ointment)						
22 LHBs Wales	2.0 [-4.2 – 5.4]	5.4 [0.0 – 7.7]	0.007*	5.4 [0.0 – 7.7]	-7.8 [-10.7 – -5.3]	<0.001*
15 PCTs South East of England	4.2 [0.8 – 7.9]	7.7 [5.1 – 11.3]	0.06	7.7 [5.1 – 11.3]	-16.3 [-18.7 – -13.1]	0.001*
16 PCTs North East of England	1.6 [-3.0 – 5.3]	13.8 [7.3 – 16.2]	0.001*	13.8 [7.3 – 16.2]	-17.3 [-19.2 – -10.4]	<0.001*
Five most deprived (WIMD) LHBs Wales	-5.2 [-8.2 – -0.3]	0.1 [-6.3 – 3.4]	0.08	0.1 [-6.3 – 3.4]	-8.0 [-15.7 – -5.9]	0.04*
Five least deprived (WIMD) LHBs Wales	2.0 [-1.8 – 5.9]	5.8 [1.5 – 7.9]	0.22	5.8 [1.5 – 7.9]	2.7 [-6.5 – 3.8]	0.14
Chloramphenicol eye drops						
22 LHBs Wales	7.1 [-2.5 – 11.6]	10.0 [6.9 – 13.6]	0.04*	10.0 [6.9 – 13.6]	-8.9 [-13.1 – -4.4]	<0.001*
15 PCTs South East of England	6.1 [0.5 – 18.2]	11.6 [4.9 – 20.8]	0.34	11.6 [4.9 – 20.8]	-20.3 [-24.2 – -16.1]	0.001*
16 PCTs North East of England	1.1 [-2.3 – 5.6]	18.3 [10.5 – 24.2]	0.001*	18.3 [10.5 – 24.2]	-22.1 [-23.3 – -12.2]	<0.001*
Five most deprived (WIMD) LHBs Wales	-2.2 [-7.6 – 6.5]	4.9 [-1.5 – 7.5]	0.22	4.9 [-1.5 – 7.5]	-9.5 [-12.5 – -8.2]	0.04*
Five least deprived (WIMD) LHBs Wales	6.9 [-4.0 – 9.2]	12.0 [10.8 – 18.6]	0.04*	12.0 [10.8 – 18.6]	-0.6 [-9.4 – 1.5]	0.04*
Chloramphenicol eye ointment						
22 LHBs Wales	-3.6 [-8.1 – 0.4]	-0.5 [-4.7 – 2.9]	0.20	-0.5 [-4.7 – 2.9]	-4.7 [-9.6 – 2.2]	0.17
15 PCTs South East of England	0.2 [-3.4 – 2.0]	3.9 [0.6 – 7.9]	0.08*	3.9 [0.6 – 7.9]	-9.2 [-11.8 – -8.0]	0.001*
16 PCTs North East of England	3.2 [-1.6 – 5.7]	4.1 [0.4 – 8.0]	0.34	4.1 [0.4 – 8.0]	-11.9 [-15.6 – -8.1]	0.001*
Five most deprived (WIMD) LHBs Wales	-9.2 [-14.0 – -5.0]	-4.5 [-11.7 – -0.9]	0.34	-4.5 [-11.7 – -0.9]	-5.3 [-20.8 – -2.1]	0.14
Five least deprived (WIMD) LHBs Wales	-0.2 [-2.9 – 3.6]	-3.0 [-9.8 – -1.1]	0.14	-3.0 [-9.8 – -1.1]	3.9 [-3.1 – 8.6]	0.08*

Results presented as median [interquartile range]. LHB = Local Health Board, PCT = Primary Care Trust, WIMD = Welsh Index of Multiple Deprivation. Year 1 = June 2002 to July 2003, Year 2 = June 2003 to July 2004, Year 3 = June 2004 to July 2005, Year 4 = June 2005 to July 2006. †Wilcoxon Signed Rank test. *Statistically significant

Twelve months following reclassification the number of items of chloramphenicol eye drops sold in Wales was 11.9 items per 1000 population, 16.3 items per 1000 population in the South East of England, and 12.3 items per 1000 population in the North East of England (Table 3.12).

Although declining trends in the number of dispensed prescription items for ophthalmic chloramphenicol preparations were observed in the 12 months after the reclassification of chloramphenicol eye drops the combined number of prescription and OTC items appeared to have increased in all settings (Figures 3.14 and 3.15).

LHB deprivation was significantly associated with the sale of OTC chloramphenicol eye drops in the first 12 months after reclassification (July 2005 to June 2006) ($r = -0.44$, $p = 0.04$) (Figure 3.16). Although 14.7 [8.6 – 17.1] items per 1000 population of OTC chloramphenicol were sold in the five least deprived LHBs this was not significantly different to that sold in the five most deprived LHBs (9.9 [6.8 – 11.8]; $p = 0.22$).

Table 3.12 Items of OTC chloramphenicol eye drops sold in different settings

	22 LHBs Wales	**15 PCTs South East of England**	**16 PCTs North East of England**	**Five most deprived (WIMD) LHBs Wales**	**Five least deprived (WIMD) LHBs Wales**
Jul 05 to Jun 06 (OTC Year 1)	11.9	16.3	12.3	10.2	12.6

Results presented as total items per 1000 population

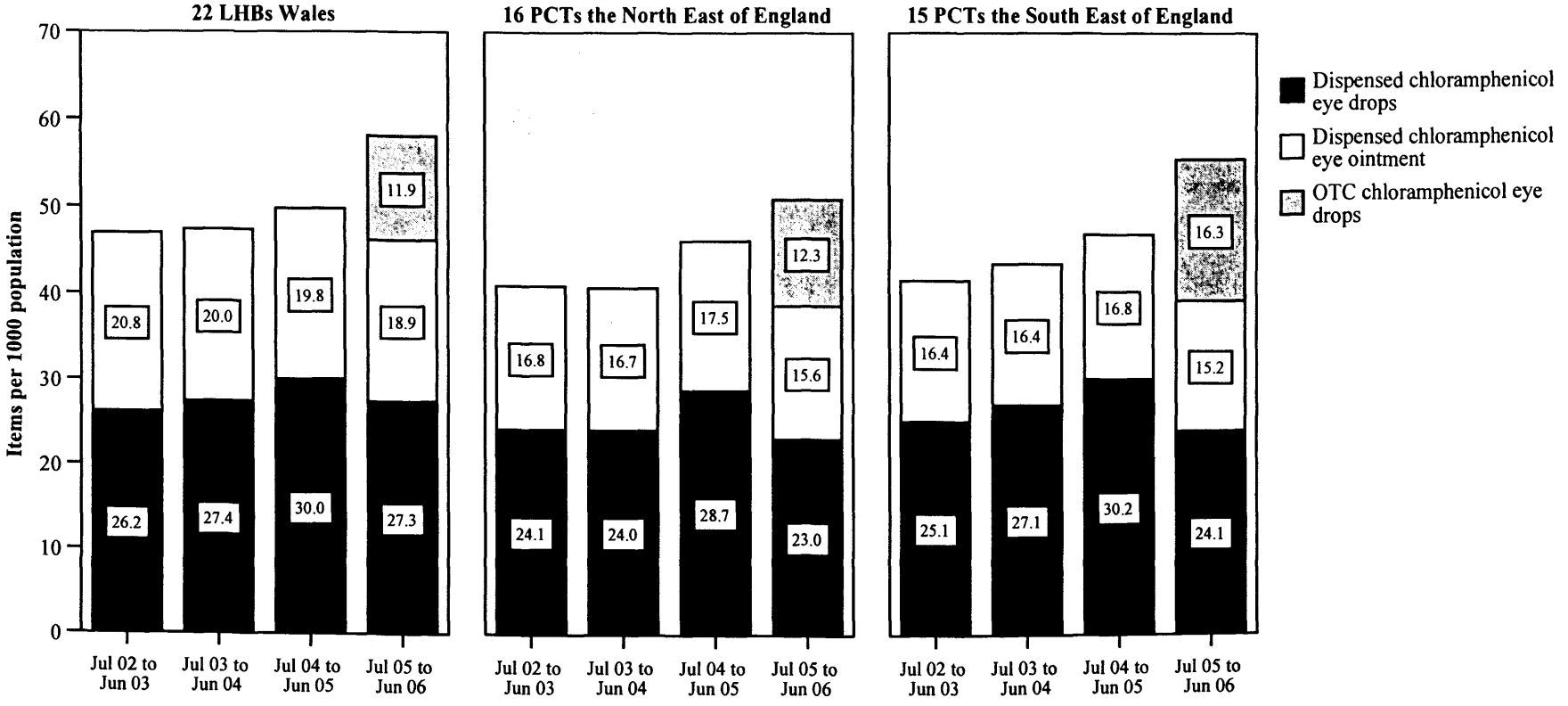


Figure 3.14 Items per 1000 population of dispensed and OTC ophthalmic chloramphenicol preparations supplied in different settings

Figure 3.15 Items per 1000 population of dispensed and OTC ophthalmic chloramphenicol preparations supplied in the five most deprived (WIMD) and the five least deprived (WIMD) LHBs in Wales

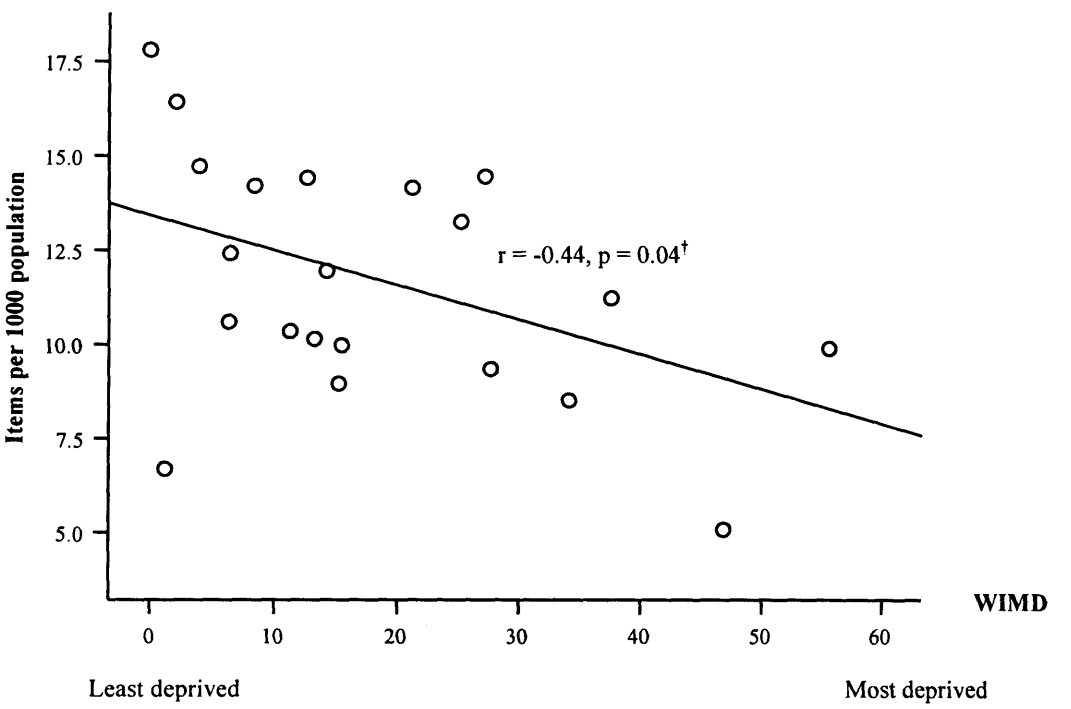


Figure 3.16 Deprivation score and sale of OTC chloramphenicol eye drops in the 22 LHBs in Wales in months 1-12 after reclassification (July 2005 to June 2006). †Spearman's rank order correlation coefficient

3.5 Discussion

3.5.1 Methodology

3.5.1.1 Settings

Changes in the pattern of medicines prescribed or sold OTC were determined in PCOs from two UK constituent countries, i.e. Wales and England. It was anticipated the impact of reclassification would vary between the countries particularly because of the ongoing phased reduction of the prescription charge in Wales at the time.

The South East and the North East regions of England were considered good candidates to compare with Wales (as discussed in Chapter 2) and, thus, were included in this study. Five LHBs in Wales were allocated to each of the most and least deprived groups to produce intuitively appropriate sample sizes to compare the sale of reclassified medicines in areas with contrasting levels of deprivation.

In October 2006 there was a reorganisation and subsequent amalgamation of a number of PCTs in England in which resulted in the number of PCTs being reduced from 303 to 152. Lists of PCTs presented in the IMS database during February 2005 to January 2007 were based on the boundaries of the restructured PCTs. As a consequence, the number of PCTs in the South East and the North East of England in the IMS database for the periods August 2002 to July 2003 and May 2003 to April 2006 were different from those supplied for the period February 2005 to January 2007 (Appendices 6 and 7). However, the population studied remained the same during the period studied. The impact of the variable number of PCTs in England on the presentation of results in the present study will be discussed in section 3.5.1.5.

3.5.1.2 Unit of measure

Although the unit of measure for the prescribing and sales of medicines were items per 1000 population, the amount of medicine per item prescribed and sold varied and depended on whether prescribed or sold. Generally, it is impractical to compare prescription item with sale item. However, there is an exception to this particularly for medicines that are supplied in a unit dose and where retail OTC packs contain the same quantity as the prescribed packs. For example, more than 90% of prescriptions for chloramphenicol eye drops are for a single preparation pack of 10 ml which is the same pack size as that available OTC.

3.5.1.3 Over the counter sell-in data

OTC sell-in data used in the present study were extracted from Regional Sale Analysis (RSA) data developed and maintained by IMS Health. RSA data represents the sale of pharmaceutical preparations from a main supplier, that is, full-line wholesaler, short-line wholesaler and parallel importers, or self-distributor to retail pharmacy (Figure 3.17).

IMS Health claim their sell-in data is accurate and covers 97% of invoice/transactions in the UK. The remaining 3% is derived from the projection of the shop sample information (panel retailers). This involves the collection of invoice data from a panel of approximately 700 retail pharmacies. The most notable omission of data from the IMS database is that for Alliance Boots pharmacies. This multiple pharmacy chain does not supply a comprehensive dataset to IMS due to their own privacy policy.

Figure 3.17 Data collection diagram for Regional Sales Analysis (RSA)

It should also be noted that the IMS data used in this study does not represent sale from a pharmacy to a patient. However, as community pharmacies only remain viable by maintaining a high stock turnover and do not generally keep a large backup stock, OTC sell-in data is considered a good proxy marker of sale from a pharmacy to a patient once the sale of particular medicine has reached its steady state.

Utmost caution is, however, required when analysing sell-in data immediately following the reclassification of a new product. According to the preliminary analysis, sell-in data for reclassified medicines during the first six months are disproportionately high until a steady state status is achieved in the following periods. For instance, sales of OTC simvastatin in Wales during the first six months after its reclassification (July to December 2004) accounted for 0.6 items per 1000 population whereas sales in the following two consecutive six month periods (January to June 2005 and July to December 2005) both accounted for 0.1 items per 1000 population. The high "sale" of reclassified medicines in the first six months of

a new product launch are probably associated with various promotional and advertising initiatives that encourage pharmacies to hold significant stocks at product launch.

3.5.1.4 Data organisation

To minimise the impact of seasonal trends on data analysis prescription and sell-in data for all medicines studied were aggregated into 12 month blocks. In the case of OTC H_2 antagonists and omeprazole sell-in data were organized in six-month blocks. This approach is essential to present sales of OTC H_2 antagonists in two periods prior to the reclassification of omeprazole (Figure 3.2). If the 12 month block approach had been employed for this data it would have only been possible to organise the sale of H_2 antagonists over one period (April 2003 to March 2004) prior to the reclassification of omeprazole (Figure 3.17). This is because data for OTC H_2 antagonists were only available for the period August 2002 to September 2006. A comparison of two periods is required to identify if there are any changes in the sales of these medicines. Therefore, a 12 month block approach would provide insufficient periods to determine the change in pattern of sales of H_2 antagonists before the reclassification of omeprazole.

