

**Deciding about research for others: normative,
empirical, and legal accounts of proxy decision-making
for research and the development of a decision
support intervention**

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Doctor of Philosophy**

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DECLARATION

This work has not been submitted in substance for any other degree or award at this or any other university or place of learning, nor is being submitted concurrently in candidature for any degree or other award.

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Summary

Research involving adults who lack capacity to consent, and who therefore require alternative decision-makers, encounters a number of ethical, legal, and practical challenges. Legal frameworks in the UK require proxy or surrogate decision-makers to make decisions based on what the person's own wishes and feelings would be. However, this may be difficult to determine or can be unknown. The aim of this thesis was to explore the ethical basis of proxy decision-making, how decisions are made in practice, and the support needs of families acting as proxies.

This thesis examined the context within which decisions are made through systematic reviews of current evidence and normative literature, and empirical research undertaken to address the evidence gaps identified using survey and content analysis methods. A qualitative study explored proxies' experiences and established their decision support needs.

The findings show that proxy decisions are contextually dependent in practice, founded on relationality and trust, with proxies aiming for authenticity rather than accuracy. Current legal frameworks and ethical accounts do not reflect the duality of the proxy's role and their obligations to both represent the person's preferences and interests. An alternative account of proxy decision-making is proposed which moves away from an autonomy and consent-based paradigm, and towards an approach centred on respect for persons.

Some family members acting as proxy experience an emotional and decisional burden and may benefit from decision support. A complex intervention was developed to support informed decision-making, which focuses on the proxy using their relationship and knowledge of the person's own values and preferences.

This thesis extends ethical understandings about the basis for proxy decisions for research, identifies areas of divergence from the legal frameworks, contributes new empirical evidence about real world decision-making, and provides a mechanism by which family members can be supported when faced with often difficult decisions.

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“If I have seen further it is by standing on the shoulders of Giants”

Isaac Newton Letter to Robert Hooke (1675)

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List of abbreviations used

CRPD	Convention on the Rights of Persons with Disabilities
CTIMP	Clinical trial of investigational medicinal product
CTR	Medicines for Human Use (Clinical Trials) Regulations 2004
DA	Decision aids
GT	Grounded Theory
HRA	Health Research Authority
IPDAS	International Patient Decision Aids Standards
IRB	Institutional Review Board
LPA	Lasting Power of Attorney
MCA	Mental Capacity Act 2005
MGT	Modified Grounded Theory
MRC	Medical Research Council
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
ODSF	Ottawa Decisional Support Framework
RA	Risk Assessment
REC	Research Ethics Committee
SOP	Standard Operating Procedures
UKCTG	UK Clinical Trial Gateway
UN	United Nations
VCM	Values clarification methods

Preface

This research originally arose out of my interest in the ethical and legal aspects of treatment decisions made on behalf of critically ill patients during my career as a critical care nurse. As I moved into a research career, I found that the same questions still arose but became even more complex when applied to decisions about research participation. My role as a researcher in a clinical trials unit has given me an opportunity to see first-hand the impact of these ethically and legally challenging issues, and the need for research in this previously under-explored area. My background in nursing also enabled me to see the need for developing practical tools to help address these complex issues. This thesis represents my exploration of proxy decision-making for research from a range of different perspectives, and the development of the first intervention to support those involved in making such decisions.

A number of manuscripts reporting various aspects of this work (including the dissertation from my preceding MA in Healthcare Law and Ethics) have been published in peer-reviewed journals or are due to be published shortly. Others are currently under review. These are summarised below:

Published:

Shepherd V. Research involving adults lacking capacity to consent: the impact of research regulation on 'evidence *biased*' medicine. *BMC Medical Ethics* 2016; 17:55 <https://doi.org/10.1186/s12910-016-0138-9>

Shepherd V, Wood F, Griffith R, Hood K, Jordan A, Sheehan M. Ethical understandings of proxy decision-making for research involving adults lacking capacity: a systematic review (framework synthesis) of empirical research. *American Journal of Bioethics: Empirical Bioethics* 2018; 9(4):267-286 <https://doi.org/10.1080/23294515.2018.1513097>

Shepherd V, Griffith R, Sheehan M, Wood F, Hood K. Healthcare professionals' understanding of the legislation governing research involving adults lacking mental capacity in England and Wales: a national survey. *Journal of Medical Ethics* 2018; 44:632–637 <https://doi.org/10.1136/medethics-2017-104722>

Shepherd V, Wood F, Griffith R, Sheehan M, Hood K. Research involving adults lacking capacity to consent: a content analysis of participant information sheets for consultees and legal representatives in England and Wales. *Trials* 2019; 20:233 <https://doi.org/10.1186/s13063-019-3340-5>

Shepherd V, Wood F, Griffith R, Sheehan M, Hood K. Protection by Exclusion? The (lack of) inclusion of adults who lack capacity to consent to research in clinical trials in the UK. *Trials* 2019 <https://doi.org/10.1186/s13063-019-3603-1>

Shepherd V, Hood K, Sheehan M, Griffith R, Wood F. 'It's a tough decision': A qualitative study of proxy decision-making for research involving adults who lack capacity to consent in England and Wales. *Age and Ageing* 2019; 48(6) <https://doi.org/10.1093/ageing/afz115>

Shepherd V, Griffith R, Hood K, Sheehan M, Wood F. 'There's more to life than money and health': family caregivers' views on the role of Power of Attorney in proxy decisions about research participation for people living with dementia. *Dementia* 2019 <https://doi.org/10.1177/1471301219884426>

Under review:

Shepherd V, Wood F, Griffith R, Sheehan M, Hood K. Development of a decision support intervention for family members of adults who lack capacity to consent to trials. *BMC Medical Informatics and Decision Making*

Chapter 1 Introduction

1.1 Background

1.1.1 The importance of including adults who lack capacity in research

It has been estimated that around 2 million adults in the UK have significantly impaired decision-making ability. Up to half of patients in acute medical and psychiatric healthcare settings lack decision-making capacity (1,2), rising to around 70% in settings such as care homes (3) and approaching 90% in intensive care settings (4). The coming decades are expected to see a significant rise in health challenges resulting from ageing populations, with a proportionate rise in conditions characterised by cognitive disorders such as dementia. Research involving those who lack capacity to consent is essential to ensure that these populations receive effective and evidence-based care. Ambitious UK research agendas have been set out in order to address these challenges, such as 'Dementia 2020' (5), however delivering this much needed research will require the involvement of substantial numbers of research participants at all stages of the condition.

Informed consent is fundamental to ethically conducted medical research (6), but obtaining valid consent can be particularly challenging in specific practice contexts (7). Individuals may be unable to provide consent for themselves due to an impairing medical condition that strikes suddenly (like a stroke) or causes a gradual loss of capacity (such as dementia), or due to profound learning disabilities. Research involving vulnerable groups, such as adults lacking mental capacity, raises many ethical and legal issues: particularly with respect to informed consent for them to be included in a project (8,9). As a result, recruitment of vulnerable groups to research is a complex process (10,11) and the exclusion of people with cognitive impairment from research is widespread (12,13). Under-recruitment to research into conditions such as dementia is one of the key challenges to advancing understanding of these conditions and improving the care and treatment of those who live with these conditions (14). The exclusion of those who lack mental capacity from participating in research has been highlighted as a concern (3), as it results in a lack of evidence-based care for populations who may already experience significant health disparities (4).

Research ethics has historically been concerned with the protection of 'subjects' from participation in research and as a result the discourse on consent has focused on the negative or protective dimension of autonomy (15). By contrast, there has been much less concern about ensuring that individuals are not denied the opportunity to receive the potential benefits of participation (15). The recent update of international ethics guidelines (CIOMS), where there is now a need to justify exclusion (16), has been seen as marking a paradigm shift from overprotection to inclusion (17). In addition to this consequentialist argument that exclusion from research leads to a reduced evidence base and hence poorer quality of care for those affected, enabling greater inclusion also appeals to an ethics of justice, both epistemic and distributive in nature. Inclusive research practice recognises the richness of the lived experience of those considered to be 'voiceless' in society, and enables them to contribute knowledge that is recognised as having value (18). However, decision-making lies at the foundations of research ethics and how we think about informed consent (19), and decisions made on behalf of someone else are perhaps the most ethically challenging of all.

1.1.2 Proxy decision-making for adults who lack capacity to consent

Adults are presumed to have capacity to make autonomous decisions about themselves unless it is determined otherwise (20). Capacity is not a global concept and the ability to perform a specific task, such as providing informed consent, will vary depending on a number of factors. However, for practical and regulatory purposes, threshold levels, rather than degrees, of competency are required (21). The Mental Capacity Act 2005 provides a comprehensive framework for decision-making on behalf of adults aged 16 and over who are unable to make decisions for themselves (20). The Act has laid out a two-stage test of mental capacity, and has codified, clarified and supplemented the common law in relation to adults who lack capacity.

Where an adult is unable to provide their own consent for decisions about research participation, another person is required to make decisions on their behalf, usually termed a proxy or surrogate in the literature. Although often considered equivalent and used interchangeably, in this thesis the term proxy is used rather than the term surrogate as the meaning of 'proxy' (from *procurator* (the act of appointing another as agent or attorney, or the authority vested in one)) being to represent, or to represent the value of something, indicates a sense of closeness or attempting to be as close as possible to something, contrasted with surrogate (which comes from the Latin *super* (over) and *rogare* (ask)) is often

thought of as standing in for something or someone – being a substitute or placeholder. From a legal perspective, a person can become a proxy in several ways: formally designated as the proxy by the person themselves, an undesignated family member or significant other volunteering to act as proxy, or through being appointed by a court to act as proxy. The circumstances leading to the requirement of a proxy include where the person affected has lost capacity progressively as a result of a condition such as dementia, or suddenly due to a stroke or critical illness, whilst for some, such as families of someone with profound or multiple learning disabilities, it may be a continued role from the beginnings of parenthood. Family members or close friends of adults lacking capacity are usually called upon to act as proxy, although someone acting in a professional role may do so under certain circumstances.

The legal provisions enabling a proxy to act in these capacities, and the relative scope of their decision-making authority, differ between legal jurisdictions and decision contexts. For decisions about whether the person who lacks capacity should take part in a research project or not, in England and Wales the person acting as proxy (termed a ‘consultee’) is required to provide advice based on what the person themselves would have decided if they had capacity to do so. The provisions of the Mental Capacity Act 2005 (MCA) (20) require that the consultee provides advice to the researcher as to whether the person should take part in the project, and what, in his opinion, their ‘wishes and feelings about taking part in the project would be likely to be if they had capacity’ (s30-33). Alternatively, the Medicines for Human Use (Clinical Trials) Regulations 2004 (22) (CTR) which governs clinical trials involving medicinal products requires that informed consent given by a legal representative for an incapacitated adult in a clinical trial shall represent that adult’s ‘presumed will’ (Schedule 1 Part 5). The incoming Clinical Trial Regulations (23) does not fundamentally change these provisions, but has left a wide margin for the application of consent by proxy, such as leaving the Member States to determine the legally designated representatives of incapacitated persons. In this thesis, the term proxy is used to refer to those acting as either a consultee or a legal representative. Whilst accepting that the term ‘decision-making’ may not reflect the legal requirement under the MCA to provide advice (s32(4(a)) [20], or that it can be viewed as not so much a decision as accepting or rejecting a proposal (24), the literature overwhelmingly describes the phenomenon as ‘decision-making’ and so the term is a pragmatic choice for this thesis.

1.1.3 Challenges of proxy decision-making for research

There are significant differences between decisions relating to medical treatment of adults lacking capacity, and those concerning their participation in medical research. Decisions regarding the participation of adults lacking mental capacity in medical research are complex and raise considerable legal and ethical issues. The ethical basis for proxy decision-making is an important practical issue, with substantial implications for the treatment and welfare of such individuals (25). The normative basis for proxy decision-making will depend upon which principle of proxy decision-making is accepted: substituted judgement where the proxy uses their knowledge of the persons' preferences to make the decision they would have made if they had capacity, or a best interests decision where the proxy makes a decision based on their assessment, rather than reconstructing what they would have decided, although the wishes and feelings of the person may be taken into account (26). This has been described as the 'time of the triumph of autonomy' in bioethics in which the autonomy of the patient paradigm dominates ethics and law (27). As a result, there is an attempt to ground all decisions in autonomy, even when the person is no longer able to express an autonomous wish (28). However, little is known about the ethical basis on which proxy decisions are made and, in the light of this autonomy-focused paradigm, the ethical legitimacy of current proxy decision-making has been questioned.

The development of ethical theory and the law are not always synchronised and are not necessarily evidence based. In proxy decision-making for research there appears to be tension between the legal standard required, the ethical basis, and the empirical evidence around how decisions are actually made in practice. This may be due to a lack of a clear ethical theory about informed proxy consent and decision-making. Whilst the law does not necessarily need to incorporate a specific ethical theory, and rarely does, the law does at least need to be compatible with, and supported by, plausible ethical theory (29). Theory can be held as being based in experience, where practice can help to formulate and reformulate ethical theories in order to ensure that they are nuanced and appropriate for the problems they are supposed to address (30). The field(s) of empirical ethics or applied ethics deals with the 'translation' of theoretical principles into workable practice rules, making them available for everyday judgements and decisions (31). Findings from a mixed methods study that examined proxy decision-making about research participation for patients with Alzheimer's disease, concluded that legislation and policy making rested on thin evidence – with an

artificial separation in law between differing ethical principles that was not evidenced in practice (32).