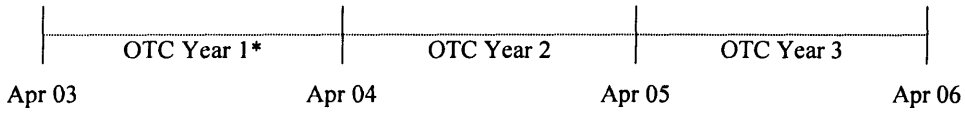


Figure 3.17 Model of the organisation of OTC sell-in data for H_2 antagonists (OTC Year 1), and both H_2 antagonists and omeprazole (OTC Year 2 to OTC Year 3) into 12 month blocks. OTC = over the counter sell-in data. *Period immediately prior to the reclassification of omeprazole (POM to P) in March 2004

3.5.1.5 Presentation of results

Unlike the volume of prescriptions dispensed, which were presented as the median number of items per 1000 population, the volume of sales were presented as total number of sales per 1000 population for each setting studied. This is because it was considered inappropriate to present the median of sale for settings in England where the number of PCTs was not consistent throughout the period studied due to the amalgamations of PCTs. The number of PCTs in the data analysis for the English regions varied during the study because of the NHS reorganisation, which presented in the IMS data supplied for the period February 2005 to January 2007. As a consequence it was not statistically appropriate to compare median values when the number of observations (PCTs) varied (Appendices 6 and 7).

3.5.1.6 Analysis

The impact of the reclassification of omeprazole and simvastatin on the pattern of prescribing of these agents was not analysed. The high level and increasing pattern of prescribing of omeprazole and simvastatin coupled with changes in clinical guidelines for the prescribing of proton pump inhibitors[169] and statins[144] generated confounding issues.

As discussed previously, the volume of sales was presented as total number of items per 1000 population for each setting studied. This measure did not support statistical analysis to evaluate changes in the sales of medicines. Therefore, descriptive statistics were used when comparing sales of OTC medicines.

3.5.2 Impact of reclassification on prescribing and sale

3.5.2.1 Omeprazole

A decline in the prescribing of H_2 antagonists and an increase in the number of prescriptions for proton pump inhibitors were observed in all settings over the study period. This was probably influenced by the accumulating evidence base for the superior efficacy of omeprazole[170-172] and incorporation into guidelines.[169, 173] This increase in prescribing may also reflect an increase in prevalence of disorders which proton pump inhibitors are indicated for such as dyspepsia and GORD. Changes in lifestyle associated with dyspepsia and GORD, such as being overweight or obesity, smoking, alcohol consumption[174-176] and physical activity at work[177] may also be responsible for an increase in the prescribing observed.

The sale of OTC H_2 antagonists in all settings studied decreased following the reclassification of omeprazole. This reduction was in contrast to the increase that had been observed over previous periods and probably, at least in part, reflected the impact the reclassification of omeprazole had on the market. It appeared, however, that the market shift was not straightforward. The sales of OTC omeprazole did not simply replace the decrease in sales of OTC H_2 antagonists as the combined sales of both omeprazole and H_2 antagonists decreased following the reclassification of omeprazole. Several variables were considered as factors that could have influenced this, including the availability of OTC H_2 antagonists as GSL medicines from retail outlets which were not included in the IMS data. Whilst it is possible that there were significant marketing and promotional initiatives in the grocery sector, ranitidine and famotidine had been available as GSL medicines since 1999 and 2000, respectively.

One factor that could have contributed to the downward trend in sale of H_2 antagonists and omeprazole is, perversely, associated with the efficacy of omeprazole. Omeprazole effectively reduces heartburn symptoms and maintains remission[178] and could thereby reduce the number of heartburn patients seeking repeat medication. However, due to the relatively high cost of OTC omeprazole, some patients who had tried and experienced the effectiveness of OTC omeprazole may have been influenced to subsequently request this medicine or other proton pump inhibitor on prescription for long term management of heartburn. Whilst there is little to support this hypothesis it is plausible and further work is required to confirm or refute it.

Whilst an explanation is elusive it is interesting to note that sales of stomach upset remedies, according to the classification used by the Proprietary Association of Great Britain (PAGB), declined in the UK in 2004 and 2005 by 1.2%[179] and 1.4%,[180] respectively. Data presented in these reports represent sales through pharmacy and grocery outlets in Great Britain and exclude sales through health food stores and mail order.

In the present study it was noted that sales of OTC omeprazole were small compared with the volume prescribed, e.g. 1.2 items per 1000 population of OTC omeprazole were sold in Wales during the period April 2005 to March 2006 compared with 698.9 prescription items per 1000 population for proton pump inhibitors that were dispensed over the same period. Several factors may have contributed to the relatively low level of sales of omeprazole compared to the high volume prescribed. Such factors could have included the cost of the packs available for sale, the limited

indications for which the product could be supplied when purchased, and the need for a pharmacist to be aware or involved in each sale.

In 2004, a pack of omeprazole in the UK contained fourteen 10 mg tablets at a cost of £9.49 and compared unfavourably to the prescription charge of £6.40 in England and £6.00 in Wales. Moreover, the availability of a higher strength and wider indication when supplied on prescription together with the common practice of issuing 28 days supply on prescription only serve to reflect that there was probably little incentive for the majority to buy omeprazole.

The need to involve a pharmacist in each sale and the requirement to follow RPSGB guidance[134] probably acted as barrier to selling more omeprazole. The RPSGB guidance issued at the time indicated that OTC omeprazole was appropriate for use in recurrent attacks of heartburn, but antacids or H_2 antagonists should be recommended for discrete attacks. In those situations where a patient presented in the pharmacy and requested omeprazole, the pharmacist was required to assess his/her clinical symptoms and follow the guideline. Whilst this guidance may well have promoted appropriate use, it could have deterred individuals from requesting the product or directed the pharmacist to supply an alternative product.

3.5.2.2 Simvastatin

The Joint British Societies' guidelines[144] on the prevention of cardiovascular disease published in 2005 state the threshold for primary prevention is a 20% risk over 10 years and support the use of appropriate drug therapies to achieve the recommended LDL cholesterol target. This, together with the enormous evidence base for the

efficacy of simvastatin has been a major factor that has contributed to the increasing number of prescriptions for statins observed in the present study. However, not all studies would support this observation. Filion et al[181] showed that the prescribing rate for statins in the four quarters after the reclassification of simvastatin appeared to reduce when compared to the increase that had been seen prior to the reclassification. This study, using the General Practice Research Database (GPRD) of approximately 3.5 million patients in England, monitored prescriptions for simvastatin on a quarterly basis from the first quarter of 2001 to the second quarter of 2005. The researchers suggested that the reclassification of OTC simvastatin in the UK had had a significant impact on statin prescriptions and that it also lead to less aggressive statin therapy.

The above study received a rapid rebuttal[182] and criticism[183] of the results presented and it was suggested that the data was not an accurate reflection of prescribing patterns in the UK. The decrease in the prescribing rate for statins observed was somewhat at odds with the general increase in the number of prescription items for lipid-regulating drugs including statins, presented in the official reports for prescribing issued in Wales[184, 185] and England.[186] Filion et al.[181] also reported a similar decline in the number of prescriptions for several other cardiovascular medicines including beta blockers, diuretics and warfarin. It is likely that the alleged reduction in the number of statin prescriptions was influenced by the same, unknown factor that was influencing a decrease in the overall prescribing of cardiovascular drugs. Prescribing data for England and Wales clearly show this not to be the case and therefore some clarification is required from Filion and his co-workers. The study[181] was undertaken in Canada and utilised data from the UKGPRD. This

database has been widely used in prescribing research studies[187-190] and the quality and validity of the data has been varied.[191, 192] This, therefore, would suggest a problem with data interpretation.

To further highlight the concerns with the Filion paper[181] it is worth considering the relative size of the sales market to the prescription market. In Wales, only 0.7 items per 1000 population of OTC simvastatin were sold during the first 12 months following reclassification. This was very small in comparison to the number of dispensed prescriptions for statins over the same period (930 items per 1000 population). Considering the small scales of OTC simvastatin sales, it is unlikely that their availability would have any impact on reducing the number of prescriptions for statins as reported.

The low sales of OTC simvastatin found in the present study were similar to another small study conducted shortly after the reclassification of simvastatin.[193] That study found only one purchase had been made in the three pharmacies in Bristol in the four weeks after simvastatin became available OTC. In a questionnaire administered to 102 people, 45% of respondents claimed they were willing to purchase OTC simvastatin, but 94% of those willing to buy the product would do so only after consulting their general practitioner.

Results from another recent study[194] which investigated the experience of community pharmacists with OTC simvastatin revealed a number of themes which were regarded as barriers to sale. These included the retail cost of the product, the need for access to clinical information, and the lack of evidence for a beneficial effect in

primary prevention in patients at moderate risk of coronary heart disease using a dose of 10 mg. The need for long term use and for a pharmacist to be involved in each sale may also have contributed to the low level of simvastatin sales. Johnson & Johnson MSD Consumer Pharmaceuticals, the manufacturer of OTC simvastatin (Zocor Heart-Pro) were particularly aware of these factors. The company have tried to address some of the modifiable issues by reducing the original retail price from £12.99 for a pack of 28 tablets when launched in July 2004 to £7.99 per pack in April 2005. The Zocor Heart-Pro questionnaire used to assess a patient's risk factors on first presentation has also been modified to be more user-friendly and less time-consuming. These improvements seem to have done little to increase the sales of OTC simvastatin.

Finally, it is perhaps worth reflecting on how the product was originally marketed and that it might have been preferable to target female consumers, rather than men, because it is usually women who are responsible for buying OTC medicines.[195] Whatever the explanation for poor sales the availability of OTC simvastatin has had negligible impact on health care and lessons need to be learned from this scenario.

3.5.2.3 Hyoscine butylbromide

Twelve months after the reclassification of hyoscine butylbromide prescriptions for antispasmodics as a group remained unchanged in all settings studied. An increase in the number of prescriptions for hyoscine butylbromide were seen in Wales and the South East of England, whilst there was no changed observed in the North East of England following reclassification.

Studies of the impact of advertising on patterns of prescribing and sales of OTC medicines in the UK are limited, whilst this has been researched elsewhere. Direct to consumer/patient advertising has been found to affect doctor–patient relationships[196] and influence prescribing decisions by increasing the volume of prescriptions for the same or similar medicine advertised.[197-199] Patients who requested advertised drugs were nearly 17 times more likely to receive one or more prescriptions compared to patients who did not request medicines,[200] and around 71% of the family doctors felt pressured by requests from their patients to use drugs that they would not ordinarily prescribe. It should be noted, however, that the majority of the available studies have focused on the impact of advertising of prescription medicine. This may, at least in part, explains the increase in prescriptions for hyoscine butylbromide seen in Wales and the South East of England which may have been influenced by advertising campaigns as a consequence of the renewed marketing following the reclassification of hyoscine butylbromide to a GSL medicine.

Most doctors have tended to view direct to consumer advertisements negatively and have expressed concern that such adverts often contain biased medical information and increase inappropriate prescribing practices.[201, 202] Why a consistent impact on all areas studied was not seen is unclear. Perhaps factors such as the influence of the prescribing support infrastructure may have played a significant role. Areas such as the North East of England have a robust support system in place[203] and this, thereby, may have ensured that the renewed marketing and advertising of hyoscine butylbromide did not translate into additional prescriptions.

The number of prescription items dispensed for antispasmodics and hyoscine butylbromide in the five most deprived LHBs was relatively high compared with those in the least deprived LHBs. Whilst this was consistent with the findings of a questionnaire survey study[204] of 1000 adults which identified that poverty, assessed by income had a strong association with IBS it is possible the hyoscine butylbromide was used for other off label indications. Anecdotal information has suggested it is used to alleviate abdominal cramping associated with opioid misuse, a problem known to be more prevalent in deprived areas across Wales.[205]

Changes in the sale of both hyoscine butylbromide P and GSL preparations from pharmacies in the 12 months following reclassification were more than 20% higher than in the previous year when only P hyoscine butylbromide was available. Even this increase is probably an underestimate of the increase in purchase of hyoscine butylbromide as the figures shown in the present study do not include sales through other general retail outlets. Overall, the increase in the sale of hyoscine butylbromide from pharmacies was probably related to consumer advertising and the availability of the GSL product for self selection.

Availability of a medicinal product for self selection is known to have an impact on sales in pharmacies. Results from a pilot study approved by the RPSGB[206] which allowed patients to self select both P and GSL medicines showed that 95% of patients preferred to buy medicines from open displays rather than on request from behind the pharmacy counter. In the present study, the increase in sales of hyoscine butylbromide occurred even though the GSL product was virtually the same (same pack size and same price) as that when previously available as a P medicine. This,

therefore, probably serves as an example of the restraining influence of the pharmacist on the sale of P hyoscine butylbromide.

An increase in the sale of both hyoscine butylbromide P and GSL preparations in the 12 months following reclassification in the most deprived LHBs appeared relatively small (5.9%) compared with an increasing sale in the least deprived LHBs (56.0%). This was probably a combination of the relatively high prescribing rate for this product in the deprived areas and unwillingness to purchase the medicine.

3.5.2.4 Chloramphenicol eye drops

Although the prescribing pattern for chloramphenicol eye drops prior to reclassification showed a steady increase, there was a decrease in all settings studied following reclassification. Although factors such as the availability of alternate medicines, an increased incidence of drug resistance and new treatment guidelines could have created a decrease in the prescribing, no evidence for such interventions could be observed during the period studied. It is, therefore, likely that the reclassification of chloramphenicol eye drops from POM to P was the major factor contributing to this.

Bacterial conjunctivitis is usually self-limiting and takes seven to ten days to resolve. Most patients, however, seek immediate and appropriate treatment.[207] Ophthalmic chloramphenicol is the drug of choice for this and the price of OTC chloramphenicol eye drops when launched at £4.79 was relatively low compared with the prescription charge in England (£6.25). In Wales, the prescription charge at the time was £4.00. This low retail cost together with the convenience of obtaining an effective product

from a pharmacy rather than waiting several days for a GP appointment may have promoted the sale of OTC chloramphenicol eye drops as found in this study.

It is not known whether advertising from pharmaceutical companies that manufactured chloramphenicol eye drops had an impact on generating an awareness of the availability of OTC chloramphenicol and encouraged patients to seek advice from their community pharmacy when they suspected conjunctivitis associated symptoms such as red eye and yellow discharge. However, it was suggested prior to reclassification that community pharmacists normally saw a couple of cases of infective conjunctivitis each week but at the time did not have access to effective therapy.[160] It was also suggested that 62% of pharmacists in the UK personally recommend most of the medicines they sell.[208] After chloramphenicol became available as a P medicine it is likely that community pharmacists would have recommended the medicine when they encountered patients with symptoms that met the treatment guidelines for the management of bacterial conjunctivitis.

In contrast to the other medicines studied, with chloramphenicol eye drops a prescription item and an item sold were comparable in quantity (section 3.5.1.2). However, because of the variation in the number of PCTs in England presented in the IMS data, it was not statistically appropriate to present median values for the sales of chloramphenicol eye drops (section 3.5.1.5). For consistency, both prescription and sales data for chloramphenicol eye drops were presented as the total number of items per 1000 population. As a consequence, descriptive statistics were used when evaluating the volume of both prescription items dispensed and items sold (section 3.5.1.6).

An increase in the combined use of prescription and OTC chloramphenicol eye drops was seen following reclassification. This suggested that the availability of OTC chloramphenicol eye drops may have promoted the use of chloramphenicol to treat bacterial conjunctivitis, or was the outcome of improved access.

The sale of OTC chloramphenicol eye drops in the first twelve months following reclassification in the South East of England appeared higher than in Wales and the North East of England. Socio-economic status including a higher level of disposable income and awareness may have contributed to this.

3.5.3 Impact of deprivation on the sale of reclassified medicines

From a study involving a range of medicines only the sale of chloramphenicol eye drops showed a significant relation to deprivation. The association between deprivation and sale of OTC chloramphenicol for self care management of bacterial conjunctivitis was similar to results from other studies which showed that self medication was more prevalent among individuals with higher educational levels[209] and less in those with a low level of education.[210]

The absence of a relationship between deprivation and the sale of omeprazole, simvastatin, and hyoscine butylbromide was probably due to the relative small scale of product sales. For example, sales of OTC omeprazole in Wales in the period used in correlation analysis were 1.2 items, 0.2 items for OTC simvastatin and 1.9 items per 1000 population for OTC hyoscine butylbromide. In contrast, sales of OTC chloramphenicol eye drops were 11.9 items per 1000 population.

An additional explanation for the lack of an association with deprivation was that the geographical area studied in an LHB was sufficiently large (population range 55981 – 305353) and may not reflected variations of both deprived and affluent areas within the LHB. It is possible that LHBs with such a variation were allocated an average score for deprivation which would mask any marked variations of the deprived and affluent areas within a single LHB.

3.6 Summary

Following reclassification:

- Sales of OTC omeprazole and simvasatin accounted for less than 1% of the volume of their prescription counterparts. In contrast, sales of OTC hyoscine butylbromide and chloramphenicol eye drops were more than 20% of the number of items dispensed.
- Twelve months after reclassification it was found that there was an increase in the prescribing of hyoscine butylbromide, whereas prescriptions for chloramphenicol eye drops decreased.
- The combined sales of both P and GSL hyoscine butylbromide from pharmacies were higher than the sale of P hyoscine butylbromide alone before the reclassification.
- Deprivation was associated with the sale of OTC chloramphenicol eye drops with more being sold in the least deprived LHBs. No correlations with deprivation were observed with the sale of omeprazole, simvastatin, and hyoscine butylbromide.

CHAPTER 4

GENERAL DISCUSSION AND CONCLUSION

Learn from yesterday. Live for today. Hope for tomorrow. The important thing is not to stop questioning (Albert Einstein, 1879 – 1955).

Since 2000 several public health policies have been introduced in the UK as a whole, and in Wales in particular. These policies have been developed to improve health and well being, remove inequities in health and better manage the increasing costs of running the NHS. Among the many policies the abolition of the prescription charge in Wales and the efforts to encourage the reclassification of more medicines from POM to P have focused on removing barriers to the access of medicines and both were the subject of study in this thesis. The intention was to explore the impact of the reduction of the prescription charge in Wales and the reclassification of medicines on the volume of medicines prescribed in primary care and the sale of OTC medicines from community pharmacy, respectively.

This discussion will first draw together and summarise the key findings of the research. The issues that underpin the results observed will then be considered, followed by a discussion of the implications of these findings. The limitations of the two studies that looked at the reduction of the prescription charge in Wales and the impact of medicine reclassification will then be explored, along with suggestions for further work. Finally, the conclusion of the thesis will be presented at the end of the chapter.

4.1 Summary of findings

The predicted impact at the outset of the study of the reduction of the prescription charge in Wales and medicine reclassification is summarised in Figure 4.1. Prior to the study being undertaken it was expected that the reduction of the prescription charge in Wales would increase the number of prescriptions dispensed and generally decrease the sale of OTC medicines from community pharmacy. In contrast, it was assumed the reclassification of medicines would increase the sale of OTC medicines whilst decreasing the number of prescriptions, at least if there was no interrelationship with the ongoing reduction of the prescription charge. A number of the findings from the present study did support the above predictions and are summarised below.

4.1.1 Reduction of the prescription charge in Wales

The impact of the reduction of the prescription charge on the number of prescriptions dispensed in primary care in Wales and selected PCTs in England was studied for three years before and two years after the first reduction of the prescription charge in Wales. It was found that the prescribing of non-sedating antihistamines and laxatives in Wales increased during the phased reduction of the prescription charge, whilst prescribing for loperamide and fluconazole 150 mg remained unchanged (Table 4.1).

No correlation between deprivation and changes in the prescribing of the drugs examined was identified in Wales (see sections 2.4.1 – 4). However, the prescribing of non-sedating antihistamines and laxatives over the period of the reduction of the prescription charge and between groups of LHBs with contrasting levels of deprivation did reveal different patterns (see sections 2.4.1 and 2.4.3). This highlighted the potential effect deprivation could have on prescribing patterns.

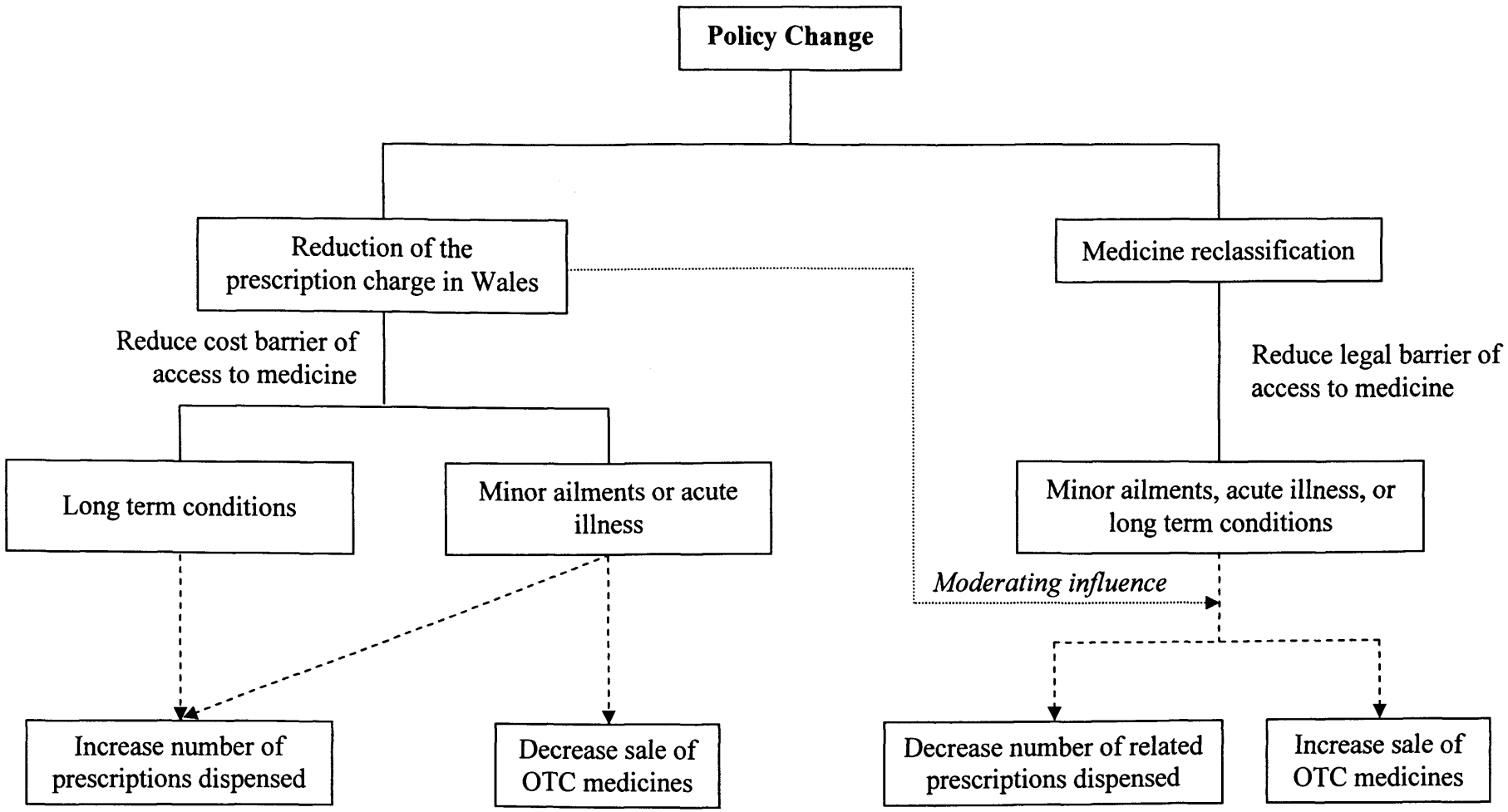


Figure 4.1 Anticipated effects at the outset of the study of the reduction of the prescription charge in Wales and medicine reclassification on prescribing and sale of medicines

Table 4.1 Summary of results relating to the impact of the reduction of the prescription charge in Wales on selected prescribed items

	Non-sedating antihistamines	Loperamide	Laxatives	Fluconazole 150 mg
Changes in prescribing*				
Wales	Yes ($p < 0.001$)	No ($p = 0.11$)	Yes ($p = 0.04$)	No ($p = 0.52$)
South East of England	No ($p = 0.73$)	No ($p = 0.57$)	No ($p = 0.23$)	No ($p = 0.36$)
North East of England	Yes ($p = 0.005$)	No ($p = 0.23$)	No ($p = 0.88$)	No ($p = 0.08$)
Five most deprived LHBs in Wales	No ($p = 0.08$)	No ($p = 0.50$)	Yes ($p = 0.04$)	No ($p = 0.69$)
Five least deprived LHBs in Wales	Yes ($p = 0.04$)	No ($p = 0.34$)	No ($p = 0.34$)	No ($p = 0.08$)
Relationship with deprivation†	No ($r = -0.14$, $p = 0.54$)	No ($r = 0.15$, $p = 0.50$)	No ($r = 0.22$, $p = 0.34$)	No ($r = -0.14$, $p = 0.54$)
Notes				
Indication	Allergic disorders	Acute and chronic diarrhoea	Constipation	Vaginal candidiasis
Retail cost of OTC medicines‡	£8.95 for Zirtek (cetirizine: 21 tablets per pack)	£3.15 for Imodium (loperamide: 6 capsules per pack)	Ranged from £1.13 for Dulco-Lax (bisacodyl: 10 tablets per pack) to £7.75 for Laxoberal (sodium picosulfate 300 mL)	£12.50 for Diflucan One (fluconazole 150 mg: one capsule per pack)

* Difference of percent change in the number of dispensed prescription items before and after the first reduction of the prescription charges in Wales (Wilcoxon Signed Rank test). †Relationship between changes in prescribing and deprivation scores (WIMD) in Wales (Spearman's rank order correlation coefficient). ‡Selected brand preparations.

4.1.2 Reclassification of medicines

Sales of selected OTC medicines from main wholesalers to retail pharmacies in Wales and England were monitored for at least 12 months following reclassification. The results showed product to product variation in the volume of sales of the medicines reclassified (Table 4.2). Sales of OTC omeprazole and simvastatin were relatively small (less than 1%) when compared to the volume of their prescription counterparts, whilst the sale of OTC chloramphenicol eye drops was about one third of the number of items dispensed on prescription. It should, however, be noted that OTC omeprazole and simvastatin are indicated for a certain treatment period (long term for simvastatin for CHD risk prevention) and this inferred that one pack purchased of these products may only represented a fraction of the treatment course of an individual. In contrast, chloramphenicol eye drops are indicated for the treatment of a single episode thereby one pack purchased was equivalent to a complete treatment course for each individual.

Changes in prescribing patterns were observed following the reclassification of both hyoscine butylbromide and chloramphenicol eye drops, although the changes were different. Twelve months after their reclassification, prescriptions for hyoscine butylbromide demonstrated an upward trend, whilst prescriptions for chloramphenicol eye drops demonstrated a downward trend. In terms of the combined effect of prescription and OTC sale volume both hyoscine butylbromide and chloramphenicol demonstrated an increase. It was also noted that sales of OTC hyoscine butylbromide from pharmacies increased following reclassification. This suggested the availability of OTC medicines may have been influential in promoting self medication and, in the case of OTC chloramphenicol eye drops, could have reduced GP workload.

Table 4.2 Summary of results relating to the reclassification of selected medicines

	Omeprazole	Simvastatin	Hyoscine butylbromide	Chloramphenicol eye drops
Item sold* (items per 1000 population)				
Wales	0.5	0.2	1.9	11.9
South East of England	0.7	0.6	2.6	16.3
North East of England	0.3	0.2	1.2	12.3
Five most deprived LHBs in Wales	0.4	0.1	2.4	10.2
Five least deprived LHBs in Wales	0.6	0.2	2.0	12.6
Impact on prescribing[¶]				
Wales	N/A	N/A	Increased ($p = 0.007$)	Decreased ($p < 0.001$)
South East of England	N/A	N/A	Increased ($p = 0.02$)	Decreased ($p = 0.001$)
North East of England	N/A	N/A	No change ($p = 0.30$)	Decreased ($p < 0.001$)
Five most deprived LHBs in Wales	N/A	N/A	No change ($p = 0.22$)	Decreased ($p = 0.04$)
Five least deprived LHBs in Wales	N/A	N/A	No change ($p = 0.34$)	Decreased ($p = 0.04$)
Impact on sales of OTC medicines[§]				
Wales	Decreased from 17.7% to -14.4%	N/A	Increased from 6.8% to 31.1%	N/A
South East of England	Decreased from 22.4% to -16.7%	N/A	Increased from 5.7% to 37.5%	N/A
North East of England	Decreased from 24.6%to -18.3%	N/A	Increased from 6.7% to 27.2%	N/A
Five most deprived LHBs in Wales	Decreased from 20.0% to -18.0%	N/A	Decreased from 30.1% to 5.9	N/A
Five least deprived LHBs in Wales	Decreased from 5.5% to -1.9%	N/A	Increased from -6.8% to 56.0%	N/A
Relationship with deprivation[†]	No ($r = 0.09$, $p = 0.70$)	No ($r = -0.40$, $p = 0.07$)	No ($r = 0.18$, $p = 0.43$)	Yes ($r = -0.44$, $p = 0.04$)
Notes				
Indication	Heartburn symptoms	Prevention in people at moderate risk of CHD	Abdominal cramp associated with IBS	Bacterial conjunctivitis
Retail cost	£9.49 for Zanprol (omeprazole 10 mg: 14 tablets per pack)	£12.99 for Zocor Heart-Pro (simvastatin 10 mg: 28 tablets per pack)	£4.39 for Buscopan IBS Relief (hyoscine butylbromide 10 mg: 20 tablets per pack)	£4.79 for Optrex Infected Eyes (chloramphenicol 0.5% eye drops: 10 mL)

*Number of items sold during the period April to September 2005 (for omeprazole), or July 2005 to June 2006 (for simvastatin), January to December 2005 (for hyoscine butylbromide), or July 2005 to June 2006 (for chloramphenicol eye drops). [¶]Difference of percent change in the number of dispensed prescription items before and after medicine reclassification (Wilcoxon Signed Rank test). [§]No statistical analyses were undertaken (see section 3.5.1.6). [†]Relationship between changes in prescribing and deprivation scores (WIMD) in Wales (Spearman's rank order correlation coefficient).

When the impact of deprivation on the sale of reclassified medicines in Wales was considered it was found that deprivation was associated with the sale of OTC chloramphenicol eye drops with more being sold in the least deprived LHBs. No similar relationship between deprivation and the OTC sale of omeprazole, simvastatin, or hyoscine butylbromide were observed.

4.2 Rationale for the changes observed

Several variables were considered to have influenced the results obtained. Those factors that may have been influential on patient decision making to obtain a prescription or purchase an OTC medicine are discussed below.

4.2.1 Cost

Results from several studies have shown that cost is a major barrier to patients having their prescription dispensed.[17-27] Despite this evidence base, cost sharing and the patients own financial contribution to the cost of a dispensed medicine is generally on the increase in many healthcare and insurance systems worldwide. There are few healthcare systems where the patient's contribution to cost sharing has gone in the opposite direction. Studies in Russia[211] and Sweden,[212] where there is full exemption from cost sharing for prescription medicines, demonstrated an increase in prescription items when introduced. The available evidence suggests it is sensible to presume that increasing the prescription charge is associated with a reduction in the demand for prescription medicines and vice versa (see Figure 4.2).