There is an important disparity between the proxy's authority under the MCA, and the CTR that govern clinical trials of medicines (33). For research that is not a clinical trial, under the MCA provisions the consultee provides advice about what the person's wishes and feelings would be about taking part in the project if they had capacity, or if they were likely to lead them to decline to take part. The researcher is then responsible for deciding whether the person should be included in the research (20). This effectively gives the consultee the right to veto research participation. For clinical trials the legal representative does provide informed consent on the person's behalf, and that consent represents the person's presumed will (22). There is no requirement under the MCA or CTR for the proxy to confirm that they are accurately representing the person's presumed will or wishes when providing or withholding consent or providing advice or veto for the person's participation. No guidance is provided about how proxies can determine the wishes or will of the person. In practice this legal standard appears difficult to achieve, particularly for those who have never expressed, or perhaps even held, relevant views. As a result, there is uncertainty whether proxies have sufficient moral authority to make such decisions under the current legal framework (26), whether the legal and ethical requirements can always be met (9), and whether the present legal basis provides an adequate standard for substituted decision-making (34).

Despite the rising prevalence of conditions such as dementia, there is a dearth of information or support available for those involved in making proxy decisions about research participation. Involvement in making decisions about research participation can be overwhelming for proxies (35), with nearly all proxies experiencing some degree of burden (36). One study of family members of critically ill patients found that being asked to provide consent for research was associated with post-traumatic stress symptoms in 35% of family members interviewed, compared with less than 10% in those involved in 'everyday' decisions about clinical care (37). Recently released NICE guidelines on 'Decision-making and mental capacity' (NG108) (38) excludes decisions about research, and the guidelines for people living with dementia and their carers (NG97) (39) highlights the importance of research for people with all stages of dementia but contains no guidance about how the involvement of those in the later stages might be enabled. A recent emphasis on improving informed consent processes in research has focussed on improving information provision (40), understanding

(41), and the quality of informed consent (42), as well as interventions to support the decision-making process (43). Decision support tools are increasingly being used to effectively support preference-sensitive decisions in clinical practice (44). However, despite the ethical, legal, and practical challenges outlined here, there is a paucity of research on how such proxy decisions are operationalised (45) or supported. There have been calls for future research to be directed towards how to develop a better appreciation of the struggles and difficulties people actually experience when acting as a proxy (24). Exploration of the ethical and practical factors influencing these decisions is a key area for future research (45), and interventions to inform and support those involved are urgently required in order for adults lacking capacity to have the opportunity to participate in research.

1.2 Aim of thesis

The aim of this thesis is to explore the normative, empirical and legal accounts of proxy decision-making for research involving adults who lack capacity to consent; to present the beginnings of an account (understood as a statement or exposition) that is grounded both empirically and theoretically; make recommendations for clarifications and amendments to the current legal frameworks in England and Wales; and the development of a novel decision support intervention set within the ethical and legal frameworks.

1.3 Scope of thesis

This thesis explores the inclusion of adults lacking capacity to consent to research, where the term 'research' is used to include clinical trials of medicines as well as trials of non-medicinal interventions, and other types of non-interventional research such as observational studies and qualitative research. The influence of the nature of the research on an individual's decision to participate has been previously noted (46). Decisions about participation in a clinical trial may differ compared with a longitudinal observational study, for example, due to the perceived level of risk and the greater time commitment required (46). Proxy decisions about research may similarly differ depending on the type of study, particularly where their role might be to provide either advice or consent depending on the study type, or where the risks or benefits of the study may vary considerably. The inclusion of different study types in

this project has allowed a broader exploration of the underpinning ethical issues and legal frameworks and enabled a richer understanding of the specific contexts within which the type of study and relevant regulatory frameworks affect the experiences and decision-making processes of those involved. However, research in emergency situations was not included as it may not be practicable to consult a proxy in these situations and so alternative consent arrangements such as deferred consent may be used (47).

Decision-making ability and the capacity to consent to research are not universal or static constructs (20). Situations where capacity is lost following a sudden and catastrophic event will differ from those where the lack of capacity has been progressive (e.g. associated with dementia) or where the person may have a lifelong disability that impairs decision-making capacity. Therefore, the context within which person's capacity is impaired and proxy decisions are subsequently required will similarly affect the experiences and decision-making processes of those involved. Whilst the legal frameworks apply regardless of the context within which the person's capacity to consent is impaired, which may be problematic in itself and is discussed in this thesis, the range of ethical issues engaged, and empirical data collected will be highly context specific. The datasets presented in this thesis are discussed within each chapter in relation to the sampling approach, research and decision-making context, and subsequent limitations, however the qualitative data is primarily derived from proxies representing people with a progressive loss of capacity. Thus, the broad scope of the thesis includes all populations who may lack of capacity to consent, but a number of the findings are of greatest relevance to those who have previously had decision-making capacity and experienced a progressive loss of capacity requiring the involvement of a proxy decision-maker.

1.4 Methodological approach

Given the interdisciplinary nature of the topic of this thesis, the methodological approach adopted necessarily includes a broad range of methods in order to capture the epistemological complexity and pluralities involved. The project spans both normative exposition and empirical enquiry, from systematic review methods to intervention development, in order to comprehensively explore the ethical, legal, and practical dimensions of proxy decision-making. Complicated areas of decision-making raise ethical

questions that should be clarified in such a way that the results are helpful for those who are practically involved (48). So whilst empirical ethics is a candidate for being one of the most theoretically complex forms of research (49), the mixed-methods approach used in this thesis seeks to bring much needed clarity to a complex area of decision-making, which can only be achieved by examining and synthesising the wider contexts involved.

Empirical (bio)ethics is characterized by the use of socio-empirical research and ethical analysis to address concrete moral questions (50). The interaction between empirical data and normative elements has been extensively debated in recent years (51). Empirical work is often seen as the 'handmaiden' just providing the facts and as secondary to normative ethics which does the 'real' and important work of resolving value questions by defining concepts, building valid arguments, and reaching practical conclusions (52). In contrast, empirical ethics approaches go beyond this false separation. There is a growing consensus that it is the integration of empirical research with normative-ethical research that is at the root of empirical ethics, although there is disagreement about the meaning of 'integration' and what the concept implies (53). This has led to a number of different approaches to the integration of empirical and normative ethics including various typologies of empirical ethics (52). Regardless of the empirical ethics approach used or position taken, the methods should be rigorous, transparent and appropriately described (53).

Approaches to empirical ethics have been described as being located on a continuum stretching from empirical studies that do ethical work to research that does sociological work (52), where either theory or practice are seen as 'trumping' the other (30). The approach used in this thesis is one where empirical data and normative analysis are viewed as mutually informing, seeking a form of reciprocity between the empirical and the normative rather than attempting data integration. This approach recognises the importance of the circumstances and context within which the ethical practice takes place, whilst ensuring that ethical theory still has a key role to play (30). The aim is to examine the ethical issues around proxy decision-making for research and explore the beginnings of a more nuanced account which retains its normative function whilst being attentive to the particular contexts in which such decisions take place.

In order to bring structure to the thesis as a whole, concepts from a framework proposed by Kon have been adapted to act as an organising construct (54). The original framework identified four hierarchical categories: Lay of the Land, Ideal Versus Reality, Improving Care, and Changing Ethical Norms. This categorisation is said to illuminate the interaction between descriptive data and normative-ethical issues, where the scientific work of the higher categories builds logically on the insights derived in the lower categories (54). *Lay of the Land* studies seek to define current practices, opinions, beliefs, or other aspects that may be considered the status quo, and can set the stage for further research. The next level, *Ideal Versus Reality*, starts with a premise regarding the 'ideal' ethical norms (and legal frameworks) and then seeks to assess the extent to which actual practice reflects this ideal. By illuminating areas of dissonance, these studies can be catalysts of change to more closely align reality with our ideals (54). The next higher-level categories explore the implications of this proceeding work focusing on three different areas, ethics, the law, and in practice, and outlining the development of new approaches. In *Changing Ethical Norms*, a review and analysis of the empirical findings leads to an adaption of the ethical norms relating to specific aspects of practice. *Improving Care* (or here *Improving Decision-making*) describes the design and test of a novel methods aimed at ensuring 'compliance' with ethical (and legal) norms. In addition to those outlined by Kon, a third area *Recommendations for Amending Legal Frameworks* has been developed, which identifies areas of the law governing research involving adults who lack capacity that are in need of clarification and amendment.

A number of limitations of Kon's framework have been recognised (55,56), not least the suggestion that empirical research can produce general truths, as implied by the term 'Changing Ethical Norms' (57). Kon's framework, and indeed other 'tools' have been criticised as adopting a methodological toolbox approach to empirical ethics which lack substantive content and are inherently vague (56). In addition, by treating data as 'fact' and creating a hierarchy, Kon's approach creates a dichotomy between the empirical and normative (57) and also fails to acknowledge the constructivist nature of empirical data (56). This risks adopting a naïve and over-simplistic account of empirical research that does not accord with recent developments in the social sciences or empirical ethics (56). Other criticism relates to Kon's claim as the framework being able to 'lay the foundation for a more universal ethic' despite lacking an account of how it operates to address the limits of empirical research (57). Empirical work is meant to bring ethics closer to the detail of everyday life through providing the details needed to inform contextualized, responsive, and appropriate judgments, rather than making sweeping claims (57). Thus, the use of frameworks such as Kon's must consider

the interpretative limits of empirical ethics approaches in light of the range of the different perspectives, practices and ethical theories (55).

It is with these limitations in mind that the framework is not used in this thesis as a fully-fledged 'ethical framework'. The work and individual empirical studies contained in this thesis are not considered to form a hierarchy, nor, in recognising its methodological limits, does it claim to seek to or achieve normative and empirical integration. This thesis also considers the role of the legal frameworks and hence extends beyond an empirical ethical body of work. Alternatively, useful concepts from the framework have been borrowed and adapted as they provide a helpful typology for work such as this, which seeks to map ordinary practices, compare the everyday to the ideal, test the effects of interventions, and deliberate over the ethical implications of previous research (57). The use of Kon's framework merely offers an organising structure which provides a narrative to the ordering of the individual chapters, with the explicit acknowledgement of what Frith refers to as the symbiotic relationship between theory and practice (30). These methods therefore can be seen as a way of moving towards 'better' and more nuanced accounts to deal with the issues that arise in practice, rather than necessarily as a way of delivering 'the truth' (30).

1.5 Thesis synopsis

The six chapters that make up the *Lay of the Land* examine the core issues of proxy decision-making from a number of different perspectives in order to define current practices and beliefs of researchers, ethicists, health and social care practitioners, and family members. This begins in **Chapter 2**, which summarises and appraises the existing literature on proxy decision-making from the perspective of normative ethics and law and identifies some of the theoretical and practical problems with existing approaches. **Chapter 3** synthesises the existing empirical research using framework synthesis and presents an empirically informed conceptual framework of proxy decision-making. **Chapters 4** and **5** explore the context within which proxy decision-making occurs through an examination of the knowledge and understanding of those likely to be approaching proxies, and an analysis of the information currently provided to proxies about their role and basis for their decision. **Chapter 6** presents the first analysis of the qualitative data from the DECISION Study. The study explored how family members make proxy decisions in the real world, and this analysis used thematic analysis methods to analyse proxies' experiences. The second analysis of the dataset is presented in **Chapter 7** which used modified grounded theory to explore the ethical practice

of proxy decision-making. It also revisits the conceptual framework from Chapter 3 and presents an updated and more informed and refined framework.

The thesis then moves into the *Ideal Versus Reality* stage with **Chapter 8**, which builds on the work presented in the previous chapters and uses triangulation methods to explore the normative, empirical, and legal accounts of proxy decision-making and identify areas of convergence and disjuncture. The seeds of a new account of proxy decision-making, one that is grounded both normatively and empirically, are then sown.

As a move towards *Changing Ethical Norms*, **Chapter 9** extends this critique to focus on the role of autonomy with respect to adults lacking capacity and the role this plays in the requirement for informed consent, and to develop a new approach based alternatively on respect for persons.

Next, **Chapter 10** focuses on the implications of the findings of the preceding work on the current legal frameworks and makes a number of *Recommendations for Amending Legal Frameworks*.

Lastly, **Chapter 11** introduces the concept of decision support as a move towards *Improving Decision-making* and describes the development of a novel tool to support proxy decision-making using theoretically informed development frameworks.

The thesis ends with a summary of the key findings and novel contributions from this thesis in **Chapter 12**, which concludes with proposals for the future direction of this work.

1.6 Public and Patient Involvement

Involving members of the public and patients in research is increasingly being seen as an essential part of how research is identified, prioritised, designed, conducted and disseminated (58). Patient and public involvement (PPI) includes involving patients, potential patients, carers and people who use health and social care services as well as people from organisations that represent people who use services, and has been defined as research being carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them (59). This includes working with research funders to prioritise research, offering advice as members of a project steering group, commenting on and developing research materials, and undertaking interviews with research participants (59).

Members of the public with lived experience as carers, family members, and advocates of people with a range of cognitive impairments were actively involved throughout this doctoral research project. Prior to starting the project, two members of the public were invited to form a lay advisory panel to review the funding application and initial draft of the plain English summary. Once the project was funded, two additional members were recruited to join the lay advisory panel. The project benefitted enormously from their involvement in the first drafting of the research questions, through to ensuring that the information provided to potential participants in the qualitative interview study (Chapters 6 and 7) was accessible and appropriate, refining the interview topic guides, and the development of the intervention itself (Chapter 11). Their involvement has made a significant contribution to the project as a whole, and particularly during the development of the decision support intervention which is further described in section 11.2.9 Collaborative development with stakeholders).

Engagement in research is defined as a process of information and knowledge about research being provided and disseminated to audiences (59). For this project, the lay advisory group had a key role in helping draft the findings from the research, particularly those from the qualitative interview study, for dissemination to the participants and wider public audiences. This included providing written summaries of the findings which were sent to all those who had taken part, as well as a short animation of the findings. A link to the animation was also sent to participants and shared on social media.

An important part of involving the public is to recognise and value the contribution they make to the research project. Towards the end of the project an exercise to 'map out' the involvement of the lay advisory group throughout the project was undertaken in order to identify when and how the group had helped shape the project. Together with the group a 'map of the PPI journey' was designed, together with additional information provided about their involvement at various stages (see **Appendix 1. Public and Patient Involvement in doctoral project**).

Chapter 2 Proxy decision-making for research involving adults lacking capacity – a critical review of the normative ethics literature

2.1 Introduction

Proxies need to rely on some kind of normative standard to guide their decision-making, however the theoretical basis underpinning the proxy's role differs depending upon which principle of proxy decision-making is adopted (26). The two widely recognised decision-making standards in healthcare ethics are substituted judgement and best interests. In cases of substituted judgement, the wishes of the patient prevail; in cases of best interests, the benefit to the patient surmounts all else (60). In order to utilise the substituted judgement standard, there are three ways the proxy can know what the person would have wanted: the person could have explicitly told the proxy either personally or in written advance directives; they could have implicitly voiced their wishes, perhaps by comments made in passing; or they could have revealed enough about their thoughts and values so that the proxy knows what the person wants, even though the matter was never discussed or even mentioned (60). Although the latter is considered by some commentators to be an extremely weak basis for substituted judgement, it may be valid in some cases (60). Other commentators go further and argue that substituted judgement is not a usable mechanism when proxies have to make decisions for adults who never experienced decision-making capacity (61) or, if they had, had never revealed enough for the proxy to know what they wanted.

There are significant differences between consent for healthcare decisions and decisions about research participation. These primarily relate to the processes for prior ethical review for research, the evolution of the legal framework, and the aims of the intervention and therefore the associated level of risk and benefits permitted (62). Valid informed consent for treatment requires three components to be present: capacity, voluntariness, and disclosure of information (21). Similarly, research participants must show that they understand the purposes, procedures and duration of the research, risks and benefits, alternatives to participation and the voluntary nature of participation (63–65). The elements of proxy consent for research have not been clearly defined, although the components of capacity, voluntariness, being informed, and freely given consent will apply to the proxy, with the additional requirement that the proxy is legally permitted to provide such consent. The most

significant difference between the two areas of decision-making is that best interests is the dominant standard for treatment and care decisions for those lacking capacity, but cannot be the standard for decisions about research as best interests is considered an ethically weak basis for enrolling those without capacity into research which is not intended (or likely) to benefit them (66). Questions remain about whether there are differences in terms of the moral authority for proxy decision-making, the normative requirements for a decision-making standard, or evidence of decision-making in practice between decisions for treatment and those for research participation.

The heterogeneous nature of the types of decisions made by proxies for adults who lack capacity, and the current dearth of empirical studies examining proxy behaviour, may make systematic generalisations about how proxies actually make decisions impossible. Johansson and Brostrom (67) outline a number of problems with drawing normative conclusions about substituted judgement from empirical studies which, they suggest, allegedly show that proxies cannot successfully apply this standard. However, given the much cited difficulties of applying substituted judgement in practice that have been identified in empirical studies, such as the accuracy of proxy predictions, there may be value in using empirical evidence to elucidate and analyse the practical, and theoretical, difficulties with substituted judgement and the proposed alternative decision-making standards. As Johansson and Brostrom acknowledge, substituted judgement first needs to be evaluated on moral grounds, to establish whether it is best thought of as a tool for decision-making or an objective measure of when a decision is morally justified. Only then can the empirical issue of understanding what is the best way to make surrogates actually make the decisions for patients be explored (67).

This review of normative ethics literature will examine the standard interpretation of substituted judgement, and the theoretical and practical difficulties it presents. Alternative interpretations of the decision-making standard will then be analysed, and conclusions drawn about the problematic nature of these alternatives, before some suggestions for a new approach to proxy decision-making for research are presented.

2.2 Methods

A systematic search to identify relevant literature was performed following development of a search strategy for the systematic review of empirical research presented in Chapter 3. The search combined terms including informed consent, research, proxy, surrogate, ethical principles, and decision-making. Bibliographic databases were searched: Ovid MEDLINE, Ovid EMBASE, Ovid CINAHL, Ovid PsycInfo, ISI Web of Science, EUROETHICS and Scopus. Supplementary searches were conducted using hand searching, reference lists from included papers, and citation tracking, to ensure a comprehensive review. A wide range of literature covering research that involved adults lacking capacity from the fields of ethics, law, medicine, psychology, and research methodology was reviewed. This review represents the breadth of topics of interest identified from the literature with relevant themes presented. A number of problematic areas are identified, and alternative interpretations are discussed. The discussion section provides an opportunity to present some potential alternative approaches which form the basis for the following chapters.

2.3 Results

2.3.1 Differences between medical treatment and medical research

Decisions made for oneself, and for others, are specific to the decision in hand, the context, and the choices available from which to choose to accept and which to reject. Decisions made on behalf of another person regarding medical treatment and care may be very different from those made about research participation, although many research opportunities will occur within a healthcare setting and will need to be weighed amongst a range of treatment options. The differences, and indeed similarities, between medical treatment and research have been widely debated, and continue to be the subject of much discussion, particularly in randomised controlled trials where participants are usually assigned to receive the intervention under investigation or the usual or standard treatment (or placebo). The debates include the relative functions and aims of research and treatment, and the misconceptions that subsequently arise.

2.3.1.1 Aims of research vs medical treatment

In many instances, research involves performing activities that are indistinguishable from other activities that are performed in a non-research context, such as carrying out a blood test or administering an existing and widely used medicine. However, the key difference between the activities is the purpose of the activity, as there are distinctively different goals of medical care and research. Medical treatment aims to promote the well-being of individual patients, however the essential purpose of clinical research is to produce generalizable medical knowledge that will improve care for future patients (68). Knowledge is needed because there is uncertainty about whether the treatment or intervention is effective, or whether it is the most effective compared to other alternatives. This imposes risks for participants, who are unlikely to benefit directly themselves, in a situation awash with uncertainties and where trust between all parties is essential. What makes research more ethically problematic is that it introduces new risks that would not otherwise be present that are governed by a complex research protocol that may be difficult to understand sufficiently well to allow informed consent. When this is considered in the context of a historical background of atrocities carried out in the name of research and the fact that the participant/researcher relationship is inherently power-imbalanced, these risks are not insignificant. This exposure to risk within ethical relationships, Hunter and Wilson argue, is why research is ethically distinguishable from medical treatment and why research merits stringent regulation – which they term ‘research exceptionalism’ (69).

Similarly, differentiating between medical research and what constitutes innovative therapy is widely debated. For a therapy to be ‘innovative’ it needs to be newly introduced with an unproven effect or side effects, and is undertaken in the best interest of the patient (70). Innovative therapies have their experimental nature in common with research but differ in that their goal is to benefit the person directly and are therefore exempt from direct governance by research ethics committee oversight. This materially changes the risk/benefit profile, and the ethical and legal obligations. It also raises many concerns about why an ‘innovative’ therapy would be attempted in place of research studies, where there are proper arrangements for safety monitoring and data collection (71).

2.3.1.2 Therapeutic misconception

Where there is a conflation of research with medical care, this confusion about what is routine medical care and what is research activity constitutes a ‘therapeutic misconception’.

The term therapeutic misconception was coined by Appelbaum et al (72) to describe how participants interpret, and even distort, the information they receive to maintain their view (presumably based on their wishes) that the research was designed to benefit them directly. This is problematic as it may undermine the basis for informed consent, and there are also concerns that proxies making decisions for people unable to provide their own consent for research are not immune to therapeutic misconception (73). However, the moral implications of therapeutic misconception are unclear, and the extent of the phenomena has been much debated (74). Sulmasy et al (75) propose that rather than expressing misunderstanding when asked about the purpose of the research, some participants are really expressing their optimism that the research will benefit them directly. Similarly, Kim et al (76) suggest that when asked to estimate the probability of benefit, they are not always expressing mathematical probability, but their own expressions of hope, wish for luck, or the need to stay positive. Being motivated by a desire for benefit should not imply a faulty understanding of research, illustrated by Kim et al through the reminder that one can rationally buy a lottery ticket hoping to win, whilst also understanding that the purpose of the lottery is not to enrich the buyer of tickets, but rather to raise funds (76). Both authors acknowledge that therapeutic misconception exists but argue that it may not be as 'ubiquitous' as some commentators suggest. Sugarman et al's (36) study with proxies of people with dementia showed that similar views are expressed by proxies, who understood that the medication might not help the patient, although all hoped that it would. However, distinguishing hopes from expectations regarding the research was difficult for some proxies (36).

2.3.2 Different standards of decision-making

Two guiding principles or standards for decisions made by proxies on behalf of another person, substituted judgement and best interest decisions, are well-recognised in the 'liberal' model that has been emerging in the United States (77) and beyond (26). Proxies should appeal to the substituted judgement standard where decisions are made in 'good faith' based on what the proxy considers the person would have chosen if they were capable of doing so (78). Decisions made under the provisions of the Mental Capacity Act (MCA) (20) and Medicines for Human Use (Clinical Trials) Regulations (CTR) (22) are based on the person's 'presumed will', or what the person would have decided if they had capacity, and are therefore considered to use the substituted judgement standard, although the term is not used in the legal instruments. Proxies should be appropriately qualified through being

suitably acquainted with the patient, and not subject to potential conflicts of interest (78). However, this standard is frequently unrealistic as proxies often do not know a person's previous preferences (78), particularly about research participation. Hope (79) describes this approach to decision-making as hypothetical choices, either in an external sense - what the person would have put in an advanced decision shortly before losing capacity, or an internal sense - what the person would now choose if they were (magically) to regain capacity for long enough to make a valid choice. Ultimately the moral criterion of proxy decision-making is the 'right reason' and, as a moral agent, the proxy is responsible for their actions (60).

The second standard of decision-making is deciding what the proxy considers would be in the best interests of the person, which may be used when making treatment and care decisions (80). Hope (79) defines best interests as the decision that would maximise the person's wellbeing, although competent people's choices may be valid even when that choice does not maximise their wellbeing. Individuals can be mistaken about what is best for them, or they can make a valid decision knowing that it is unlikely to be in their best interests. Hope et al (79) present a checklist of factors that may assist when determining best interests, including current and past wishes and values, and the strengths with which they were held, which might be used and weighed in coming to a judgement about treatment or care decisions. Although best interests forms the legal basis for decision-making generally under mental capacity law in England and Wales (20), it is not considered an appropriate standard for making decisions about research participation, as participation is not intended to benefit the person directly and hence cannot be weighed alongside other options that may confer a benefit to the person. A third standard is discussed in the literature – known wishes, where a person with capacity provides a direct expression of their preference. This is discussed further at a later point in the chapter, but in practice it is rare to encounter individuals who have left clear and unambiguous directions about research participation (or indeed other decisions) that can be applied directly without interpretation or evaluation as to its meaning and application to the situation at hand.

These separate standards (known wishes, substituted judgement, best interests) are considered by some to form a sequential bioethical hierarchy, despite empirical research on proxy decision-making showing a departure from these standards when actual decisions are made in practice (81). Other commentators note that it does not reflect the clinical reality of medical decision-making, or the interests of patients and families (82). Dionne-Odom and Bakitas (80) point out that the fixed three-standard hierarchy implies that proxies use these

abstract principles like a 'skeleton key that can open the doors of decision making in all cases'. They suggest that people in real-life settings are typically variantists, who use different criteria in different situations, which varies over time (80). Although these three standards are problematic when applied to decisions about research, Berger (66) and many others find the best interests standard to be the most problematic.

2.3.2.1 Substituted judgement – legal origins and the standard interpretation

The substituted judgement standard is used by surrogates where there is no exact knowledge about the preferences of the person who lacks capacity, and instead an attempt is made to 'infer from their knowledge' of the person what they would have decided (83). The standard interpretation of substituted judgement is that proxies are required to make the decision the person would have made in the circumstances, if they were competent to do so (84). To stand in the shoes of their charge (85), or 'don the mantle' of the person (86). The appeal of the substituted judgement standard is that it is said to 'support the patient's autonomy by leading us to the decision that the patient would have wanted' (28) even if they did not provide definitive guidance (84). However, the exact definition of substituted judgement is widely disputed and has been the subject of disparate interpretation in the courts (83).

The evolution of substitute decision-making in England and Wales from the 19th Century probate courts dealing with distributing the property of incompetent individuals has been well described elsewhere (87). Harmon (87) controversially argues that substituted judgement is a dangerous legal fiction which was borrowed irresponsibly from the law of 'lunacy' and management of property - 'doing that which it is *probable* the lunatic himself would have done' - into the law of informed consent for medical treatment and beyond. She describes it as an Alice in Wonderland agency relationship, where those deciding on behalf of another run the risk of forgetting that they are required to justify their assertion, confusing the probable intent of the person with certainty about their intentions (87).