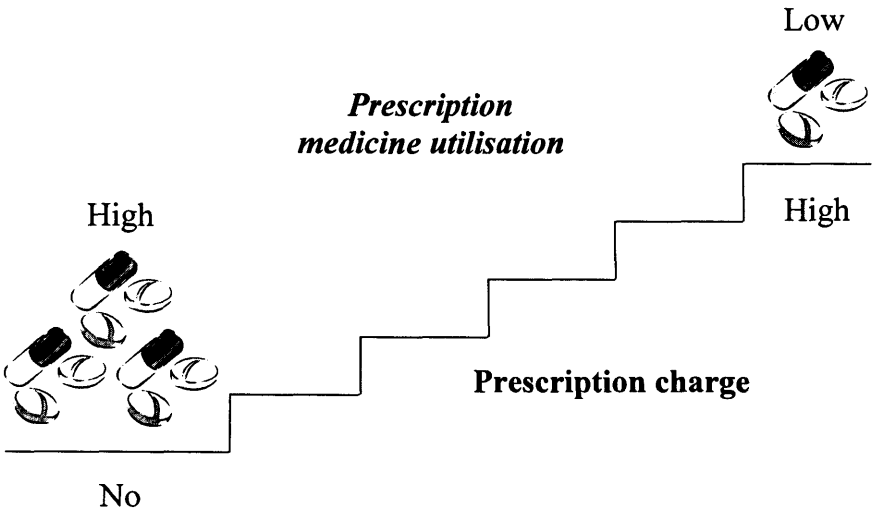


Figure 4.2 Hypothetical model illustrating the association between the prescription charge and prescription medicine utilisation

The reduction of the prescription charge in Wales increased the prescribing of non-sedating antihistamines and laxatives and was consistent with the anticipated effect of the reduction of the prescription charge. However, this was not a universal pattern with all medicines studied as it was found that the prescribing of loperamide and fluconazole 150 mg showed no change. This was unexpected considering the cost of OTC fluconazole 150 mg was relatively high (£12.50 for the branded product and £6.99 for the generic) compared with the prevailing prescription charge in Wales of £3. In addition, the volume of sales of OTC fluconazole 150 mg appeared similar to the volume prescribed throughout the study and regardless of the timescale studied. Before the study commenced this ratio of prescription items to sales items suggested fluconazole was a good candidate to monitor the impact of the reduction of the prescription charge. Why this did not materialise remains unclear. Perhaps many individuals continued to self medicate because it was quicker and more efficient than seeking treatment from GPs.[213]

Cost may also have been considered by the pharmaceutical manufacturer as a major barrier for patients to purchase OTC simvastatin. However, a reduction of the retail price of OTC simvastatin from £12.99 to £7.99 per pack in April 2005 did not increase the sales of this medicine.

It follows from the above scenarios which focused on the prescribing of fluconazole 150 mg and the sales of OTC simvastatin, that factors other than cost may have a significant role to play in a patient's decision to obtain a prescription or purchase an OTC medicine. These are discussed in the following section.

4.2.2 Medical condition

According to published guidance on self care support,[6] medical conditions can be classified as an acute illness, minor ailment or long term condition and the course or duration of required treatment may vary among conditions within the same category. For example, the treatment of a minor ailment such as vaginal candidiasis may require a single oral dose of fluconazole whilst allergic rhinitis, which is also classified as a minor ailment,[214] may require a daily dose of a non-sedating antihistamine over several weeks or months.

The self management of any medical condition requires a knowledge of the disorder including the duration of treatment, the perceived urgency of the condition and the availability of effective treatment. In the present study an increase in the volume of prescriptions for non-sedating antihistamines and laxatives was observed following the reduction of the prescription charge in Wales. Both of these OTC medicines are normally indicated for a treatment course of longer duration than with loperamide

(up to five days for acute diarrhoea) and fluconazole 150 mg (single dose for vaginal candidiasis or candidal balanitis). The fact that there was no change in the prescribing of loperamide and fluconazole 150 mg during the study implied that a substantial portion of individuals who continued to use these medicines required prompt access to treatment when affected and self medicated rather than obtain the same medication on prescription.

The sales of those reclassified medicines indicated for a long duration of treatment such as OTC simvastatin were minimal compared with the volume prescribed, whilst sales of OTC chloramphenicol eye drops, indicated for a short course of therapy, were relatively high. It should, however, be noted that the strength, pack size and indication of OTC chloramphenicol are similar to that of the prescription product whilst OTC simvastatin has a lower strength, smaller pack size and limited indications compared to their prescription counterparts.

The use of prescription and OTC medicines for the management of any medical condition are not, and probably never have been, mutually exclusive. OTC hyoscine butylbromide (both P and GSL) is indicated for the relief of gastrointestinal spasm associated with irritable bowel syndrome, a chronic condition with frequent, recurrent, exacerbations. An individual who suffers from the related episodic pain may well benefit from prompt access to a short course treatment of OTC hyoscine butylbromide. Those who find it effective may consider using it long term and also decide to request it on prescription from their GP. This could, in part, explain the increase in both prescribing and sale of OTC hyoscine butylbromide observed following reclassification. The impact of a renewed advertising campaign on

prescribers, although targeted at patients, also cannot be ruled out as influencing the subsequent prescribing of hyoscine butylbromide.

The results of the present study suggest that as the prescription charge diminishes individuals are generally more willing to obtain prescription medicines for the management of medical conditions that require a long course of treatment or do not bring about prompt symptomatic relief whilst they appear more willing to purchase effective OTC medicines for conditions that can be managed with a short course of therapy. The range of medicines studied in this thesis has, however, been limited and the findings may not be generalisable. This is well illustrated even with the few drugs studied.

OTC omeprazole is indicated for the relief of heartburn symptoms for a maximum of 4 weeks. In the present study sales of omeprazole were small and lower than H_2 antagonists although it is arguably the most effective product available OTC for the treatment of this condition. This suggests that there are many factors at play when an individual decides to purchase a medicine other than relative effectiveness and the evidence base.

4.2.3 Convenience of access

The OTC market in the UK includes medicines in both the P and GSL categories. The sale of P category medicines requires supervision by a pharmacist and might be perceived as the "behind the counter" category to differentiate it from "off the shelf" or GSL medicines. In contrast, medicines in the POM category require a prescription from a designated healthcare professional and, therefore, may be referred to as the

"in the dispensary" group. The ease and convenience of access to medicines is higher for those with lower levels of controls such as GSL medicines, and declines as the level of control increases (Figure 4.3).

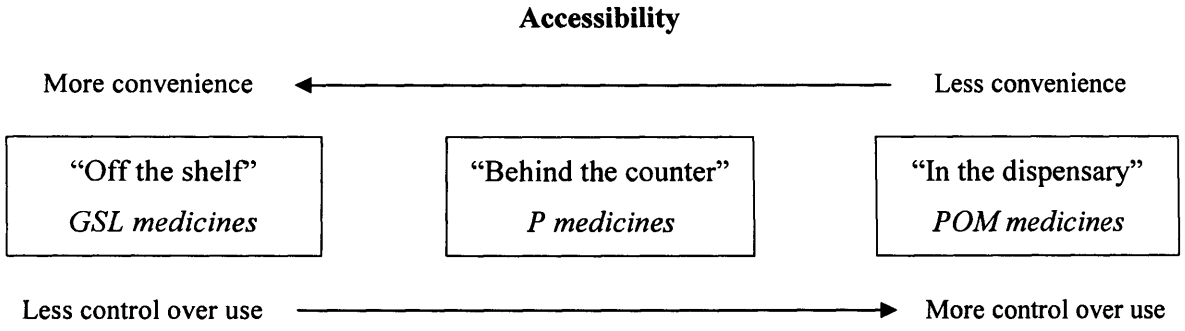


Figure 4.3 Access to medicines (modified from Blenkinsopp and Bond)[215]

The availability and ease of access to OTC medicines may outweigh the disbenefit of cost and the delay in waiting for an appointment with a GP. This may therefore promote sales and encourage self medication. It has been suggested[216] that patients prefer to buy medicines by self-selection, and sales of medicines increase when they are available for self-selection. Although not designed to test this, the results from the present study with hyoscine butylbromide support this hypothesis. When hyoscine butylbromide was reclassified to a GSL medicine there was an increase in sales compared with the period when it was available as a P medicine despite the fact that the strength and pack size of both P and GSL preparations are virtually the same. This may also serve as an example of the obstacle pharmacists may present to the sale of P medicines although, once again, the impact of a renewed advertising and promotional campaign cannot be quantified. A similar example also arose with the sale of omeprazole which requires a pharmacist to be involved in each sale in accordance with RPSGB guidance.[134] This again may act as a barrier to selling more

omeprazole, especially when individuals can self select H_2 antagonists which are available as GSL medicines for the same indication.

The pharmacy supervision requirement for the sale of medicines in the P category requires the pharmacist to be both present in the pharmacy and aware of all such sales. In 2001, the RPSGB allowed a few pharmacies to undertake trials in which P medicines were displayed for self-selection. Since then an increasing number of pharmacies have expressed an interest in making P medicines available for self-selection and in March 2007 the Society initiated a consultation on whether pharmacies should be able to display P medicines for self-selection.[217] Following a six-week consultation, the RPSGB concluded that the restriction on the self-selection of P medicines should remain in place thereby favouring the protection of patient safety.[218] This implies the only process which allows a medicine to be available for self-selection is to classify it as a GSL medicine.

4.2.4 Other factors

The three factors discussed above, i.e. cost, medical condition and convenience of access, are probably the main themes which impacted on the results in the present study. There are, however, other factors which also contributed to the decision of an individual to obtain a prescription or purchase an OTC medicine and these are discussed as follows.

4.2.4.1 Deprivation

Deprivation comprises a wide range of socioeconomic markers which may include income, employment, education, housing, physical environment, and geographical access to services. These factors are also related to each other, for example patients with lower educational attainment tend to earn less income, live in poorer areas, and suffer more ill health, than those from a higher socioeconomic group. It was found in a study undertaken in Spain that the prevalence of self medication with OTC medicines was higher among those with higher educational qualifications and those living in large cities.[209] Intuitively this scenario would also be expected to apply to the UK and was observed in the present study where deprivation was found to be associated with the sale of OTC chloramphenicol eye drops. The absence of a relationship between deprivation and the sales of omeprazole, simvastatin, and hyoscine butylbromide as seen in the present study may have been due to the low statistical power of the study design to detect an effect of these relatively small scales of product sales.

4.2.4.2 Advertising

The advertising of medicines in the UK is controlled by a combination of statutory measures enforced by the Medicines and Healthcare products Regulatory Agency (MHRA). Advertising to the public is only permitted for medicines legally classified as P or GSL medicines[219] and is one of the important tools used by pharmaceutical companies to promote the sales of their products. It has been stated by the director of the Proprietary Association of Great Britain (PAGB) that "If companies can't advertise their products then switching is not going to happen."[220] This statement

only serves to reiterate the importance of the financial dimension of reclassifying a medicine and the important part advertising plays.

Robust published studies relating to the impact of advertising on the decision to purchase an OTC medicine are limited as most of the studies undertaken have focused on the impact of advertising prescription only medicines directly to consumers. Amongst those studies undertaken few have shown a significant correlation between the number of advertisements seen and the number of pharmaceutical products used.[221-223] In the present study an increase in the sale of OTC hyoscine butylbromide observed following reclassification may have been partly influenced by advertising as the manufacturer utilised the opportunity to remarket the product to the consumer via television[224] and media press.[225]

4.2.4.3 Other factors

There are many other factors which influence an individual's decision to purchase an OTC medicine, none operate in isolation, and a number are listed below:

- Confidence and belief in the ability to control a given minor or self-limiting illness[226]
- Past experience of symptoms and problems caused by the condition[227]
- Need for ability to function or work[213, 228]
- Advice from social network[229]
- Wish to avoid a clinical examination or discuss embarrassing symptoms[230, 231]

Overall the decision by an individual to purchase a medicine is a complex multifactorial process (summarised in Figure 4.4).

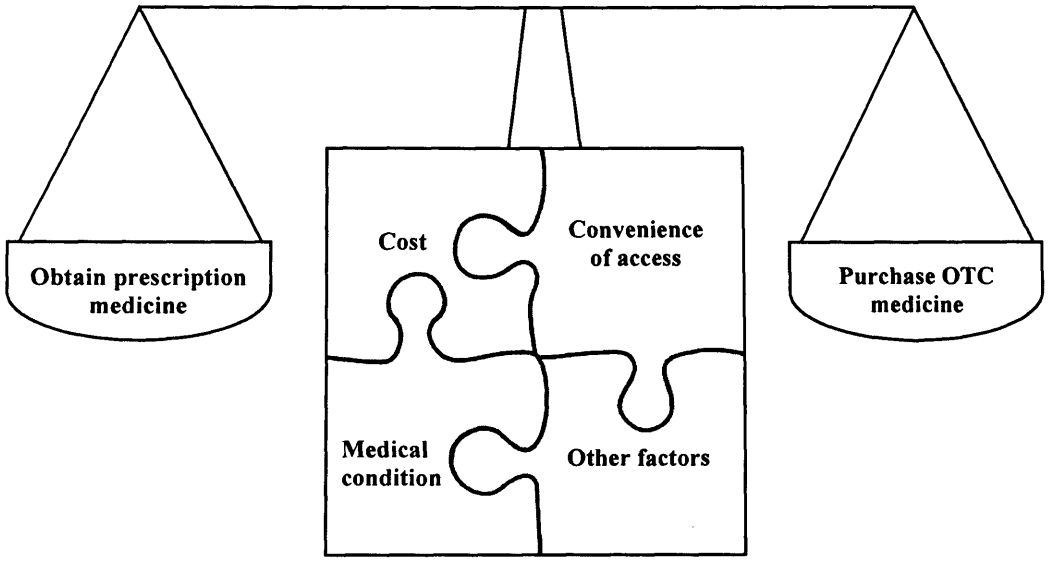


Figure 4.4 Model to illustrate the factors associated with a patient's decision to obtain a prescription or purchase a medicine

4.3 Implications of research findings

4.3.1 Government/policy maker

One reason for having a prescription charge in place is to discourage the use of non-essential medicines. The prescription charge may, however, also act as a barrier for patients to access essential medication, especially for those suffering from non-exempt chronic medical conditions and those on relatively low income whose earnings are just above the threshold for exemption under the low-income scheme. Findings from several studies[10, 12, 232] have revealed the inequities in the UK healthcare system created by the prescription charge. A number of options have been proposed[106] to reduce these inequities and include:

- Abolish the prescription charge
- Introduce a lower charge with fewer exemption categories
- Introduce reference pricing whereby a basic medicine is paid for by the NHS but patients can opt for a more expensive treatment if they pay the difference
- Extend the list of chronic conditions exempt from the prescription charge
- Make prepayment certificates cheaper

Perhaps the simplest way of addressing the inequities created by the prescription charge is to abolish the charge completely. From a political perspective this approach is likely to attract public support and has been adopted by the Welsh Labour Party and more recently the Scottish National Party[112] as part of their respective manifestos to help them win their national elections. Whether England will also follow has not yet been resolved. It is likely the Westminster Government is watching the impact of the abolition of the prescription charge in Wales and the pending changes in Scotland before making a final decision.

From a government perspective the abolition of the prescription charge results in a loss of revenue which, in Wales, accounts for about £29.5m per annum on a recurring basis to the income of the NHS.[233] The net income from the prescription charge is far less than the figure quoted above when administration expenses such as the cost of collecting the fee, handling pre-payment certificates, and the hidden legal costs of prosecuting those who try to avoid charge evasion are all taken into account. Although the prescription charge can never be a major source of revenue, the amount raised in Wales was not negligible and in all likelihood will have to be found from other sources.[234]

It has been suggested that the prescription charge deters the use of essential medicines in people with non-exempt chronic conditions thereby contributing to adverse consequences on their health and unplanned hospital admissions.[106] As a consequence there may be hidden savings associated with the abolition of the prescription charge by preventing more serious health problems and hospital admission costs because vulnerable and low income individuals may be less likely to avoid collecting the medication prescribed for them.

A major concern with the abolition of the prescription charge is that it will increase the number of individuals consulting their GP for medicines to treat minor ailments which they may have previously purchased over the counter. This issue has not only attracted attention from Governments and policy makers but also from the general public. A snapshot survey of prescribing in Wales reported in the local press[235] suggested patients were being prescribed cheap OTC medicines such as Vaseline, Bonjela and paracetamol which should otherwise have been purchased. There was also a call from the Welsh Shadow Health Minister that "The Government has to firm up the guidelines on prescribing and ensure that these items, which are relatively cheap and which anyone can afford – regardless of whether they are on benefits or are a millionaire – are not part of free prescriptions." This concern should, however, be interpreted with caution.

Firstly, it seems illogical for patients to have time off work and travel to the surgery to consult their GP to save the cost of less than £1 or £2 for a cheap medicine such as paracetamol. Secondly, prescribing trends are generally increasing year on year and therefore any increase in the prescribing of a specific agent should be compared with

the rate seen in previous years or with other settings which could serve as a control. Whilst unlikely, it is not incomprehensible that cheap medicines could be prescribed to save prescribing more expensive alternate agents where the diagnosis and outcome is less than clear and the evidence to prescribe a more expensive item is weak.