Dresser (88) offers a reminder that the original court rulings related to the incompetent person's *surplus* income, ensuring that sufficient resources were retained to cover their care. Buchanan and Brock argue that this would also be applicable to healthcare decisions – that a course of action cannot serve the interests of others at the expense of the person's basic interests (29). This arguably also applies to decisions about research participation, and

echoes ethical guidance that the rights, safety and well-being of the participants are the most important considerations and should prevail over the interests of science and society (65).

2.3.2.2 *Practical difficulties of substituted judgement*

Buchanan and Brock describe substituted judgement as the proxy choosing 'as the patient would choose if the patient were competent and aware of both the medical options and the facts about his or her condition including that fact that he or she is incompetent' (29). The key difficulty of substituted judgement is the question of whether one person can ever simulate the decision-making processes of another (25). The problem of how to identify the 'correct' substituted judgement leads to a major stumbling block when attempting to apply this literal interpretation of the standard to medical or research decisions. The person in question will never have experienced exactly the same set of circumstances before, and therefore has never had the same choice to make from the same set of options. This means that the proxy is required to undertake the near impossible task of 'choosing as the patient would choose' in a scenario that the patient had never, and probably could never, have imagined they would be facing. This has led to the critics of substituted judgement claiming that substituted judgement amounts to nothing more than complicated guesswork (84).

Proxies' substituted judgements about participation in research are likely to be 'highly speculative as most incompetent people...were never presented with such a choice in the past and are unlikely to have formulated and expressed opinions on the matter' (89). Substituted judgement requires imagination on the part of the proxy, involving extrapolation, and real effort to utilise all of the evidence for assuming that the decision is what the person would have wanted (67). Even so, the proxy is unlikely to identify the choice an incompetent person would have made if they were competent (84). It has been noted that predicting decisions about research participation may be even harder than those about medical treatment (83). The difficulties encountered when patients *themselves* are asked to predict now what decisions they would make at a specific point in the future are further addressed in the discussion of patient predictions and accuracy below.

2.3.2.3 *Known wishes*

In order to provide a substituted judgement for medical treatment or research decisions for a person who lacks capacity, proxies are required to follow the persons' prior direct expression of their preference (66), their 'known wishes'. This could be informally stated

during conversations with family and friends, or in the form of a formal written advance directive or decision, which will be discussed shortly. Establishing what the person would have decided may be extremely problematic, given the (probably unexpected) circumstances of their loss of capacity and the likelihood of one or more medical outcomes. Empirical studies have shown that patients rarely effectively discuss their treatment preferences with their proxies, even around high-profile decisions such as preferences for end-of-life care and organ donation (90). This is partly as a result of patients and their family members finding these conversations difficult (90). Additionally, the substituted judgement standard is even more difficult to apply in research because research decisions are usually more complex than decisions about treatment and, in practice, people rarely anticipate these choices with specificity sufficient to meet this standard (66). There may also be an expectation (a legal requirement in the USA) that the degree to which consent for research must be informed is greater than it is for treatment (66).

There is some evidence that conversations about their treatment preferences do not significantly increase proxy accuracy (91,92), or when they had previously discussed involvement in research protocols (93). Proxies' confidence in their ability to make a decision that would be consistent with the person's wishes, may be more important than actually knowing their wishes. An empirical study exploring the determinants of surrogates' confidence regarding an intensive care unit (ICU) patients' participation in genetic research found that prior discussion about research participation was not significantly associated with surrogates' confidence in their ability to provide substituted decisions (94). However, surrogates who were confident in their ability were more likely to accurately represent patients' wishes and agree to their participation (94). It has also been suggested that substituted judgement could reduce the burden of the decision felt by proxy decision-makers, by framing it as the person's choice rather than the proxy's (28). There is some empirical evidence that nearly all proxies experience some degree of burden in making decisions regarding research participation (36). It is not clear whether using substituted judgement, or an alternative decision-making standard, does reduce the burden felt by proxies in practice.

The fundamental area where known wishes and substituted judgement are most problematic is for individuals who have never experienced capacity for making complex decisions, such as those with profound intellectual or learning disabilities, or those who once had such capacity but have no close surviving relationships or evidence of their wishes and

hence have no representation by someone who knew the person when they did so. For these individuals, their views about participating in a research study can never be determined. A blanket requirement for decisions about research participation to be based on 'presumed will', regardless of the possibility of determining their known wishes, is not addressed in the ethical literature. The question has similarly been side-stepped by the courts considering medical treatment decisions, who have been accused of 'tenaciously clinging to the assumption that a failure to exercise the right of self-determination...is to discriminate against the incompetent individual' (29). Cases involving medical treatment for people who have a lifelong disability that impairs decision-making capacity, such as Saikewicz (86), have resulted in the courts making 'heroic but confused attempts' to determine something the person was incapable of ever conceptualising, in order to protect the right of self-determination that they were never capable of possessing (29).

2.3.2.4 *'Failure' of proxy predictions*

A number of commentators have questioned the congruency or accuracy with which proxies predict patients' treatment preferences (95,96). To understand the extent and causes of any incongruence, researchers must therefore compare surrogates' decisions to those that patients who currently have capacity believe they would make for their future, incapacitated selves (97). A number of empirical studies involving patient and proxy dyads have investigated the accuracy of proxies' predictions for agreement to hypothetical medical treatment scenarios. A systematic review of studies that provided empirical data on how accurately surrogates predict patients' treatment preferences found that, overall, surrogates predicted patients' preferences with 68% accuracy (98). The review also found that neither patient designation of surrogates nor prior discussion of patients' treatment preferences improved surrogates' predictive accuracy. Those acting as proxy family members designated to serve as surrogate decision makers failed to accurately consent to research for critically ill patients in one-third to nearly one-half of cases (99).

Studies involving hypothetical treatment or research scenarios have been widely cited as evidence that family members do not know the patient as well as they - and the patients themselves - think they do, and used to question the moral authority of substituted judgements themselves (26). The lack of predictive ability has led to the conclusions that surrogates' decisions using substituted judgement is an inadequate method of gaining consent (26), is no better than random chance (100), and may be seriously flawed (101).

Johansson et al (102) suggest that surrogate accuracy is not, in reality, one issue but several issues that differ in respect to their relative moral importance. However, these studies have limitations, most fundamentally that they are based on the assumption that surrogates and patients have similar decision-making patterns in hypothetical and actual treatment situations (97). There are also significant issues with the methodology used in such studies (103) which limits their influence when examining proxy decision-making. Methodological shortcomings include that participating proxies are typically those who accompany the patient to a clinic and are therefore selected through convenience rather than being a patient-designated proxy; the 'patient' may be a healthy volunteer, or may already be experiencing a neurodegenerative condition that may affect their decision/prediction ability; and assumes that a single unambiguous preference exists which the proxy can provide. The dichotomisation of participant responses of 'unsure' or 'don't know' being grouped together with positive predictions that the patient would agree to treatment/research, rather than used as an indication of uncertainty, may also be problematic (103). In Shalowitz et al's (98) systematic review of surrogates' predictions of treatment decisions, seven out of the nine studies included in the review used this dichotomisation. However, the greatest issue is that they are 'predictions' rather than decisions, which raises questions about whether they are of any value in terms of determining normative authority.

The empirical studies which match proxy predictions with what individuals say they would prefer in various future hypothetical scenarios simply do not show that surrogates have made inaccurate substituted judgements (67). A decision - as distinguished from a preference or a prediction - involves carefully identifying the factors that are under consideration in this instance, for this person, with respect to the person (and surrogate's) history and selecting the 'best' choice from the available options (104). Decisions about important issues require thoughtful reflection and nurturing. To suggest that the proxy's knowledge of the patient should enable them to have a fully formed, precisely focused decision tucked neatly away, and they would be able provide that decision on command via substituted judgement has been described as 'irrationality on stilts' (104).

Debating the failure of proxy predictions as a result of proxies inaccurately matching patients' prediction fails to take into account the fundamental reason for resorting to a substituted judgement - that the proxy is needed to decide for the person because the person themselves has become incompetent. What the person would have decided while healthy and competent and not in need of treatment or care is materially different in

circumstances where there is now a need for treatment, care, or research decisions to be made. In these empirical studies the patient themselves is required to imagine what that future incompetent self would be like, and what that fictitious future-self would choose for themselves in a hypothetical scenario. The accuracy of their own prediction cannot be measured, but is used as the 'true' or 'correct' outcome that the proxy's prediction must be matched against, the 'gold standard', even though it is known that people have difficulty with 'affective forecasting' – predicting their future emotional states and reactions (97). Proxies in such studies are faced with a monumental task. They would not only have to anticipate what being in such a state of incompetence would be like, but also imagine it from the point of view of the person they represent, who themselves would have to anticipate what such a future state would be like. Focussing on the accuracy of surrogates' decision-making in hypothetical scenarios when examining the normative conclusions of proxy decision-making studies may be misleading and may be best thought of as merely matching a guess (104).

2.3.2.5 *Stability of preferences*

Understanding the conditional nature of substituted judgement is an important feature in the debate about its validity. Brostrom et al (105) describe this fundamental problem of making assumptions when using substituted judgement - the undetermined decision conditions - as what degree of competence is the person imagined to have. What beliefs, preferences, values, emotions, intentions are relevant to the situation at hand? The lack of specific context mean that the proxy has little or no guidance when considering just how competent they should imagine the person to be, or how they should envision the person's hypothetical outlook, and the circumstances surrounding their decision-making (106). This leaves the proxy unsupported when selecting which decision conditions they think the person should have, whether they should be making a decision based on the person's last competent decision condition, favourable conditions when they were most likely to protect their own interests, or peak decision conditions when they were 'at the height of their powers' (106). They suggest that the most appropriate decision conditions may be those that are sufficiently recent, favourable and characteristic of the person, although problems with the underdetermined decision conditions of substituted judgement remain.

Another example of a problem associated with the standard interpretation of substituted judgement can be found in the moral psychology of decision-making, and in particular the

stability of individuals' preferences over time. A number of empirical studies have demonstrated that individuals' treatment preferences change over time (107,108). Dionne-Odom (80) describes how ethical standards and values that seem appropriate currently might appear inappropriate later, over time this change in preferences may be triggered by new information and/or affectivity (beliefs about how one will feel emotionally in the future). In proxy accuracy studies it is explicitly or implicitly assumed that the patients' predictions are true/correct. If the surrogate's prediction does not match, the surrogate's prediction is considered to be a failure (103). Overall surrogate accuracy is determined by the success rate of matching all predictions made in the test (103).

Decision-making is known to be a complex process of assessing and weighing both short-term and long-term costs and benefits of the various competing actions and is subject to the moderating effect of social context (109). The social environment may influence decisions, for example it may create a tense or relaxed atmosphere, which then influences the person's emotional state and thereby their decisions (110). Individuals may also alter their decisions depending on who is with them, or who they consider to be their 'reference-point' at the time of the decision (109). Studies that have compared patients' and proxies' choices regarding hypothetical research studies ignore crucial factors about decision-making in practice versus hypothetical scenarios. There are huge gaps between decision-making in real life situations, where influences of the social environment are extensive, and decision-making as measured in these studies, which is often done without any social influences. Individuals may be less affected by stressful conditions when accompanied by friends or family, which will reduce the effect of the stress on their decisions, while showing high levels of stress when deciding alone in a study interview, with resulting effects on decision-making (109).

This raises doubts about empirical studies exploring hypothetical preferences and attempting to match proxy and patient predictions. Johansson and Brostrom (67) argue that if changes of mind are common, what is the justification for singling out a patient's (or indeed proxy's) answer at a certain point in time as defining the 'correct' answer. The argument from changes of mind theory therefore undermines the assumption made in studies testing proxy accuracy for decisions about medical treatment that there is a straight forward way to assess surrogates' capacity to comply with the substituted judgement standard (67). This is likely to be also true for decisions made about research participation, raising questions about the use of the standard under its original interpretation.

2.3.2.6 *Poor decisions and systematic mistakes*

A practical difficulty may arise when proxies attempt to make a decision for a person whose tendency was to make systematic mistakes and poor decisions in certain settings (84). There is growing evidence that individuals make important systematic mistakes in decisions, such as those about medical treatment (111,112), which are likely to be replicated in decisions about research participation. Cognitive scientists have identified a wide range of biases and heuristics, which may give way to predictable biases and errors in judgement and decision-making (113). These include commission bias (a tendency toward action rather than inaction) and relative risk bias (a stronger inclination to act when presented with the relative risk than when presented in terms of the absolute risk) (113) which may be very relevant when making a decision about whether to participate in a research study. A proxy may be faced with replicating the person's decision, including that it would have been subject to bias, poor judgement, or systematic mistakes, when attempting to decide as the person themselves would have if competent.

Systematic mistakes also arise in recalling past experiences, as well as predicting how good or bad future ones would be (114). Other examples, such as those in dealing with probabilities that also lead to mistakes, are of great importance in medical treatment decision-making (114) and likely to be as important, if not more so, when considering participating in research that may involve the probability of being allocated to an intervention arm versus placebo, potential side-effects, or relative risk of benefits versus harm. An example may be where a person's decisions have consistently been systematically subject to order effects (or primacy/recency framing) bias when provided with choices, where information or choices presented at the beginning or end of a series is remembered and chosen more often than information presented in the middle of the series (113). When presented by their physician with possible options for aggressive treatment, conservative management, or participating in a clinical trial of a novel experimental treatment, they may well have chosen the latter merely because their bias led them to select the final option presented. An extraordinarily insightful proxy deciding on that person's behalf may have been aware of their framing bias, and when faithfully attempting to replicate their decision would intentionally select the last option presented. Some individuals may be aware that their behaviour is as a result of a cognitive bias, and later regret the choices they have made and express the desire to counter this bias in future. However, there would appear to be little value in continuing this pattern of biased decision-making, other than to appeal to the

preservation of autonomous decision-making as obliging the proxy decision-maker to enact the person's previously autonomous preferences.

Proxies themselves may also be subject to the effect of a range of biases and heuristics, which may result in biases and errors in their judgement and decision-making. This, among other factors, may contribute to the previously discussed difficulties in accurately predicting patients' decisions, as empirical studies have shown. Attempting to replicate a person's biases or heuristics, while attempting to eliminate the effect of the proxy's own biases, may be an impossible task.

2.3.3 Theoretical difficulties with substituted judgement

The justification for appealing to the substitute judgement standard is intended to continue to respect a person's autonomy, even after they have lost decision-making capacity (115).

2.3.3.1 *Informed consent and respect for autonomy*

There have been many accounts of autonomy offered, however, a basic framework of two key elements emerges – what Schwab (116) calls 'formal autonomy' and 'effective autonomy'. Formal autonomy refers to the conditions under which a person's desires, preferences, and decisions are thought to be their own, in order to be considered to be self-governing, or self-determining. Effective autonomy refers to the match between a person's autonomous desires, preferences, and decisions and their actual decisions, choices, and behaviours – or authenticity. These elements can be viewed as two components of autonomy (117), or as two separate types of autonomy (116). Most commentators agree that any meaningful analysis of autonomous action will integrate both concepts, so it is important to represent each (113). Brudney (118) helpfully illustrates this framework of dual components using Frank Sinatra's classic song – what is thought to be important is both that "I did it" (self-determination) and that it is "my way" (authenticity). Chan (77) adds a third component – self-sufficiency.

Autonomy has been described as a fundamental value in society (28), requiring a social nexus (119), that runs as deep in the common morality as any ethical principle (21). Autonomy encompasses self-rule without any controlling influences or limitations that prevent meaningful choice and, conversely, those who lack mental capacity and are incapable of deliberating or acting on the basis of their desires or plans have diminished autonomy (21).

In healthcare, respect for autonomy requires that a patient's treatment preference is respected (120). The adoption of an autonomous framework for medical decision-making, with a move away from a traditional paternalistic approach, is described by Torke et al as the most important change in medical ethics in the past 30 years (28). Informed consent is commonly viewed as key to respecting patients' autonomy in medical treatment and research (121). Adults lacking capacity who have diminished autonomy are unable to provide informed consent for research, and therefore must receive adequate protection that reflects their vulnerability (122). The principle of respect for autonomy requires respect for a competent person's preferences and decisions, but there is less agreement that it requires respect for preferences established earlier by a person who has since lost capacity (120).

Proxy decision-making on behalf of a person after they have lost the ability to make their own decisions is intended to continue the respect for the person's autonomy, even if they did not provide definitive guidance regarding their preferences (84). Childress and Beauchamp (21) maintain that substituted judgement is a weak standard of autonomy. Others suggest that respect for autonomy (or 'self-determination') is no longer relevant for those who have lost the ability to make decisions if they did not leave directives; that they are no longer self-determining is the very reason they require a proxy (118). Jongsma and van de Vathorst (123) argue that decisions made by proxies do not respect the autonomy of research participants who lack capacity as they do 'little justice to the preferences' of incapacitated participants. They consider proxies to be a 'poor means to extend the person's voice' in the decision-making process (123). As determining a person's exact decision in a previously unencountered scenario is challenging for many proxies, it is not clear how satisfying the person's purely hypothetical decisions is a way of respecting this right (105). Brudney (124) describes this attempt to preserve a person's autonomy as conveying a 'large rhetorical punch'. The problematic area of respect for autonomy forming the basis for proxy consent is revisited later in the thesis as part of the *Changing Ethical Norms* work (Chapter 9).

2.3.3.2 *Is precedent autonomy binding?*

If the principle of respect for autonomy requires us to respect a competent person's decisions, then it may also require us to respect such decisions made in advance. For those who clearly expressed their preferences prior to the loss of capacity, it has been suggested that the principle of respect for autonomy compels others to respect such preferences, even

if they can no longer express the preference for themselves (21). A person can exercise their autonomy not only through making decisions in the present, but also by making decisions that will influence what is to happen in the future (125). The anticipated or precedent autonomy standard, provocatively termed 'pure' autonomy by Childress and Beauchamp (21), applies exclusively to those who previously had capacity and expressed an autonomous preference relevant to the current situation. However, a number of commentators have raised questions about whether preferences made by a person when competent can still be attributed to the person when they have lost capacity and can no longer understand or revoke their decision. As Stonestreet (126)[84] asks, why should the values and priorities of a person who is (at least in some sense) no longer present govern the care of someone who is, when at least some of what made that person what they are/were has been eroded?

The criteria for 'satisfactory evidence' of a person's preferences has been widely disputed and, as Childress and Beauchamp (21) emphasise, even evidence in the form of an oral or written advance directive needs to be evaluated carefully to establish whether it constitutes an autonomous preference that is relevant to the decision in hand. Buchanan and Brock state that decisions that shaped and gave meaning to the life of the person who has lost capacity should be respected (29), to which Jongsma and van de Vathorst (123) add the proviso that only if the decision is not changed or renounced in the meantime. Dionne-Odom and Bakitas (80) point out that preferences do change over time, and that ethical standards and values that seem appropriate now might appear inappropriate later. Individuals' preferences may be altered at any given time, which may be triggered by new information and/or affectivity (beliefs about how one will feel emotionally in the future) (80). Those who no longer have capacity to make decisions have also lost the ability to understand and reaffirm prior expressed wishes. Jongsma and van de Vathorst (123) emphasise that not reaffirming preferences is not the same as changing or renouncing them and, in order to understand if previous preferences are still applicable, those acting as proxy should try to imagine what the person would prefer in the current situation if they were competent. This appears to invoke the substituted judgement standard, as discussed in more detail below.

However, others consider that the difference between autonomy and precedent autonomy is merely that precedent autonomy involves a longer passage of time, and that the moral authority of an agent's autonomous act is not altered by the mere passage of time (127). Jongsma and van de Vathorst (123) suggest that, as other decisions are reasoned according to this principle, such as those regarding marriage and mortgage arrangements, there is no

reason to presume that an autonomous decision concerning research participation should be treated differently. Davis (120) contends that a preference includes (and is not merely supported by) the *reasons* that the person had for that preference. If the reasons for that preference concern properties of the person which were then lost through the circumstances surrounding their incompetence (such as dementia), then the reason for them having that preference are gone – therefore those reasons are no longer valid (120).

This raises doubts about whether attempting to use the precedent autonomy standard, in reality, results in proxies using their own judgement about the person's preferences, rather than any extension of autonomy (128). Arguably, the proxy's interposition as arbiter of how and when previous preferences should be applied exerts an element of 'control or limitation' that may deny the person's own 'meaningful choice' that Childress and Beauchamp (21) assert is the very essence of autonomy. If doubts exist about the obligation to respect a person's autonomy, following their loss of capacity to be self-determining, this brings into question the justification for appealing to the substituted judgement standard as a means of continuing to honour that obligation.

2.3.3.3 *Representation*

Questions about whether a person can ever truly represent the decision-making process of another have been widely debated in the fields of philosophy and psychology, amongst others. Wrigley (26) summarises the two main theories in philosophy of mind that attempt to capture how we mentally represent others: Simulation Theory and Theory Theory. Using simulation to predict the mental processes of another person, which involves their memories, emotions, beliefs, desires, and experiences, can make simulating that person's decision-making impossible, no matter how well the person is known. The processes that allow people to reasonably determine the likes, dislikes and attitudes of another person in everyday situations, would be insufficient for medical treatment (or research) decisions as they involve such a wide and complex arrangement of values, emotions and attitudes (26). Simulation Theory, Wrigley (26) contends, is based on two assumptions: that using imagination to simulate being in a particular situation is the same mental process as when actually in that situation, and simulating the attitudes and wishes of another person and using reasoning would be similar enough to the person's mental processes to determine the answer. Wrigley (26) summarises Theory Theory as reliant on pre-established theory as to how people normally think and respond to situations (a folk psychology), however it is

extremely unlikely to capture the complexity of the thought processes involved in medical (treatment or research) decisions. Wrigley (26) argues that, if either theory is correct, this leads to the position that proxy consent on the basis of substituted judgement has such an uncertain basis that accurately determining another person's decision would be unachievable.

Construal level theory (CLT) proposes that individuals take into account hypothetical alternatives to reality by forming abstract mental 'construals' of psychologically distal objects, allowing them to make predictions about the future and imagine other people's reactions (as well as remember the past) (129). There are associations between temporal, spatial, and social distances, and hypotheticality, which affect each other, and are inferred from one another (130). Trope and Liberman (129) describe how spatial and temporal distances increase the impact of high-level information (such as theories, beliefs, and general trends) and decrease the impact of low-level information (such as specific situational and task characteristics) on predictions about the future. This has implications for proxy decision-making as they propose that values, because of their relatively abstract and decontextualized nature, can be more readily applied to, and guide decisions about, psychologically distant situations (129). CLT may also address the problems of proxy versus patient accuracy in empirical studies when presented with hypothetical future scenarios. Psychological distance is considered to be egocentric (129) and there are likely to be spatiotemporal differences between the patient and proxy's perspectives of self-versus other, which will affect their respective predictions and their confidence with the accuracy of those predictions.

Tunney and Zeigler (131) propose an alternative model of proxy decision-making that has two components, Perspective Taking and a simple Choice Rule. They suggest that decision-makers consider the choice from four perspectives: what they would do if they were in the other person's position (projection), what they believe the other person would choose to do (simulation), what they should do (benevolent), and what the best outcome is for themselves (egocentric). Their model suggests that proxies examine the relevant choices by simultaneously constructing all four perspectives, using their ability to detach from their own preference through their empathetic view (131). By capturing the impact of empathy, which they describe as a normative benchmark for the accuracy of a proxy decision-maker, they acknowledge that a proxy's ability is determined by their ability to engage in the perspective-taking component of empathy (132). However the Tunney and Zeigler (131) model centres on the concept that proxies simulate both their own preferences and their perceived

preferences of the other person when making decisions. This conflicts with the standard interpretation of substituted judgement that requires a decision based purely on what the person themselves would have decided, with no account taken of the proxy's own preferences.

The proposed theories attempt to represent the proxy decision-making process by taking into account the change in perspective from thinking for ourselves to another person, and how this affects the decisions that we make on behalf of other people. How these theories integrate with the standard interpretation of substituted judgement as a legal and ethical standard is unclear and is sadly beyond the scope of this thesis. The theories of decision-making and their relevance to how proxies make decisions are further discussed in Chapter 11.

2.3.3.4 Right-making characteristic or decision-making procedure?

Brostrom (106) suggests that there is an ambiguity in the concept of a decision-making standard, such as substituted judgement, which could be understood as a condition of adequacy, or a criterion of rightness. Accordingly, substituted judgement could be considered to be a condition that 'good decisions' ought to satisfy - an objective measure which determines when a decision is morally justified - or a tool for decision-makers that provides a way of thinking, a guide to the process of reaching a decision, which may involve reaching the 'right answer' through empathic understanding if necessary (67). Philips and Wendler (84) suggest that asking proxies to decide what the person would have decided may be a valuable heuristic of the appropriateness of a decision, rather than a decision-making standard in its own right. Johansson and Brostrom (67) propose that rather than asking proxies to 'guess' what the person would have decided and judge whether the standard has been satisfied, which is not particularly effective, it may be more helpful to instruct proxies to apply the substituted judgement principle - which will make the morally-right decision through its articulation. This, Johansson and Brostrom (67) suggest, is the distinction between 'right-making characteristics' and 'decision-making procedures' that has been well-established in moral philosophy and act-utilitarianism, as first discussed by Bales (133). More simply put, it is a measure versus a tool - the measure of a good decision but without any presumption that the principle should be used, or a tool (guide or rule) in the process of decision-making (106).

Using this distinction, it may not be true that the best chances of satisfying substituted judgement as an adequacy condition is to instruct proxies to try to apply it, and in fact it may have the opposite effect (106). Empirical evidence supports the view that instructing surrogates to identify *what the patient would have wanted* negatively impacts on their accuracy of predictions, which leads critics to conclude that substituted judgement is flawed as a measure of 'good decisions' (134). Lindemann and Lindemann Nelson (104) also question the assumption that a good proxy decision is one that merely reproduces the content of the person's choice, as in many cases, this counterfactual will have no clear content to reproduce. He suggests that what people value about making decisions is not only getting the outcome they choose, but also getting the outcome because they choose it. Lindemann and Lindemann Nelson (104) suggest that the shared bonds between a person and those close to them create a concept of shared agency, where what matters most is not so much what is decided as who does the deciding. The sharing of these bonds allow the proxy to express something of the person's own agency, which provides the proxy's moral authority as decision-maker. Johansson and Brostrom (104) suggest that what should be measured is not proxies' accuracy when being instructed to apply a literal interpretation of substituted judgement, but their accuracy in deciding as the patient would when provided with the best possible tools for making such decisions. What those tools are, and how they should be utilised, is a matter for further inquiry and debate, and is the overall focus of this research project.