Previous experience from across the UK showed there was a sharp rise (Figure 2.1) in the number of prescriptions dispensed (11%) during the period of removal of the prescription charge in 1965 (278.9 millions prescriptions) and 1967 (309.7 millions prescriptions).[114] This may not, however, be relevant in attempts to forecast the impact of the current abolition of the prescription charge in Wales. Several factors need to be taken into account to justify this statement. At this point in time many factors are different from those dominant 40 years ago and these include the growth in the economy, the higher percent of patients that were exempt the prescription charge, the rise in consumerism and self care and a wider access to more effective OTC medicines.[236, 237] A further systematic investigation following the abolition of the prescription charge in Wales is, therefore, warranted.

In contrast to the abolition of the prescription charge, there is little debate about the Government policy on medicine reclassification. One of the aims of the UK Government has been to promote the reclassification of medicines to decrease the NHS cost associated with the provision of prescription medicines. It is anticipated that if a wide range of medicines are available over the counter it will give patients more choice to access medicines and will, in turn, reduce the number of patients consulting their GP to obtain a prescription medicine. Over the counter chloramphenicol eye drops is probably the best example in recent years to illustrate

the impact of medicine reclassification on reducing the number of prescribed items of the same therapeutic agent.

Whilst the results from the present study demonstrated the marked uptake of a product for acute treatment of chloramphenicol eye drops this study also revealed a low uptake of those medicines reclassified for chronic medical conditions such as omeprazole and simvastatin. Although the potential for OTC omeprazole and simvastatin to impact on the prescribing budget is immense, the scale of sales observed suggest any impact was negligible. The reasons for this are unclear but may include perceived effectiveness, a wish to save the cumulative cost of purchasing OTC products long term by obtaining such medicines on prescription, the availability of other medicines for the same indication and the obstacles for patients to obtain these P medicines when behind the counter.

To achieve the Government's aim of encouraging the use of OTC medicines to reduce the prescription budget a variety of strategies should be considered to support the sale of reclassified medicines, particularly for those indicated for chronic conditions. This may include a financial incentive for community pharmacists to take on the management of chronic medical conditions and a link to each patient's clinical record to aid better management. The UK and Welsh Governments have already set out a number of programs relevant to support the above and these include the medicine management agenda in community pharmacy[238] and a network link to electronic patient records.[239] It may take time for these programs to be fully implemented and their full impact on patient care and the use of OTC medicines will have to be evaluated at some point in the future.

The cost of OTC medicines has been recognised as a barrier to self medication, particularly in disadvantaged area.[215] This was supported by results from the present study which showed that sales of OTC chloramphenicol eye drops in Wales were associated with deprivation, with lower sales in the most deprived areas. It is therefore necessary to develop strategy to overcome this barrier whilst still giving patients a choice to conveniently access a community pharmacy for self medication, or visit their GP. Perhaps minor ailment schemes are an appropriate way forward and these have also been shown to have the advantage of reducing the workload of the GP.[240, 241] However, such programmes may not entirely comply with the Government's aim of supporting medicine reclassification to reduce the NHS drugs bill. In these programmes pharmacists still have to be reimbursed by the Government for the cost of the medicine supplied.

In summary, the loss of revenue from the prescription charge should be weighed against the savings associated with everyone being able to access the medicines they require, the health benefit this should bring and the avoidance of some hospital readmissions.[234] The UK Government's policy on promoting medicine reclassification has been shown to fit well with their desire to increase access to medicines over the counter and reduce associated prescription volume, as exemplified by the reclassification of chloramphenicol to treat bacterial conjunctivitis.

4.3.2 Pharmaceutical industry

The results from the present study suggest a substantial number of individuals in Wales may have switched from purchasing OTC non-sedating antihistamines and laxatives to obtaining these substances on prescription. It is likely that sales of these

OTC products may have also seen a corresponding downturn and this could have an impact on the manufacturer. To maintain profits from the sales of OTC medicines, especially following the reduction of the prescription charge in Wales, manufacturers may have to pro-actively promote self medication. The OTC pharmaceutical industry, represented by PAGB, has already set out a number of interventions relevant to support self care and these include lobbying at the government level, conducting research, producing relevant publications and organising self care conference.[242] Few of these initiatives have been directed at the Welsh Assembly Government or the population of Wales and this may need to be addressed.

Medicine reclassification is normally driven by the pharmaceutical industry to increase the sales of their products and prolong the commercial life of selected medicines. The company which holds the marketing authorisation will make a request for reclassification to the MHRA. Evidence of safety and efficacy must be provided by the company to support the application for reclassification. It is likely that much of the available evidence will come from the use of the medicine as a POM. To overcome safety concerns, the dose and pack size of reclassified medicines are generally lower than those available on prescription. As a consequence, the lack of evidence of efficacy at the doses approved for OTC sale often create concern amongst healthcare professionals and informed patients. The efficacy and benefit of simvastatin 10 mg serves to illustrate this[145, 146] and may have been a small but contributory reason why sales of OTC simvastatin were relatively low following reclassification. To address this, the manufacturer would have needed to undertake new clinical trials with the lower strength proposed for the OTC market. This was clearly not feasible given the prohibitive cost and time delay this would involve.

Although cost may not be a barrier for the majority of the general population to purchase an OTC medicine for an acute condition, the cumulative cost of purchasing OTC medicines for a chronic condition may not be as attractive. This could become a particular problem if a greater number of medicines for chronic condition are reclassified, as planned, in the future.[133] It is important that there should be strategies in place to help patients or consumers cope with the accrued cost of purchasing medicines at regular intervals. One approach to consider may be the introduction of a scheme similar to a pre-payment certificate whereby the medication can be purchased at a discount by the long term user.

4.3.3 Healthcare professionals

In the present study it appeared that GPs in Wales experienced a high number of patient visits following the reduction of the prescription charge, at least for selected medicines. This was much as predicted[115, 116] although it did not apply to all the prescription medicines studied. This increase in GP workload could be countered by allowing pharmacists to supply more medicines on the NHS whether as supplementary or independent prescribers or by participating in minor ailment schemes.

There is some evidence that the attitude of GPs towards medicine reclassification in the UK has become more positive over time. For instance, the level of GP agreement to the proposal for the reclassification of chloramphenicol eye drops from POM to P increased from 34% in 1983[243] to 52% (1992),[244] 67% (1996),[245] and 80% in 2004.[246] Reasons for the shift in GP opinion may include acceptance of a now established policy, perceived lack of problems with previous switches, needing strategies to

manage their own increasing workload and increasing confidence in the performance of community pharmacy.[215]

It has been suggested that whilst GPs are often in agreement with the reclassification of medicines used to treat an acute illness, they are less supportive with medicines used in chronic conditions.[215] However, considering the trend over the past two decades and anticipated future changes, it is hoped that GPs may become more sympathetic towards the reclassification of medicines to treat chronic conditions. GPs are known to influence the use of OTC medicines in several ways, particularly by recommending or advising against the use of certain medicines. This position of influence over the use and purchase OTC is exemplified with simvastatin. It was found that 94% of individuals willing to buy this medicine would do so only after consulting their GP.[193] Therefore, if the GP is not supportive it is unlikely an individual will continue with the medicine long term.

The combination of the abolition of the prescription charge and the medicine reclassification of potent, effective medicines appears to have had an impact on the pharmacy profession in several ways. Community pharmacy in Wales has probably suffered a loss of income related to the decline in sale of some OTC medicines following the reduction of the prescription charge. The results from this study add some weight to this by demonstrating an increase in the number of prescription items for medicines such as non-sedating antihistamines and laxatives. This loss of income may have been partially offset by an increase in the number of dispensing fees because of the higher number of prescriptions being dispensed following the reduction of the prescription charge.

The reclassification of medicines provides community pharmacy with an opportunity to expand their professional role, especially in the management of chronic medical conditions. However, the low sales of OTC simvastatin as reported in this study suggest pharmacists have been unable to capitalise on this. In contrast, the high sales of OTC chloramphenicol eye drops following reclassification, which account for about one third of those previously prescribed, have allowed the community pharmacist to make a real contribution to the management of bacterial conjunctivitis. In addition, the decline in the number of prescription items dispensed for chloramphenicol eye drops imply that this reclassification was associated with a decrease in GP workload. As mentioned previously, this may help improve the attitude of GPs towards the reclassification of medicines in the future.

Unlike prescription drugs, OTC medicines can be advertised directly to the public. Consequently, both GPs and community pharmacists should expect to receive more requests for reclassified medicines. Although there is little published research on the impact of advertisements for OTC medicines in the UK, a study from the US has suggested that these adverts lack the information necessary for consumers to make informed choices.[247] As a consequence, when encountering a request for an OTC medicine from a patient, healthcare professionals need to be sure the medicine supplied is appropriate for the patient's clinical condition with minimal risk of adverse effects arising. GPs also need to make sure they do not end up in a position where they prescribe the advertised drug or similar agent because it is widely advertised and/or requested by patients.

4.3.4 Individuals

Although the abolition of the prescription charge should remove an inequity in healthcare, this policy may also have changed the health seeking behaviour and self medication habit of many individuals. In particular, it could encourage some to obtain a medicine on prescription rather than buy an OTC product. This, however, was not evident for all medicines studied and suggests that factors other than cost savings associated with the reduced prescription charge may also be at play. At the time of writing the prescription charge in Wales has been abolished for more than 6 months. Interviews with pharmacists and GPs published in October 2007[233] suggest that patients had not radically changed their behaviour in response to the abolition of the prescription charge.

In terms of medicine reclassification, the results from the present study appear similar to other work which has demonstrated that the availability of reclassified medicines have improved access,[56] made patients price aware,[248] and presented opportunities for self selection.[54] However, this benefit may not be realised if pharmacists are too restrictive with access to P medicines[249] or the individual cannot afford to purchase the medicine. In addition, the product selected by the individual may be influenced by acquired knowledge from reliable and/or unreliable sources and influenced by acquisition cost, advertising, disease awareness campaigns and any promotion, support or recommendation at the point of sale.[248] Appropriate support and advice should be given to the patient at the point of sale and monitoring systems should be in place to ensure the safe and appropriate use of OTC medicines, especially those recently reclassified.

4.4 Limitations

This study was designed to be relevant to the work of the pharmaceutical public health division of the National Public Health Service in Wales. Its purpose was to identify the impact of policy and regulatory changes on the pattern of prescribing and sale of medicines. The study was, therefore, ecological in design and intended to make use of readily available secondary data sources. As a consequence, the study had a number of limitations associated with both the method and data used and these are discussed below.

4.4.1 Experience and views of patients and healthcare professionals

To understand the impact of the results from the quantitative studies undertaken in this thesis it was important the experience and views of healthcare professionals and patients in Wales should be obtained. This, however, would have required additional skills, resources and time, and these were unavailable within the constraints of this study. Nevertheless, it is important these views are captured to identify barriers and misunderstandings that may be associated with implementing such a significant government policy.

4.4.2 Comparison of prescribing and sales data

It would appear to be a relatively straight forward task to explore a change in the sale of an OTC product and that of the same product or therapeutic group prescribed to better understand the impact of the reduction of the prescription charge on health seeking behaviour. This approach was, however, fraught with a number of problems particularly where an OTC pack could also be dispensed. Whilst it was anticipated that this would be a rare occurrence in community pharmacy anecdotal evidence

suggests this was potentially problematic where sell-in data was used as a proxy for actual sales. It was not possible to overcome this problem unless universal electronic point of sale data had been available. Nonetheless, prescribing and sales data could be compared in the present study for particular medicines such as chloramphenicol eye drops where specific branded retail OTC packs were available and could be identified as such in the sell-in data. Unfortunately, even with this scenario there was no guarantee a shortage of the prescription product would not arise thereby resulting in the supply of an OTC pack against a prescription request for the same active ingredient.

4.4.3 Medicines studied

A limited number of medicines were initially selected for study to evaluate changes in the prescribing and sale of medicines commonly prescribed and widely used OTC to treat minor ailments. Some medicines that met the selection criteria for both the reduction of the prescription charge and medicine reclassification studies were not investigated due to confounding issues and two of these examples are discussed below.

Paracetamol was initially considered a candidate drug to study and results from a preliminary analysis revealed a significant increase in the number of items dispensed following the reduction of the prescription charge in Wales. However, a comparative analysis with selected PCTs in the South East of England also revealed a similar trend. The withdrawal of rofecoxib in October 2004 followed by a general reduction in the use of other cyclo-oxygenase-2 (COX-2) selective non-steroidal anti-inflammatory drugs (NSAIDs)[250, 251] together with a number of reviews that

highlighted concerns with the use of selective NSAIDs[252, 253] may have contributed to the general increase in the prescribing of paracetamol. This was a major confounding problem with paracetamol and necessitated its exclusion from the list of medicines studied.

Hyoscine hydrobromide (Scopoderm) was also initially selected for study but the explanation for exclusion was somewhat different to that for paracetamol. When hyoscine hydrobromide was reclassified from POM to P it met all the selection criteria for inclusion in the medicine reclassification study. However, it was not studied because distribution in the first 12 months following reclassification was restricted to Boots pharmacy outlets[254] and their sales data were not routinely available in the IMS database.

Overall fewer medicines were studied than initially anticipated and this only served to further restrict the generalisability of any results obtained. To overcome this, the list of medicines studied should be expanded to better evaluate the impact of the abolition of the prescription charge on promoting the use of medicines in Wales.

4.4.4 Small area analysis

As mentioned in Chapters 2 and 3, the deprivation scores used in the present study were complied at LHB level and derived from a mix of LSOAs with high and low deprivation scores. As a consequence this could mask any effect that was specific to the most deprived areas. This could have been overcome if prescription data and OTC sell-in data had also been available at LSOA level. Unfortunately, this was not

the case but does serve to highlight an issue that needs to be addressed in any future work.

4.5 Further work

Future work needs to better understand the reasons for the changes observed in this study and expand the range of medicines studied. In addition, the duration of the study needs to be extended to cover a prolonged period following the complete abolition of the prescription charge in Wales. Suggestions for further study include

- Undertake a qualitative study (focus group and/or interview survey) to determine the reason behind the changes in prescribing volume and sales of medicines observed
- Extend the range of medicines studied
- Examine the impact of the abolition of the prescription charge on the prescribing of medicines for long term medical conditions
- Undertake a comparative analysis of prescribing and sales data to more fully investigate the impact of the abolition of the prescription charge on medicine utilisation
- Use prescribing and sales data at LSOA level to more fully explore the impact of deprivation on the change in pattern of prescribing or sales of reclassified medicines
- Undertake a longitudinal study following the abolition of the prescription charge in Wales in April 2007

4.6 Conclusion

This is one of the first studies that have explored the impact of changes in the prescription charge in Wales. It was a laudable aim of the government in Wales to remove the financial burden on individuals at the time they require a prescribed medicine. This thesis has revealed that during the period when the prescription charge in Wales was being reduced there was an increase in the prescription volume of selected medicines. From this it was implied that the policy of abolishing the prescription charge did have an impact on some of those individuals who may otherwise have purchased a medicine OTC. Whilst such an impact is understandable it does not reflect the required collective, social responsibility to constrain unnecessary demand on health service resources. Whether a similar or even greater change has occurred after the abolition of the prescription charge is unknown and clearly needs to be studied.

With respect to the UK Government policy on the reclassification of medicines this study has confirmed that the policy probably improved access to a few selected OTC medicines, especially those for acute conditions. However, despite an increase in the range of reclassified medicines to embrace chronic conditions the results from the present study suggest, to date, that public engagement with this agenda has been poor and uptake of the medicines involved small. The reasons for this need to be identified and addressed in future work.