2.3.4 Alternative interpretations of substituted judgement

Some commentators question the literal interpretation of the substituted judgement standard, or question if there is just one standard or many. Brostrom et al (105) suggest that there are various formulations of the substituted judgement standard that concern not just what the person would have *decided*, but sometimes what they would have *wanted*, *valued* or *consented* to. Johansson et al (102) suggest that the use of the everyday phrase 'what the person would have decided' results in too literal an interpretation and attempt at precision than is warranted. This, they argue, results in unhelpful philosophical scrutiny and a focus on the technical issues of the decision, which misses the true intentions behind the use of the substituted judgement standard.

They suggest rejecting what the person would have decided under certain counterfactual conditions (25), making a decision instead that is the best fit with the person's life and

character. They propose a more general vision of what this approach to surrogate decision-making is about – that of proxies trying to do good for those who are unable to decide for themselves – which provides the moral justification for its use (102). Johansson et al (102) propose that greater sensitivity should be shown towards the general moral context of proxy decision-making. They suggest it is not so much a complex task of predicting a decision using a host of factors that typically affected the choices they made, but rather identifying a limited number of core values and desires that would be most practical in the current situation (67). Childress and Beauchamp (21) suggest that this requires that the proxy should have a deep familiarity with the person, so that the judgement reflects the person’s own views and values. There is empirical evidence that patients do not want a strictly substituted judgement made for them, but want family members to take into account their welfare and current interests (28).

Many commentators have argued that there is a need for a new interpretation of substituted judgement, one with sufficient nuance and robustness (60,80,84). Dresser (88) suggests that varied interpretations of substituted judgement will not affect real-life decisions, where clinicians and proxies will attempt to respect what was important to the person whilst protecting them from pain or other suffering. Buchanan and Brock (29) further argue that a new systematic ethical framework or theory of proxy decision-making is needed. Although not specific to decisions about research, a number of alternative interpretations of substituted judgement, or alternative models of proxy decision-making, have been proposed in recent years, primarily by contemporary US bioethicists. These will now be considered in turn.

2.3.4.1 Endorsed Life

Philips and Wendler (115) attempted to clarify the substituted judgement standard through their alternative (re)interpretation of the standard using an endorsed life approach, which bases decisions on the type of life the person endorsed for themselves. They argue that substituted judgement is best understood as not attempting to replicate the person’s decision, but respecting the person’s values and allowing them to continue, as closely as possible (84). Philips and Wendler describe this as decision-making based on which option best promotes the life the patient valued for themselves, which includes the influence it would have on the lives of others – such as the proxy themselves – even if they did not actually live that life (115). They argue that the life most people value is broader than merely

the experiences they encounter but includes the impact on the lives of those around them, therefore the interests of loved ones should also be taken into account to the extent that the person themselves would have done so. They refer to decisions made in the context of clinical practice, but it is useful to explore this standard in the context of decisions about research participation.

The strengths of the endorsed life approach, they argue, is that proxies are likely to know the sort of life the person valued for themselves, even if the person had never indicated treatment or other preferences. Thus, removing the guesswork and the appeal to counterfactuals. They maintain that this approach respects autonomy by allowing the life course the person endorsed while they are competent to determine the course of their life after they have lost capacity, whilst avoiding the ‘fiction’ that the person is able to make decisions (115). They also suggest that this avoids persistent cognitive bias and systematic mistakes, by not simply making the decision they would make for themselves but considers their attitudes towards those preferences and the resulting decisions. They also propose that the burden of proxy decision-making may be reduced by recognising that there is not always one correct choice, but more than one option may be equally consistent with the life they valued (115). The endorsed life approach, they argue, has benefits to both the individual through continuing their life to be realised, and other members of society through the reassurance that their care would be based on their choices and values should they lose capacity.

Philips and Wendler (115) recognise that there are questions about *which* endorsed life the proxy should be using, as individuals change the life they endorse for themselves over time and endorse different aspects of life at different times. They propose making decisions based on the life they last endorsed for themselves when competent, although it would not hold in the unlikely event of drastic changes to a still competent person – such that they become a different person – due to the impairing condition. Importantly, values that a person abandoned when competent would not be taken into account by their proxy once they have lost capacity.

A number of questions arise about whether endorsed life is an adequate approach to decision-making. The most problematic is whether a person’s ideals about the way they would like to live, rather than how they actually lived should be given more normative weight (88). Although Philips and Wendler (84) argue that if the difference between the life the

person valued and the life they actually lived is merely that of evidence accessibility, then that is not adequate reason for giving the latter ethical priority. Dresser (88) argues that the way a person lived their life could be viewed as a more genuine indication of the life they valued. Philips and Wendler state that people typically make decisions for themselves based on the life that they value for themselves, but there is no evidence that this is the case for medical treatment decisions or decisions about research participation. Sulmasy and Sulmasy (135) criticise Philips and Wendler (115) for failing to make use of the empirical evidence that people do not want decisions to be guided purely by their own (previously stated) preferences, preferring equal weight to be given to their proxy's judgement. Dresser (88) argues that most people make decisions that reflect their actual values and preferences, not necessarily the laudable values they might aspire to, and there is no reason to suppose that proxies should depart from this.

Philips and Wendler (115) suggest that the endorsed life approach reduces the potential abuses by individuals and institutions when pursuing treatment options to achieve their own ends, regardless of the impact or the person's interests or values. Historically, research has experienced similar abuses. However, as Dresser (88) suggests, using a person's 'aspirational' life as a standard for decision-making is likely to be even more susceptible to distortion or misinterpretation than their actual life. It is possible that proxies will feel a *greater* burden if there is no one 'right' choice, but rather a range of equally correct options. The proxy's decision-making choice is perhaps made more difficult when each option will have a different outcome, even if the choice is between equivalent options.

2.3.4.2 *Authentic life*

Brudney's (118) alternative position is that the best way to use the substituted judgement standard is to continue the life the person actually lived in order to promote the authenticity of their life. An authentic choice is where the decision fits with the person's basic beliefs and values (124). For situations where the person has made an advance directive that clearly lays out what their choice would be, the proxy would do as indicated by the directive. When there is no sufficiently clear statement of the person's wishes, Brudney (118) poses the question the proxy should ask themselves as "What would the patient choose to do if he could be made aware of the choice in front of him?" In answering this, the proxy relies on their knowledge of the person's beliefs and values to figure out what their choice would be. He differentiates these as, on the one hand an *actual* choice made where a clear directive exists,

and if there is no sufficiently clear expression of their actual choice, the proxy should try to determine their *hypothetical* choice — what they would choose if competent (118). He is clear that this is merely a hypothetical choice and is quite distinct from the exercise of the person's will, which is not under consideration. He argues that what underpins the moral authority of this hypothetical choice is, not just best interests, but both elements of autonomy, in particular the value of capacity for individuality, of being a particular self, which he calls 'authenticity' (118).

Brudney (124) refers to the two concepts of autonomy previously described, as 'agency' (or 'self-determination' (136) or 'liberty' (115) and 'authenticity'. Where agency is the capacity to make a choice, to decide on the basis of reasons (including bad reasons), and authenticity is the capacity to live a distinctive life, to construct that life in accordance with distinctive beliefs and values. He differentiates between these by suggesting that agency can be fully exercised at the point that each choice is made, whereas authenticity, by contrast, is exercised over time, sometimes over a lifetime. Agency is a momentary achievement and authenticity is sustained. Authenticity is not just about making a choice, or even choices, but making a life that fits. Therefore, an authentic choice is one that makes sense within the framework of the beliefs and values that the person affirms (136), but this may be more challenging when making a decision for another.

Brudney (118) describes the ambiguity of the proxy's role as whether they are required to go over their knowledge of the person in an attempt to recall instances when the person expressed directly or indirectly what they *want done* in the current circumstances, or go over their knowledge to work out from their understanding of the person's beliefs and values, what they *would want done*. He alludes to this decision-making being a path from where the first point is a clear expression of the person's wishes, and if there is no sufficiently clear prior exercise of the person's will the proxy moves along the path to the second step (118). This path may, in practice, diverge from the straight and narrow where the person's wishes are too unclear. While Phillips and Wendler (84) point out that an authentic life may not necessarily be a 'good life', Brudney (124) does not disagree — but suggests that authenticity is just one element of a good life, others being having friends, satisfying work, and so on. As a good life may have so many elements in any given context, authenticity may become overshadowed by these other elements (124).

Brudney (118) considers that an authentic life may not carry much normative weight if the authenticity involves false beliefs, poor reasoning etc., but may be one choice amongst options such as best interests and the interests of others, such as the person's family and friends. This may not be helpful in determining which amongst options to choose. Brudney (124) rightly argues that establishing the proper moral authority for proxy decision-making is only the first question, the second – how far actually applying it in practice compromises that authority – is where the challenge really lies.

2.3.4.3 *Substituted interests*

Sulmasy and Snyder (82) propose an alternative approach to proxy decision-making which they claim allows for person-centred and individualised decisions, and which combines principles of decision-making with empirical evidence about how individuals make decisions and what holds value to them. Their model emphasises the authentic (true to who the person really is) values and interests of the person, rather than 'guessing' what the person would have decided, or focussing on autonomy that the person can no longer exercise (82). They term this a substituted interests model, that allows for a 'best judgement' to be made about which decision advances the good of the person as a unique individual. Sulmasy and Snyder (82) propose that this contextualised integrated model of substituted judgement and best interests asks the proxy to apply the person's authentic values and known wishes through describing the person's loves, beliefs, and fundamental moral commitments, even if they don't know their precise wishes about the matter in question. This, they maintain, is what the proxy is substituting for the person, and reflects how patients want decisions made for them (137) and respects the complex ways in which proxies actually make decisions.

However, the clinician has a considerable role in decision-making using a substituted judgement model. The clinician presents the clinical situation, the proxy's role is to articulate to the clinician the person's values and interests, and the decision-making process is shared. Sulmasy and Sulmasy (135) maintain that their inclusive model embraces respect for an endorsed life, as well as respecting those who would defer decision-making to their family. Sulmasy and Snyder (82) highlight the burden and stresses of decision-making felt by proxies and argue that, while they retain the primary and ultimate decision-making authority, the clinician's recommendations about the best course of action can help to shoulder the burden.

The substituted judgement model has some advantages over both the authentic and endorsed life approaches, as it incorporates wider consideration than the authentic life the person lived or the values and beliefs they endorsed for themselves. It allows a balance to be drawn between the person's life and values, known preferences, and current interests. However, the claims made about the clinician's role in sharing the decision-making and relieving burden through taking (some) responsibility raises accusations of paternalism. Sulmasy and Snyder (82) themselves acknowledge that this objection may be raised, and helpfully provide sample conversation pointers to guide clinicians through discussions in a stepwise fashion. However, they do not present any guidance about how any differences between clinician's recommendations and proxy's preferred options should be resolved, particularly where there are conflicts between the person's preferences and what would be in their interests now. There is an acknowledged lack of guidance on how clinicians should consider the current best interests of a person who lacks capacity and how to weigh them against their previously stated preferences in a particular clinical situation (138). It is also not certain that a person's interests are determined by what they prefer, independent of the extent that the person values or endorses those preferences (115). Given the uncertainty, if both clinician and proxy jointly share responsibility for the decision-making process, how can a single 'best judgement' be reached?

The role of the clinician in shared decision-making may be particularly unhelpful in decisions about research participation, principally where the clinician is also the investigator. This conflict of interest could make their recommendation of a course of action, and subsequent involvement in the best judgement decision-making process, inappropriate. Although the general approach - a contextualised balance of the person's values and preferences as a unique individual, taking into account their current interests, and their relationships with those around them - is applicable to research decisions as well as decisions about medical treatment and care.

2.3.4.4 Actuarial or preference prediction approach

For decisions regarding medical treatment, alternative models of decision-making have been proposed which attempt to predict which treatment option a given person would most likely prefer if they were unable to decide for themselves, based on their characteristics and information about which treatment preferences are correlated with these characteristics (139,140). This approach employs a statistical prediction rule that would apply the decision

of a majority of similar patients, also known as an actuarial model (141). This approach would be used in circumstances where a person has lost capacity and they did not clearly convey their treatment preferences, either in conversation or in a written advance directive (140). The prediction would be informed by the results of empirical research correlating individual characteristics with treatment preferences in different situations involving those without capacity, and incorporated into the shared decision-making process (140). As it is impossible to know what the person would have wanted in the event that they lose capacity, Rid and Wendler (140) suggest that the 'last competent' preferences the person provided is the best estimate for which treatments they would want in this situation. The proponents of this model argue that this is a pragmatic approach to a problem that cannot be 'solved' as there is currently no diagnostic method for identifying the actual treatment preferences of most people who lack capacity (140). They argue that empirical evidence suggests that the treatment preferences of the *average* person predicts patients' preferred treatment option just as accurately as surrogates (98,139,142).

The normative grounds for this approach are based on the assumption that a persons' preferences and values last endorsed prior to losing capacity should guide how they are treated because they are the best estimate of their wishes once capacity has been lost (140). However, as the authors acknowledge, there is no evidence that this is the case, and between the last competent preferences and the requirement for a decision to be made, the person has materially changed as the events have now led to the person losing decision-making abilities. They present no argument as to why treatment preferences for still competent individuals are necessarily applicable or valid for those who do not have capacity, and hence are a different population in terms of their current and future situation. As previously discussed, the premise that a person's prediction about what they would decide if they lost capacity should be treated as the 'gold standard', is not applicable to generalisations about a group of individuals who share the same characteristics such as such as age, gender, and education.

It also relies upon the person making their 'last competent' preference known about each and every situation that may require a decision to be made, with enough specificity and context to allow this preference to be applicable and valid to the situation in hand. With the exception of conditions such as dementia, loss of capacity is unlikely to be predicted in most cases. The authors suggest that the person's preference for the use of a predictor tool could be incorporated into an advance directive (140). However, if an advance directive is being

completed, this may be a more appropriate (and authoritative) means of communicating their *actual* preferences for situations likely to arise, and any instructions for leeway given to their proxy, rather than directing in advance that the preferences of those who *merely share the person's characteristics* should be followed in the event of loss of capacity. The authors also do not make clear why there is reason to believe that a person is more similar to those who share their characteristics, than their prior self, even if that prior self did not convey their preferences.

Brock (114) raises a number of questions about the use of an actuarial model in proxy decision-making and its attempt to improve decision-making by making more accurate decisions. In his view, although the approach is likely to replicate the systematic mistakes and biases that people are prone to making, such as predicting outcomes and evaluating probabilities, rather than correcting them. More importantly, he highlights that the reasons people choose close family members to act as their proxy is not solely based on their ability to predict their wishes, although this is a common reason (114). The fundamental basis for their decision-making authority is that families are where strong feelings of love and responsibility towards one another develop, which brings obligations and responsibilities to help and care for each other, and with these obligations comes some discretion about how these are fulfilled. This will not always be through a strict substituted judgement, which disregards any impact on the family members, but instead will require careful consideration between all those involved. In fact there is empirical evidence that suggests that individuals, especially older people (143) and those towards the end-of-life (144), are more concerned about *who* will make decisions for them than with *what* is decided in a particular situation.

Frey et al (141) examined members of the public's preferences about alternative approaches to proxy decision-making, comparing patient designated proxy to approaches such as a decision made collectively by the person's family through consensus, or through aggregation of the family members' individual votes using a majority rule, or use of a statistical prediction rule. Their study found that satisfaction was highest with a patient-designated proxy, followed by shared proxy decision-making approaches with least satisfaction with a statistical prediction rule. This may suggest that there are generally low levels of support for such a model, although this may have been affected by how the model and its use was framed by the investigators – whether as a stand-alone model or incorporated into shared decision-making as Rid and Wendler propose (145). Wendler et al (146) found that the majority of participants in their study endorsed the possibility of incorporating a preference

prediction into the process of shared decision-making, based on its potential to increase the proxies' predictive accuracy and/or reduce proxy distress. Part of their claim that it will be acceptable, is that they anticipate it will reduce the burden for proxies of knowing what the *person themselves* would have wanted, but it is not clear that the proxy knowing what *other similar people* would want would in fact reduce the burden or stress experienced by proxies (145). A preference prediction model lacks the richness and detail in the ways people know each other and act as proxy for one another. This is also why proxy decision-making is not simply a matter of reproducing content, people value not only getting the outcome they choose, but also getting the outcome because they choose it (104).

Whilst Frey et al's (141) alternative approaches, and Rid and Wendler's (140) patient preference indicator model, are intended for medical treatment decisions, similar arguments could be used for decisions about research participation or even more so, as both are highly contextualised decisions.

2.4 Discussion

2.4.1 Need for a different approach

The literature has given a strong indication that proxy decision-making for decisions about medical research are complex, highly contextualised decisions in practice that clearly depart from the rigid sequential bioethical hierarchy previously outlined. The standard interpretation of substituted judgement, and its attempt to extend individual autonomy beyond the loss of capacity, does not take account of the intricacy of individualistic decision-making and its inherent instability and biases. It has been suggested that substituted judgement is not an appropriate standard for decision-making where there is no clear expression of what the person would have wanted, or when proxies have to make decisions for adults who never had capacity (60). It has been noted that this standard is rarely used in proxy decisions about the participation of people with intellectual disability in research due to the problems identifying what their preferences or wishes might be (147).

For medical research, the primary objective is to generate new knowledge to improve future care, the intention is not to benefit those individuals taking part – although they may well derive some benefits – and so a careful assessment of the risks and burdens of participating

is required. For adults who do not have decision-making capacity, the legal framework in England and Wales requires decisions about research participation to be based on what the person themselves would have wanted, if they had capacity. Decisions about research participation are even more complex than decisions about care or treatment as the aims, risks and benefits are unique to each situation, and are less likely to have been the subject of prior discussions between potential participants and those acting as their proxies. Decisions about research are not based on whether it would be in the person's best interests to participate, the dominant standard for treatment and care decisions, as best interests is considered an ethically weak basis for enrolling those without capacity into research which is not intended (or likely) to benefit them. The problems with both substituted judgement and best interests standards when there is no clear expression of the person's wishes, has led to calls for an alternative interpretation or even a third standard (60).

It has been noted that currently there is no adequate theory of decision-making for those lacking capacity, with discrepancies between assumptions and reality. As the legal and ethical frameworks should be (at a minimum) compatible with, and supported by, a credible ethical theory, there is a need for a systematic ethical framework (29). Empirical research to date has focussed on how accurately proxies mirror or reproduce the judgements of those who lack capacity, Dionne-Odom (80) suggests that alternatively the focus should be on developing conceptual and theoretical models that identify key variables, and their relationships, in decision-making in practice. This needs to be developed alongside an understanding that the moral authority to make proxy decisions is bound up with the way in which the theoretical basis underpinning the decision-making is characterised (25). This combination of ethical and decision theory is supported by Sussman's (148) work on decisions made about palliative care, which proposes that the guidance offered by ethical principles can be enriched through the exploration of narrative data about the person's life, enthusiasm and relationships. In addition to alternative interpretations of the substituted judgement model, other alternative approaches proposed have included the 'reasonable treatment standard' (60), or an algorithm-based approach which may address the issue of 'surrogateless' individuals (149). Alternative approaches generated from this review of the literature will be discussed further below.

2.4.2 Thoughts about an alternative approach

Given the theoretical and practical problems associated with the standard interpretation of substituted judgement, and proposed alternative interpretations and models, a range of potential approaches have been identified through reviewing the literature. These may be seen as either becoming components of a structured multi-factorial process of proxy decision-making for research or, if merited, may be further developed and refined in their own right to form a new interpretation or model.

2.4.2.1 What can be 'saved' from the legal origins of substituted judgement?

Returning to the original legal conception of substituted judgement may provide useful 'ingredients' that an alternative approach would need to encompass. The early probate court rulings were based on the decision that would have been made by the 'sort of person' rather than attempting to determine that particular individual's wishes (150). This early position pre-dates the 'legal fiction' that the decision is 'what the incompetent person would have decided'. This is a similar concept to the 'reasonable person' standard that permeates English law (e.g. the 'man on the Clapham omnibus' (151)) and features heavily in medical jurisprudence – particularly in questions about informed consent for treatment. The 'reasonable person' standard has been described as 'independent of the idiosyncrasies of the particular person whose conduct is in question'. The reasonable man is presumed to be free both from over apprehension and from over-confidence.' (152). Although what constitutes a 'reasonable' person has been widely debated, and has evolved over time (see *Montgomery v Lanarkshire Health Board* (153)), retaining the original concept – that where that particular person's wishes cannot be determined we can consider what a person comparable to them might decide – may be helpful, particularly for deciding for those who have never had capacity. Although the reasonable person is free from the biases and idiosyncrasies that the person in question may in fact have, it may be a starting point to test whether a reasonable person would take part in the research study under consideration, before considering whether this particular person should take part. This may provide an objective test, which for those who have previously had capacity and whose wishes and values are known to some degree, could be followed by subjective values in order to inform a decision. On a practical note, it is unlikely that a study that only the unreasonable would participate in would survive contemporary research governance and ethical approval process.

Another 'ingredient' that may be worth retaining is the element of retaining the person in question's basic interests when making a decision on their behalf. The lunacy courts were deciding about the incompetent person's surplus income and ensured that sufficient funds remained to provide for the person's own needs, thereby limiting the detrimental impact on the person. The justification for this limitation is the vulnerability of the person lacking capacity and the speculative nature of the decision (29). This concept is echoed in ethical guidelines covering medical research which prioritises the welfare of the person participating in research over the interests of research institutions, scientific progress, and society more generally. The Declaration of Helsinki states that 'considerations related to the well-being of the human subject should take precedence over the interests of science and society' (64) (clause 5). The ethical position is reinforced in legal instruments, such as that the rights, safety, and well-being of participants are the most important considerations and shall 'outweigh' (20) or 'prevail over' (22) those of science and society. Unlike the principle of 'best interests' enshrined in the MCA which requires a determination or weighing of 'best' amongst all the various factors or interests to be considered (although it lays down no hierarchy) (20) this approach merely considers as a starting point whether the proposed study would be detrimental to the person's fundamental interests. These interests may be thought of in the broadest terms as encompassing their experiential interests, as well as medical interests. On a similar practical note to that above, it is unlikely that a study that would be to the detriment of a person's medical interests would be proposed by their healthcare team, and a study likely to be to the detriment of a person's fundamental interests would survive contemporary research governance and ethical approval processes, which would also require that the research question can only be addressed if people lacking capacity are included.

2.4.2.2 What about a human rights approach?

An alternative approach for proxy decision-making may stem from the UN Convention on the Rights of Persons with Disabilities (CRPD) which formally recognises the vulnerability of people with disability and, together with its Optional Protocol, has been ratified by the UK (154). Although the CRPD does not address medical research specifically, it does have much to contribute to the direction that research involving people with disabilities should take in line with a human rights approach (155). Unlike the MCA, the CRPD does not feature best interests which it claims are not based on the person's will and preferences, and instead urges that best interests approaches as part of substitute decision-making regimes should

be abolished and replaced with supported decision-making which respects the person's autonomy, will and preferences (156). The CRPD General Comment states that the 'best interpretation of will and preferences must replace the 'best interests' determinations... to ensure that persons with disabilities enjoy the right to legal capacity on an equal basis with others' (156)(para.21). Supported decision-making can be intended for those with capacity to remain the primary decision-maker, as well as other forms which includes advance directives, enduring powers of attorney, health care proxies, and nominated representatives (157). Supported decision-making is also closely aligned to the shift seen in areas such as maximising independent decision-making for those with disabilities or conditions such as dementia making employment or living arrangements, as well as the shift in clinician's approaches to informed consent following Montgomery (153).

The CRPD version of supported decision-making specifically applies to those factually incapable of making valid decisions through the requirement for the 'will and preferences paradigm' to replace best interests 'where, after significant efforts have been made, it is not practicable to determine the will and preference of an individual' (156). Ruck Keene and Ward (158) compared the CRPD with the provisions of the MCA in England and Wales and the Adults with Incapacity (Scotland) Act 2000 (AWI). They noted that when the AWI was drafted the paternalistic best interests approach was rejected as too vague on its own, needing supplementation by further factors to be taken into account, and not sufficiently taking into account the views, wishes and feeling of the person when competent (158). Ward suggested the term 'constructing decisions' for the processes of decision-making under AWI, which requires a best interpretation which respects any competent decisions (158).

This approach to constructed or interpreted decisions, rather than substituted judgement, may be useful in terms of decision-making for research. The MCA provisions covering decisions other than research expressly require decision-makers to take into account the person's past and present wishes and feelings, his beliefs and values, and any other factors that the person would be likely to consider, although the determinative standard is that it must be in the person's best interests [section 4 MCA]. The importance of considering the person's own wishes has been widely debated, particularly with the rise of person-centred care, and there have been calls for the person's values and wishes to have equal weighting with best interests (159). A recent review of the MCA by the Law Commission, although focussing on deprivation of liberty safeguards, recommended that amendments to the Act were required which would also aim to give greater priority to the person's wishes and

feelings when a best interests decision is being made (160). It has also been suggested that there is not much of a separation between substituted judgement and best interests and that, despite the labels, they might conceptually be closer than might be first thought (159). Coggon (159) hypothesises that the person-centered decision-making standard for people who have lost capacity could as comfortably be labelled best interests as substituted judgement, and cautions against the distraction of a label.

This growing move towards a 'will and preferences' paradigm in other areas of proxy decision-making, and the focus on the provision of person-centred care that puts the person's own views and wishes (both current and past) at the heart of decisions about care and treatment, may support the inclusion of the person's past and present wishes, feelings, beliefs and values, in the proxy decision about research, together with any other factors that the person would be likely to consider. This constructed decision may have more solid foundations where the proxy has an enduring, close relationship with the person in question and is confident in their knowledge of that person's values and beliefs about factors relevant to the decision. Although this approach may still allow consideration of the past and present wishes of a person who has never had capacity – as those close to the person will be aware of their likely response to research methods or procedures that participation would require. This construction might draw on knowledge about the life the person endorsed for themselves (115) as well as the authentic life they actually lived (118), as truly knowing the person would provide the proxy with the knowledge about aspects of their life or character they aspired to but did not achieve. Knowing the person and their flaws, and why it matters, is more relevant than identifying an example of a similar decision and attempting to replicate it in the current situation. Constructing this decision, through the proxy's best interpretation of what they know about the person, is likely to be challenging, but keeping these elements at the core will arguably provide a more accurate version of 'what the person would have decided, if they had capacity' than a hypothetical construction based on counterfactuals, or where substituted judgement is used as a measure of accurately matching a guess – where even the person would not have been able to forecast their prediction.