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ndary=true&ssDocName=CON009709&ssTargetNodeId=836&DynamicListQuery=&DynamicListSortBy=xCreationDate&DynamicListSortOrder=Desc&DynamicListTitle=&PageNumber=null&Title=Advertising%20of%20medicines&ResultCount=10

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Appendix 1

Population of selected Primary Care Organizations (PCOs)

PCO	Population
Wales	
Anglesey (Ynys Mon)	66829
Blaenau Gwent	70064
Bridgend	128645
Caerphilly	169519
Cardiff	305353
Carmarthenshire	172842
Ceredigion	74941
Conwy	109596
Denbighshire	93065
Flintshire	148594
Gwynedd	116843
Merthyr Tydfil	55981
Monmouthshire	84885
Neath Port Talbot	134468
Newport	137011
Pembrokeshire	114131
Powys	126354
Rhondda Cynon Taff	231946
Swansea	223301
Torfaen	90949
Vale of Glamorgan	119292
Wrexham	128476

PCO	Population
The North East of England	
Darlington	96733
Derwentside	82525
Durham and Chester-Le-Street	144715
Durham Dales	84849
Easington	95345
Gateshead	194460
Hartlepool	90019
Langbaurgh	97456
Middlesbrough	179787
Newcastle	261200
North Tees	184662
North Tyneside	196068
Northumberland Care Trust	307901
Sedgefield	90433
South Tyneside	151483
Sunderland Teaching	277441
The South East of England	
Adur Arun & Worthing Teaching	212782
Bexhill & Rother	78228
Brighton & Hove City	257368
Crawley	114018
Eastbourne Downs	260850
Elmbridge East & Mid Surrey	150241
Guildford & Waverley	167132
Hastings & St Leonards	233599
Horsham & Chanctonbury	89908
Mid Sussex	118889
Surrey East	134761
Surrey North	200915
Surrey Heath & Woking	191864
Sussex Downs & Weald	150184
Sussex West	176423

PCO	Population
Five deprived (LLTI) PCTs England	
Barnsley	224600
Derwentside	82525
Easington	95345
Knowsley	150000
Sedgefield	90433

Appendix 2

Percent of each Local Health Board (LHB) Lower Layer Super Output Areas (LSOAs) in the 20% highest deprivation scores in Wales

LHB	Percent of LSOAs in the 20% highest deprivation scores in Wales
Monmouthshire	0.00
Powys	1.25
Ceredigion	2.13
Gwynedd	4.00
Vale of Glamorgan	6.41
Flintshire	6.52
Pembrokeshire	8.45
Anglesey	11.36
Conwy	12.68
Torfaen	13.33
Carmarthenshire	14.29
Wrexham	15.29
Denbighshire	15.52
Bridgend	21.18
Swansea	25.17
Cardiff	27.09
Newport	27.66
Caerphilly	29.09
Neath Port Talbot	34.07
Rhondda Cynon Taff	37.50
Blaenau Gwent	46.81
Merthyr Tydfil	55.56

Appendix 3

Flow diagram for CASPA data transfer

1 First screen

1.1 Select "Catalogue" mode

⇩

1.2 Select time period in "Selected Periods"

⇩

1.3 Select specific drug group in "BNF Selection List"

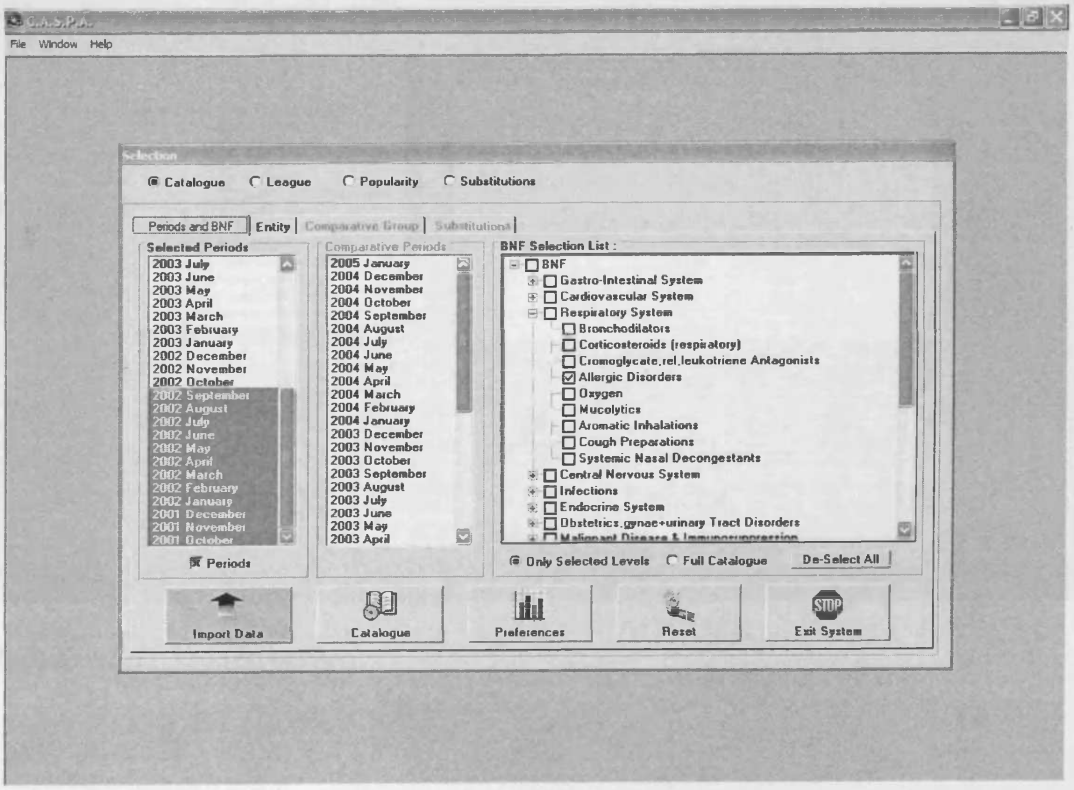


Figure A3.1: First screen

2 Second screen (Entity sheet)

2.1 Select specific LHB

⇩

2.2 Click "Catalogue" button at the bottom

⇩

2.3 The results screen, named as "LHB name (Multiple Periods)" will appear

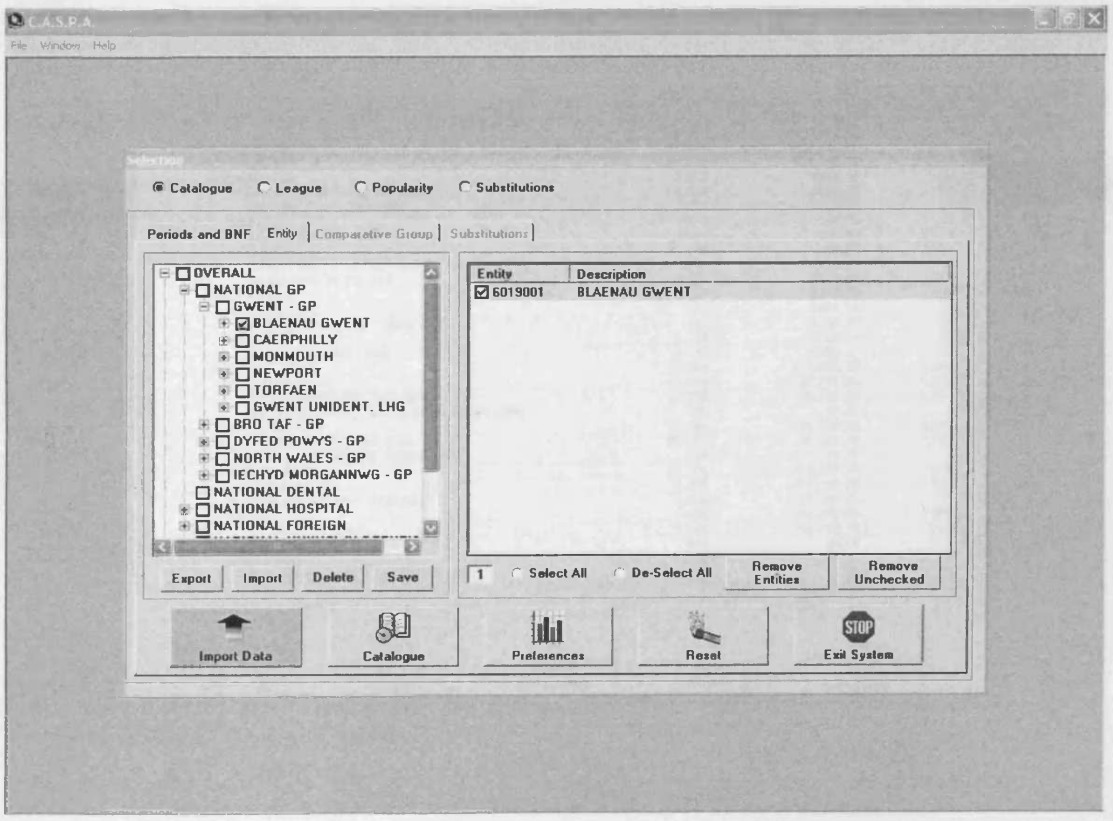


Figure A3.2: Second screen

3 Results screen

3.1 Click to highlight the section level of drug (orange color)

⇩

3.2 Click "Export" button at the bottom

⇩

3.3 The "Select Level" screen will appear

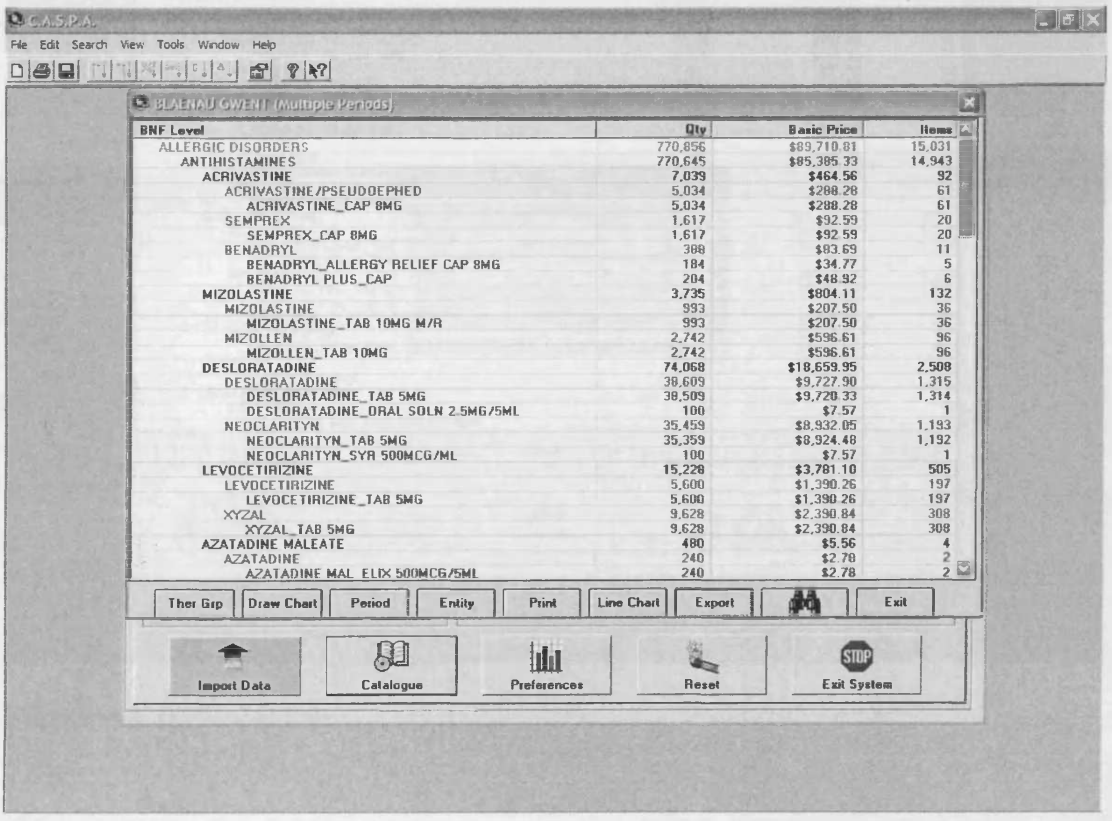


Figure A3.3: Results screen

4 Select level screen

4.1 Click "Section" button

⇩

4.2 The "Save As" screen will appear

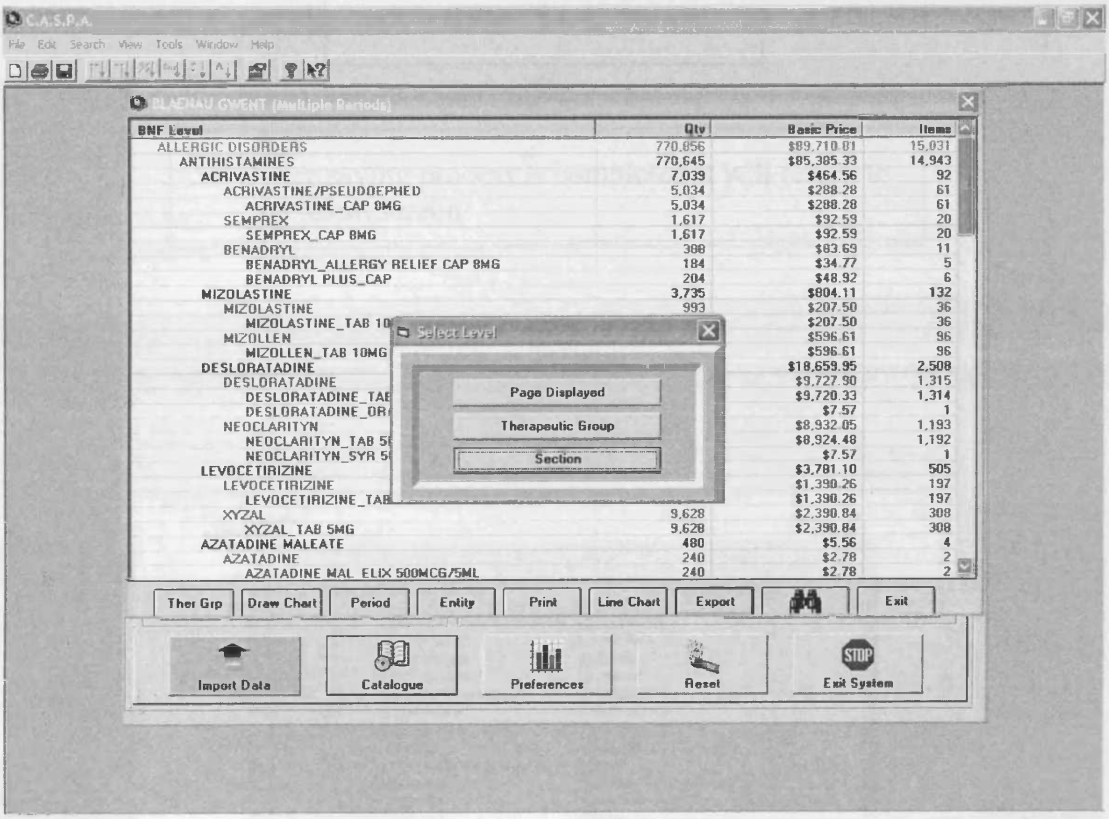


Figure A3.4: Export data

5 Save as screen

5.1 Select appropriate location for the file to be saved [normally save in Local Disk (C)]

⇩

5.2 Enter the file name

⇩

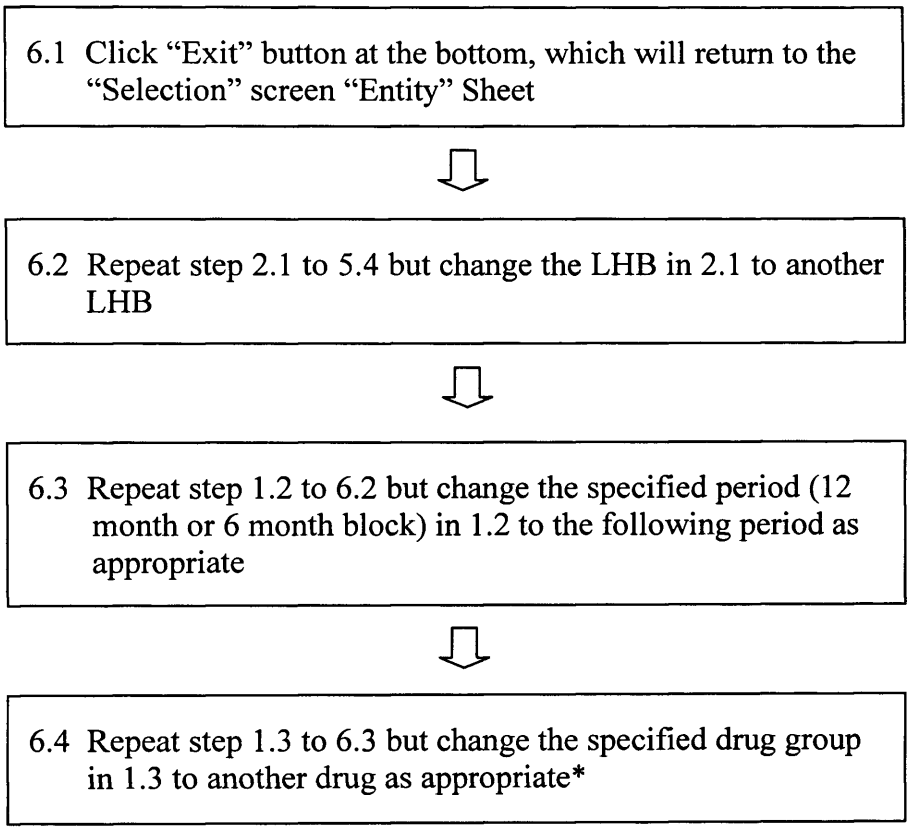
5.3 Click "Save" button

⇩

5.4 After saving process is completed it will return to the result screen

Figure A3.5: Save as screen

6 Export data for another LHB, period, or studied medicine



* Loperamide, laxatives, non-sedating antihistamines, and fluconazole 150 mg

Appendix 4

Comparative rank of limiting long term illness (LLTI) by Primary Care Organisations (PCOs)

Wales			England		
LHB	**Percentage***	**Ranking†**	**PCT‡**	**Percentage***	**Ranking†**
Five most deprived PCOs					
Merthyr Tydfil	30.0	2	Easington	30.8	1
Neath Port Talbot	29.4	3	Barnsley	25.0	11
Blaenau Gwent	28.3	4	Derwentside	25.0	12
Rhondda Cynon Taff	27.2	5	Sedgefield	24.8	14
Caerphilly	26.3	6	Knowsley	24.7	18
Five least deprived PCOs					
Powys	20.4	92	Aylesbury Vale	12.6	367
The Vale of Glamorgan	19.9	116	Wycombe	12.6	368
Flintshire	19.2	134	West Berkshire	12.4	371
Monmouthshire	19.1	139	Bracknell Forest	11.7	373
Cardiff	18.8	147	Wokingham	10.9	376

LHB = Local Health Board, PCT = Primary Care Trust, PCO = Primary Care Organisation. *Calculated from a 'Yes' response to the question in the 2001 Census: 'Do you have any long term illness, health problem or disability which limits your activities or the work you can do?' †Combined rank of both Wales and England. ‡Only local authorities that were coterminous with those of their PCTs.

Appendix 5

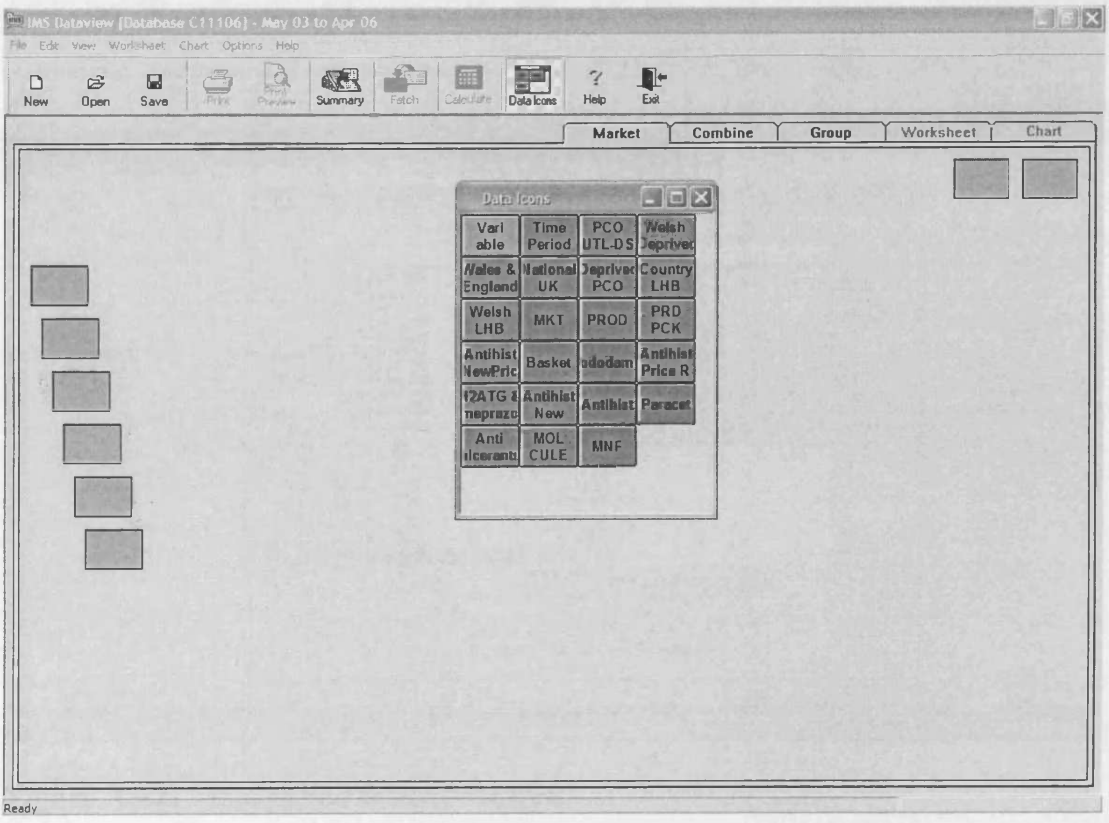
Flow diagram for IMS data transfer

1. First screen

1.1 Select "Time Period" box

⇩

1.2 The "Member Selection" screen will appear



FigureA5.1: First screen

2. Time period (member selection) screen

2.1 Select specific time period

⇩

2.2 Move the selected time period to the right column

⇩

2.3 Click "OK" button

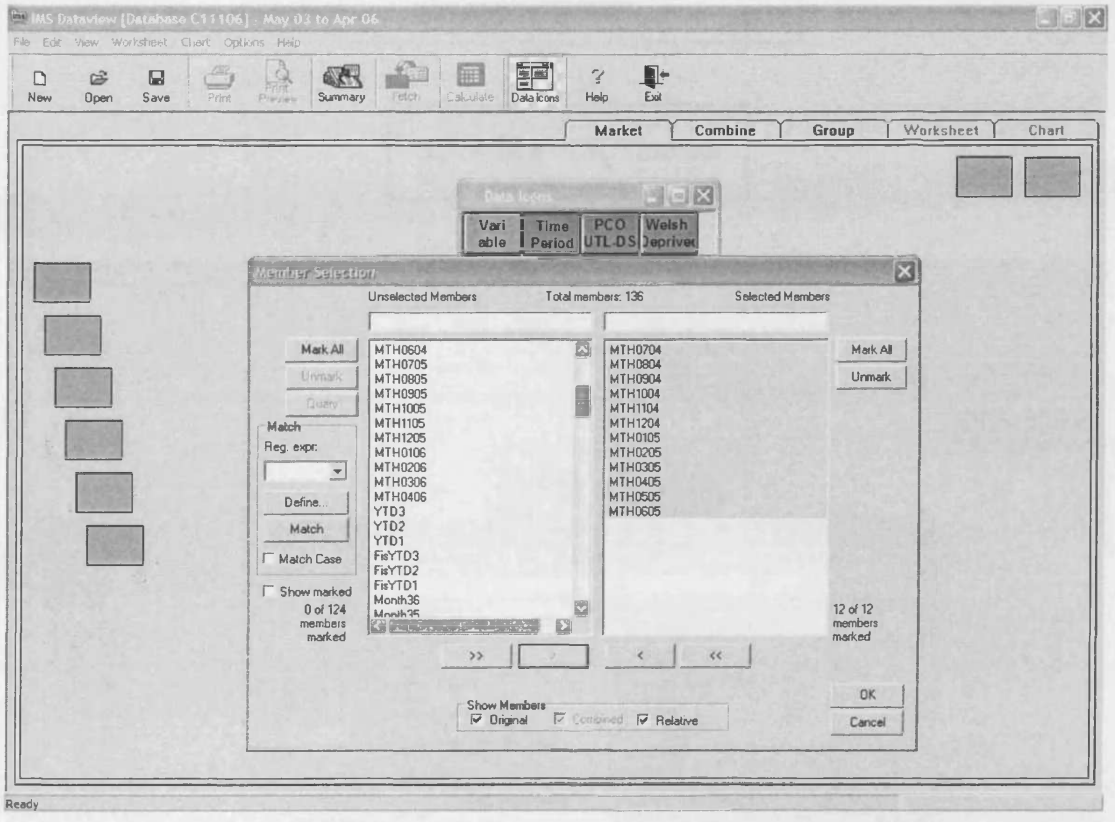


Figure A5.2: Time period selection screen

3. PCO (member selection) screen

3.1 Select "PCO" box

⇩

3.2 The "Member Selection" screen will appear

⇩

3.3 Select specific PCO

⇩

3.4 Move the selected PCO to the right column

⇩

3.5 Click "OK" button

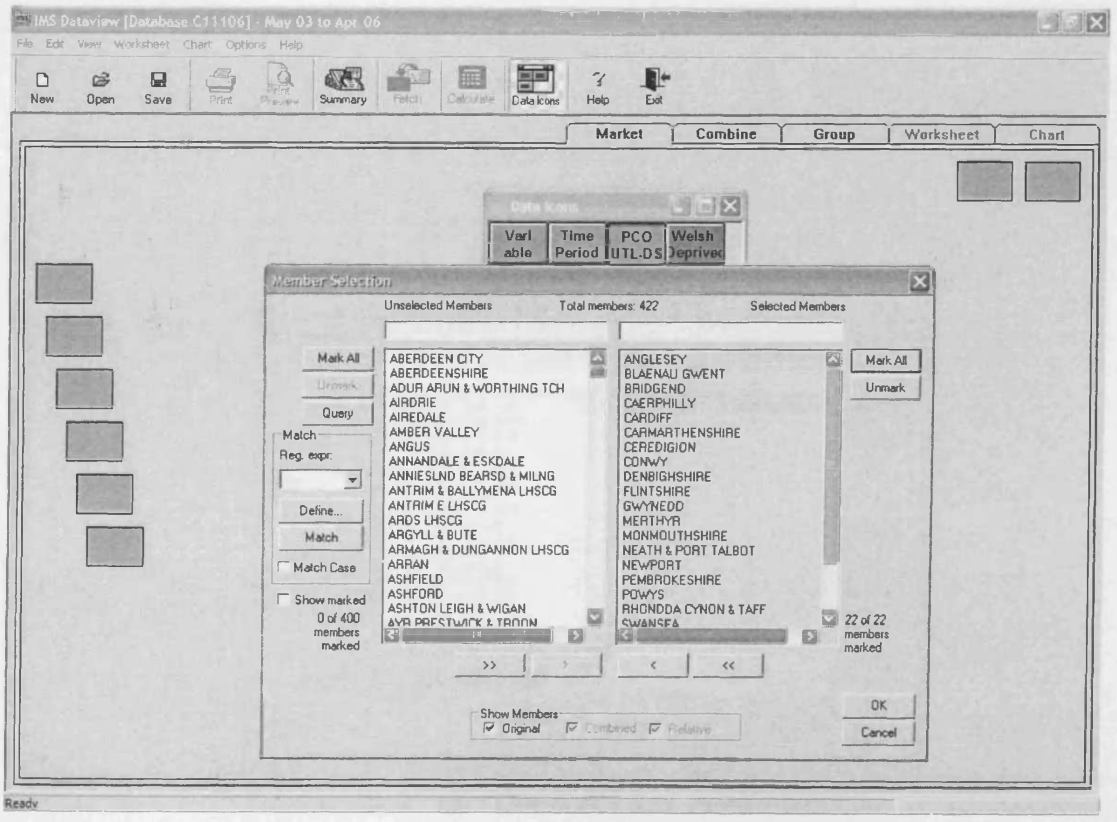


Figure A5.3: PCO selection screen

4. Product pack (member selection) screen

4.1 Select "PRD PDK" box

⇩

4.2 The "Member Selection" screen will appear

⇩

4.3 Select specific product

⇩

4.4 Move the selected product to the right column

⇩

4.5 Click "OK" button

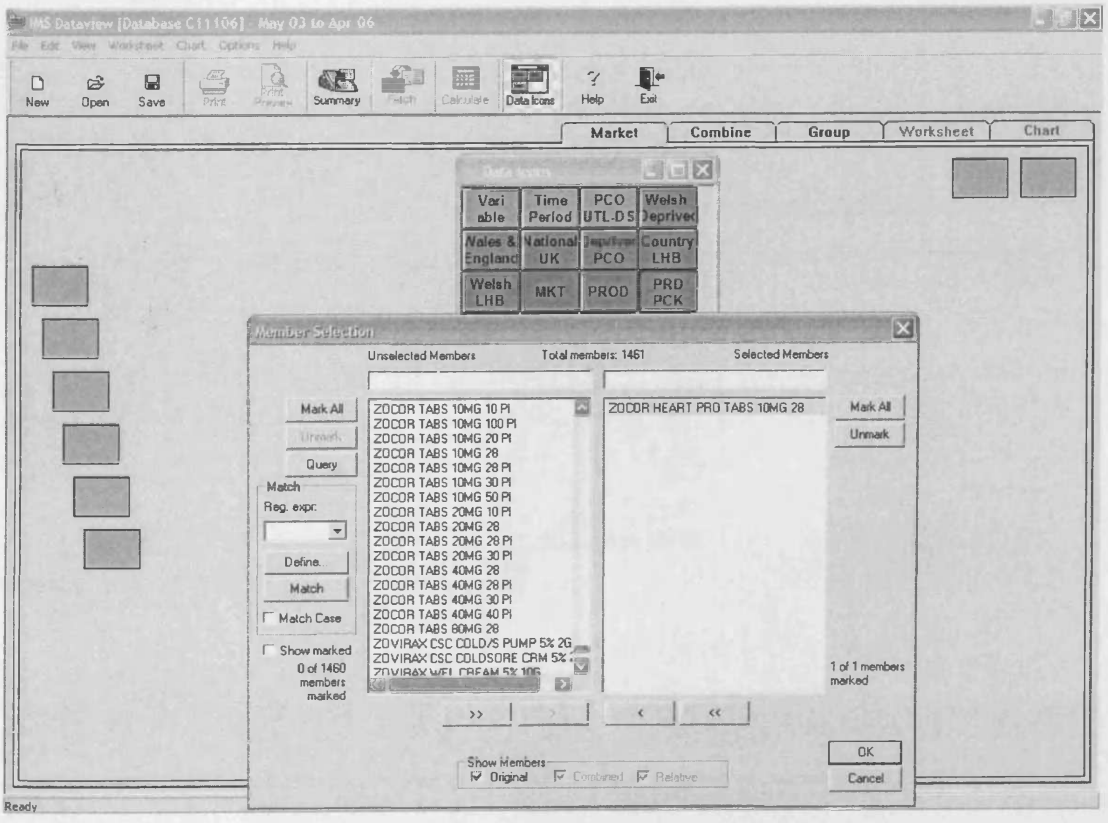


Figure A5.4: Product pack selection screen

5. Market sheet screen

5.1 Move selected "PCO" box to the first row on the left

5.2 Move selected "Time Period" box to the first column on the right

5.3 Click "Fetch" button

5.4 The "Worksheet" screen will appear

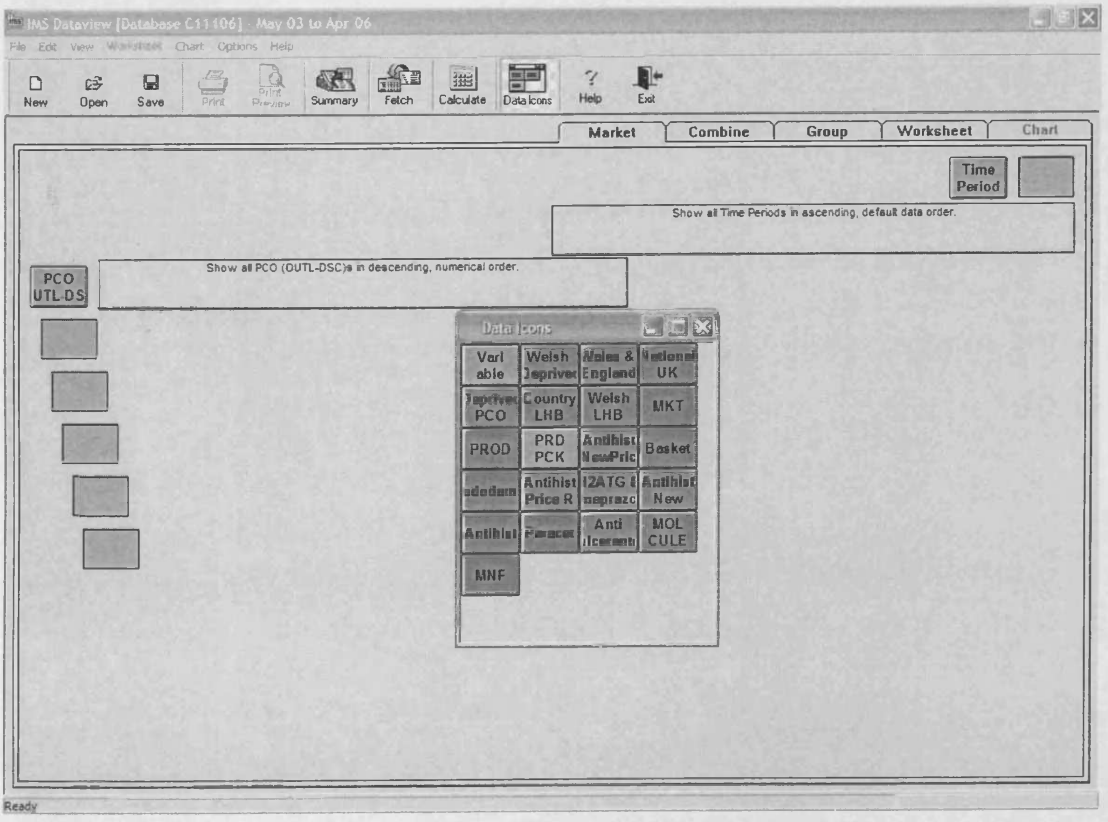


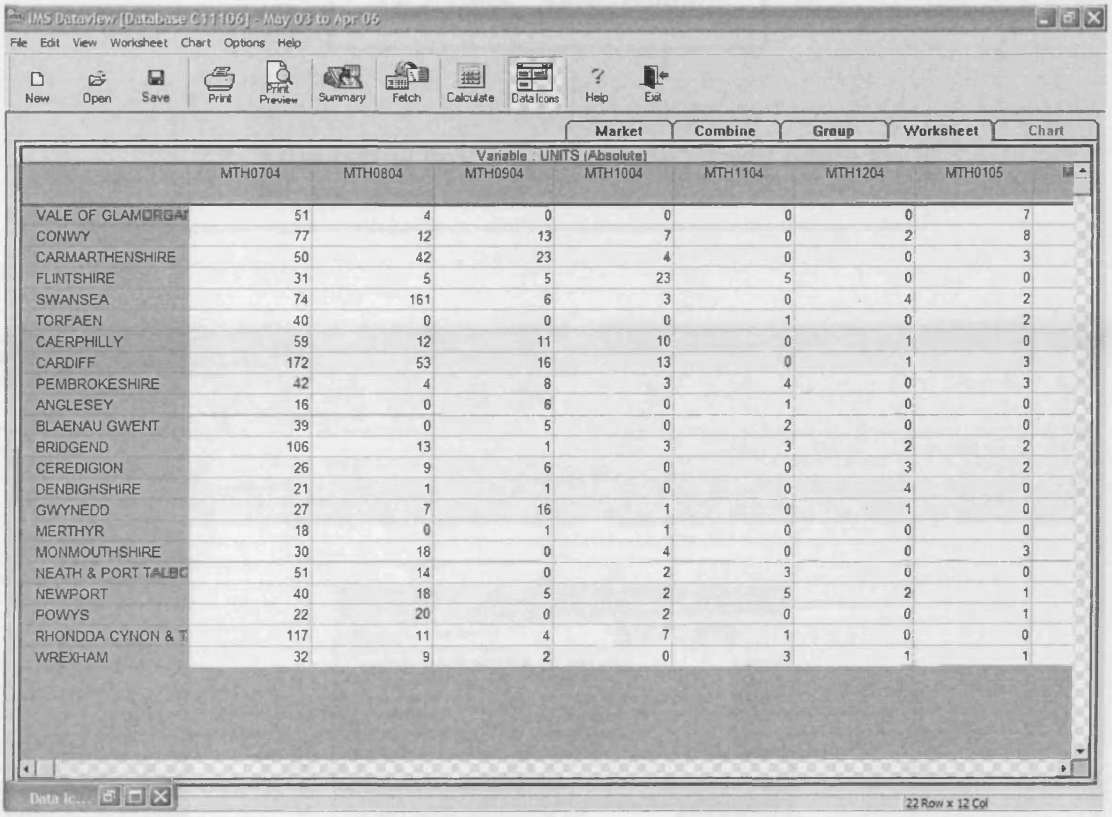
Figure A5.5: Market sheet screen

6. Worksheet screen

6.1 Select "File" button and Export to Excel

⇩

6.2 The "Save as" screen will appear



	MTH0704	MTH0804	MTH0904	MTH1004	MTH1104	MTH1204	MTH0105
VALE OF GLAMORGA	51	4	0	0	0	0	7
CONWY	77	12	13	7	0	2	8
CARMARTHENSHIRE	50	42	23	4	0	0	3
FLINTSHIRE	31	5	5	23	5	0	0
SWANSEA	74	161	6	3	0	4	2
TORFAEN	40	0	0	0	1	0	2
CAERPHILLY	59	12	11	10	0	1	0
CARDIFF	172	53	16	13	0	1	3
PEMBROKESHIRE	42	4	8	3	4	0	3
ANGLESEY	16	0	6	0	1	0	0
BLAENAU GWENT	39	0	5	0	2	0	0
BRIDGEND	106	13	1	3	3	2	2
CEREDIGION	26	9	6	0	0	3	2
DENBIGHSHIRE	21	1	1	0	0	4	0
GWYNEDD	27	7	16	1	0	1	0
MERTHYR	18	0	1	1	0	0	0
MONMOUTHSHIRE	30	18	0	4	0	0	3
NEATH & PORT TALBO	51	14	0	2	3	0	0
NEWPORT	40	18	5	2	5	2	1
POWYS	22	20	0	2	0	0	1
RHONDDA CYNON & T	117	11	4	7	1	0	0
WREXHAM	32	9	2	0	3	1	1

Figure A5.6: Worksheet screen

7. Save as screen

7.1 Select Local Disk (C) for the file to be saved

⇩

7.2 Enter the file name

⇩

7.3 Click "Save" button

⇩

7.4 After saving process is completed it will return to the worksheet screen

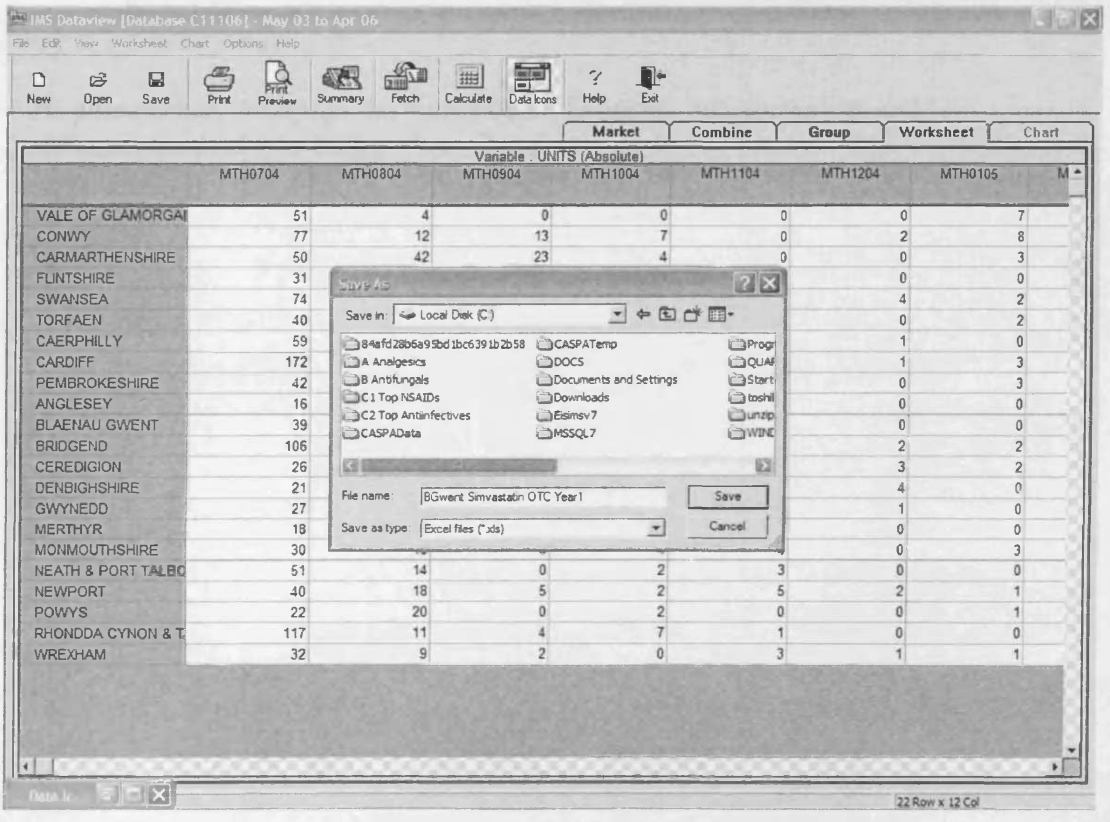
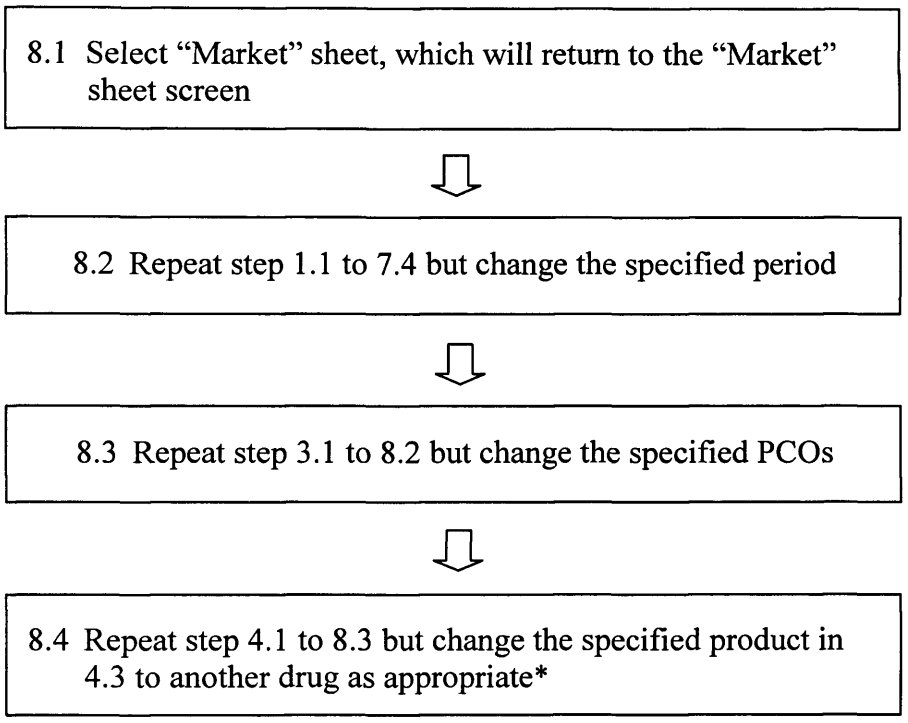


Figure A5.7: Save as screen

8. Export data for another PCO, period, or studied medicine



* H_2 antagonists, omeprazole, simvastatin, hyoscine butylbromide, and chloramphenicol eye drops

Appendix 6

Grouping of Primary Care Trusts (PCTs) in the North East of England following reorganisation in October 2006

Before October 2006	After October 2006
Darlington	Darlington
Derwentside	County Durham
Durham and Chester-Le-Street	County Durham
Durham Dales	County Durham
Easington	County Durham
Gateshead	Gateshead
Hartlepool	Hartlepool
Langbaurgh	Redcar & Cleveland
Middlesbrough	Redcar & Cleveland
Newcastle	Newcastle
North Tees	North Tees
North Tyneside	North Tyneside
Northumberland Care Trust	Northumberland Care Trust
Sedgefield	County Durham
South Tyneside	South Tyneside
Sunderland Teaching	Sunderland Teaching

Appendix 7

Grouping of selected Primary Care Trusts (PCTs) in the South East of England following reorganisation in October 2006

Before October 2006	After October 2006
Adur Arun & Worthing Teaching	West Sussex
Bexhill & Rother	Hastings & Rother
Brighton & Hove City	Brighton & Hove City
Crawley	West Sussex
Eastbourne Downs	East Sussex Downs & Weald
Elmbridge East & Mid Surrey	Surrey
Guildford & Waverley	Surrey
Hastings & St Leonards	Hastings & Rother
Horsham & Chanctonbury	West Sussex
Mid Sussex	West Sussex
Surrey East	Surrey
Surrey North	Surrey
Surrey Heath & Woking	Surrey
Sussex Downs & Weald	East Sussex Downs & Weald
Sussex West	West Sussex

Appendix 8

List of publications

1. Walker R, Dhippayom T, John D. Analysis of prescriptions dispensed out of hours by community pharmacists in Wales. IJPP 2004; 12 Suppl: R72.

2. Dhippayom T, Walker R. Impact of over the counter (OTC) omeprazole on use of prescribed and nonprescribed ulcer-healing drugs (poster presentation). In: Patient profiling: key to successful treatment. Proceedings of the 34th European Symposium on Clinical Pharmacy; 2005 Oct 26-29; Amsterdam, The Netherlands. 2005. p. 55.

3. Dhippayom T, Walker R. Impact of the reduction of the prescription charge in Wales on the prescribing and sales of paracetamol. IJPP 2006; 14 Suppl 2: B39-40.

4. Dhippayom T, Walker R. Impact of the reclassification of omeprazole on the prescribing and sales of ulcer healing drugs. Pharm World Sci 2006; 28: 194-8.

5. Dhippayom T, Walker R. Sale of over the counter simvastatin following reclassification from prescription only status (oral presentation). In: The role of communication in patient safety and pharmacotherapy effectiveness. Proceedings of the 35th European Symposium on Clinical Pharmacy; 2006 Oct 18-21; Vienna, Austria. 2006. p. 13.

6. Dhippayom T, Walker R. Impact of medicine reclassification on over the counter sale of hyoscine butylbromide (poster presentation). In: The role of communication in patient safety and pharmacotherapy effectiveness. Proceedings of the 35th European Symposium on Clinical Pharmacy; 2006 Oct 18-21; Vienna, Austria. 2006. p. 73.

7. Walker R, Dhippayom T. Does the reclassification of medicines create an inequality? (poster presentation). In: Generation to generation: sustainable directions for public health. Proceedings of the 15th UKPHA Annual Public Health Forum; 2007 Mar 28-29; Edinburgh, UK. 2007. p. 130.

8. Dhippayom T, Walker R. Impact of availability of over the counter chloramphenicol eye drops on the prescribing of chloramphenicol eye preparations: Abstracts of DURG (UK & Ireland) Conference 2007. Pharmacoepidemiol Drug Saf 2007; 16: 589-90.

9. Dhippayom T, Walker R. Impact of the reduction of the prescription charge in Wales on the prescribing of non-sedating antihistamines in primary care. Health Policy (2008), doi: 10.1016/j.healthpol.2008.01.006.