2.4.2.3 A move away from an individualistic conception of autonomy

There are grounds for considering that an approach that moves away from attempting to (re)create the person's substituted judgement may have a reasonable ethical basis. Critics have long argued that an individualistic conception of autonomy fails to recognise that

humans are not fully independent individuals and does not fully represent the scope of human interests and agency, or the relational nature of our lives (161) particularly once capacity is lost. Dewing (162) notes that current informed consent practices fail to include the person who lacks capacity (in this case as a result of dementia) in the process other than through an extension of the traditional competency-based informed consent method. She argues that continued adherence to the traditional universal system of ethics grounded in responsibilities and rights is not consistent with person-centred research which values personhood, and therefore amounts to 'exclusionary ethics'.

Dove et al (161) describes the theoretical challenges associated with a more relational form of autonomy, but argues that relational autonomy based on an ethic of care and trust in consent decisions can lead to the adoption of a shared decision-making model involving the patient, their family and healthcare professionals. He supports the notion of the socially situated person, where relational autonomy promotes decision-making guided by an ethic of care and moral responsibility (161). Although referring explicitly to people with decision-making capacity, he argues that a person's own consent can be augmented by facilitating and encouraging the relational aspects of the decision-making. This may give scope for keeping the person at the centre of the decision but, as mental capacity diminishes, then allows others to share the decision-making and eventually carry the burden for ensuring the person's voice is heard once they are no longer able to express their wishes. This could be operationalised through Holt's (163) proposal for the graduated consent process being tailored to the level of risk involved, where people with reduced capacity might still be able to express some preference and thereby exercise a degree of autonomy, particularly for low risk studies. Norman et al (164) argues for inclusivity in consent and proposes the cyclical consent model where getting to know the person, their verbal and non-verbal communication methods, and building an understanding of them, allows the person to be involved in the process and be supported to provide their own consent or agreement where possible. These concepts are aligned with the supported decision-making requirements enshrined in the CRPD.

Ho (165) suggests that the feminist notion of relational identity can help understand the moral significance of family involvement and interests, pointing out that familial care relationships are not generally based on temporary contracts but on empathy and beneficence between family members. This reciprocity means that family members care about the person's interests and well-being, such that their choices would probably match

the person's overall goals, meaning that family involvement can be compatible with or even enhance the person's autonomy (165). This 'matching the person's overall goal' may be a more meaningful interpretation of using substituted judgement as a tool, rather than an aim as encouraged by the use of counterfactuals and attempts to replicate a (non-existent) decision. Parallels can be drawn with Gilligan's (166) seminal work that led to the emergence of an 'ethic of care', which demonstrated the difference between approaching a problem through 'logic and law' (as seen in the standard interpretation of substituted judgement) compared with 'through communication in relationships' which a more nuanced approach would encourage.

2.5 Summary

Decision-making about research participation on behalf of another person is highly complex and contextualised, and current notions of substituted judgement based on individualistic autonomy and competency-based consent processes fail to reflect the intricacies of proxy decision-making in practice, or the true objective of the proxy role. The purpose of entrusting a proxy with making decisions on an individual's behalf is that the proxy understands the narrative of the person's life and their relationships, and how their values and wishes are shaped against the trajectory of that life and those around them. What is emerging is a move away from notions of autonomy based on presumed will that have no evidence-base for either the 'accuracy' of such decisions, nor any societal support, and therefore lack sufficient moral authority.

A new approach or re-interpretation may, provided there are sufficient safeguards in place to ensure that the person's interests are not harmed, focus on a person-centred approach that takes account of the context of the decision to construct a decision based on the 'building blocks' of the person's past, present, and future life. This may include elements of what is known about the person's life (both the life they lived and the life they valued), known values and wishes including any advanced decisions or directives, and their relationships with those around them and their interests. In addition, a focus on communication, supporting the person to understand and express and contribute their own view as much as possible, and to take into account their current preferences. This would signal a move from exclusionary ethics to a position of inclusion, which may be more in line

with human rights approaches to access to healthcare and involvement in decision-making. For those who have never had capacity, a greater emphasis could be placed on establishing current preferences, taking into account any negative or positive impacts from research participation. A risk proportionate approach could be adopted, rather than a fixed threshold of absolute capacity to consent, so that research involving lower risks would require graduated levels of agreement from the person, appropriate to the various aspects of the study. Independent advice about how involvement might affect the interests of the person could be sought where necessary in order to support the proxy. The overarching principle would be for those involved with the person to balance the weighting of the various elements, using ‘what the person would have wanted’ as a tool where possible, in order to reach a consensus about research participation that can be said to be the best interpretation of the person’s wishes.

These may be considered to be the seeds of a new approach – one that will require much careful consideration and refinement, but which envisages the proxy-patient relationship(s) being both the key that allows us to make decisions on behalf of another, and the tool to provide an answer.

2.6 Learning points

Normative accounts of substituted judgement based on an individualistic account of autonomy and competency-based consent processes are presented in the literature. However, important theoretical and practical problems with these accounts have been identified.

Decision-making about research participation on behalf of another person is highly complex and contextualised, and the existing normative accounts fail to reflect the intricacies of proxy decision-making in practice, or the true objective of the proxy role.

A number of proposed alternative interpretations and approaches have been identified through reviewing the literature. These include alternative interpretations of substituted judgement that attempt to better represent individuals’ wishes through basing decisions on an endorsed or authentic life or considering substituted interests instead. Alternative models

of decision-making have been proposed which attempt to more accurately predict preferences using actuarial approaches to decision-making.

Elements of a new approach that move away from an individualistic account of autonomy to one that is grounded in relationships, is attentive to care, and which values personhood, are proposed.

Chapter 3 Ethical issues in proxy decision-making for research involving adults lacking capacity – a systematic review of empirical studies

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3.1 Introduction

Proxy decision-making can be seen as comprising two main areas of ethical concern: the designation of the proxy who represents the person and why they are selected, and the nature of the decision-making itself. The ethical practice of proxy decision-making is an important issue, with substantial implications for the treatment and welfare of such individuals (25). However, little is known about the ethical basis on which proxies act as decision makers, or what factors are relevant in proxy decisions in practice, and there is a dearth of information or support available. Exploration and understanding of the ethical factors involved in these decisions ensures ethical and informed decisions are made by proxies which enables adults lacking capacity to appropriately participate in research. This chapter reports a systematic review of existing empirical research exploring the ethical issues of proxy decision-making for research.

Systematic reviews are reviews of existing research which use explicit, accountable, rigorous research methods that can inform us about *what* is known, *how* it is known, and what is *not known* about a chosen topic (168). The use of systematic reviews to address issues in medical ethics is relatively methodologically novel (169). Previous reviews have covered diverse topics such as the ethical issues in consent to clinical trials with pre-term or sick neonates (170), the use of concealed medications (171), and the care of people with dementia (172). Although the practice of conducting systematic reviews in bioethics has been widely

debated, it has been suggested that they are a necessary development in the discipline (173). McDougall outlines three main types of systematic review in bioethics: of empirical bioethics, of normative bioethics, and a review of reasons (173). The primary aim of this empirical bioethics review was to explore the ethical issues in proxy decision-making for research participation by adults lacking capacity, and the factors associated with the operationalising of proxy decision-making in practice.

This mixed methods review synthesised the empirical evidence derived from qualitative, quantitative or mixed-methods studies which examined the relevant ethical issues. The review had specific regard to: (a) how decisions were made (views, experiences, and understanding), (b) who was involved in the decision-making, (c) which factors were considered, and (d) what principles underpin proxy decision-making. Proxies were defined as individuals who have been consulted regarding an adult lacking capacity who has been invited to take part in research. This included relatives and carers who might be asked for surrogate consent on behalf of another person, and researchers who make a decision based on advice from a consultee, using both hypothetical scenarios and decisions made in practice. Decision-making includes providing legally valid informed consent, as well as providing advice, as determined by the applicable legal framework (33,174). Ethical issues may have been clearly identified as such or related to the ethical standards or principles underpinning the decision, or issues defined *a priori* which included proxy accuracy, burden, and comfort. The review then brings together the findings to provide an overarching synthesis of proxy decision-making for research participation, and the development of a conceptual framework.

3.2 Methods

An initial conceptual framework (**Appendix 2. Initial conceptual framework of proxy decision-making for research**) was developed utilising existing knowledge and the critical literature review reported in Chapter 2. The conceptual framework informed the search strategy and terms. The review was prospectively registered on PROSPERO database of systematic reviews (CRD 42017054561).

3.2.1 Search strategy

A systematic search to identify relevant studies was conducted following development of a search strategy with assistance from an information specialist, and piloting of appropriate search strategies. The search combined terms including informed consent, research, proxy, surrogate, ethical principles, and decision-making. The full search strategy is available in **Appendix 3. Search strategy for systematic review of empirical studies**. A number of bibliographic databases were searched: Ovid MEDLINE, Ovid EMBASE, Ovid CINAHL, Ovid PsycInfo, ISI Web of Science, EUROETHICS and Scopus. Studies were limited to those in the English language. The search was not limited by date or geographical location.

The searches were undertaken in January 2017. The difficulties with identifying ethical issues using standard search filters have been noted elsewhere (175). Given the problems with identifying ethical issues in studies that are rarely appropriately indexed, supplementary searches were conducted including citation tracking, reference lists of included papers, and electronic table of contents (eTOC) of key journals for the last two years. This approach aimed to identify a set of studies providing relevant empirical data on ethical issues in proxy decision-making for research participation.

3.2.2 Inclusion and exclusion criteria

Studies potentially eligible for inclusion were those reporting:

- Empirical research, using qualitative and/or quantitative methods.
- Studies aimed at understanding proxies' views about consent to research participation for adults lacking decision-making capacity.
- Studies that report patients' or researchers' views/experiences of proxy consent/agreement for research participation.
- Ethical issues arising in obtaining proxy consent/agreement for research participation (which includes proxy accuracy, discrepancy, and comfort).

Studies were excluded if they reported the views of clinicians or did not include consent for research (such as treatment only), were protocol papers, or were not empirical research (such as argument-based normative papers).

3.2.3 Study selection

Studies included in the review reported empirical primary research aimed at understanding proxy informed consent, or decisions about research participation by adults lacking capacity (in any country). The evidence base was expected to be diverse, therefore studies of any design could be included, such as: interventional studies, observational studies (cohort or case-control), mixed-methods, qualitative interviews (unstructured and structured), questionnaires, and surveys.

Titles and abstracts from the initial searches were screened for relevance based on the inclusion criteria, and a sample of around 20 papers from the initial searches were reviewed by three reviewers to ensure the accuracy of the application of inclusion and exclusion criteria. Included abstracts were independently reviewed by two reviewers. Disagreements were resolved by discussion, or in consultation with a third reviewer or across the wider team as appropriate, to make a definitive judgement. The full text of all potentially relevant studies was retrieved and assessed using the same process. Data from the included studies were independently extracted by two reviewers using a review-specific form developed following piloting with three included heterogeneous papers. Studies that were identified and included or excluded are reported using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (176).

3.2.4 Quality appraisal

Quality appraisal was conducted to assess the methodological rigour of included studies. Studies were appraised for quality using standardised frameworks appropriate to the different types of study reviewed. For surveys, the AXIS checklist (177) was used, and for qualitative research the Critical Appraisal Skills Program (CASP) checklist was used (178). Critical appraisal of all included studies was conducted, and a random sample of 10% of papers was independently appraised by a second reviewer to ensure the accuracy of the application of quality assessment tools. Studies were not excluded from the evidence synthesis based on quality assessment alone, as is increasingly the case for qualitative reviews (179).

3.2.5 Data extraction and synthesis

Two reviewers extracted data from the included studies independently; and extracted data were combined where one reviewer identified additional relevant data. Only data relevant to the aims of the review were extracted. Qualitative data were extracted and entered into NVivo 11 (180). Quantitative studies were small and highly heterogenous in populations and measures, and therefore meta-analysis was not feasible. Subsequently, quantitative data were narratively reported and entered into NVivo 11.

3.2.6 Synthesis approach

The review followed the framework synthesis approach outlined by Gough et al (168), which is based on five stages: familiarisation with the data; identifying an initial conceptual framework; indexing data; mapping and interpretation of the data; and iteratively refining and developing the conceptual framework (181). An important feature of the approach is that, unlike some other qualitative methods, it allows themes or concepts identified *a priori* to be specified as coding categories from the outset, and to be combined with other themes or concepts that emerge through inductive analysis (182).

3.2.7 Data synthesis and development of framework

Data were coded thematically, with codes both pre-specified in accordance with the conceptual framework and generated from the data itself. As themes and contexts expanded, and new themes emerged, the framework was developed, and data were coded iteratively. Definitions for each theme were developed and refined through discussions between the review team, and data were mapped and aggregated under each theme. Proxy decision-making is highly complex and contextualised; therefore, attention was paid to the context surrounding each theme and individual study.

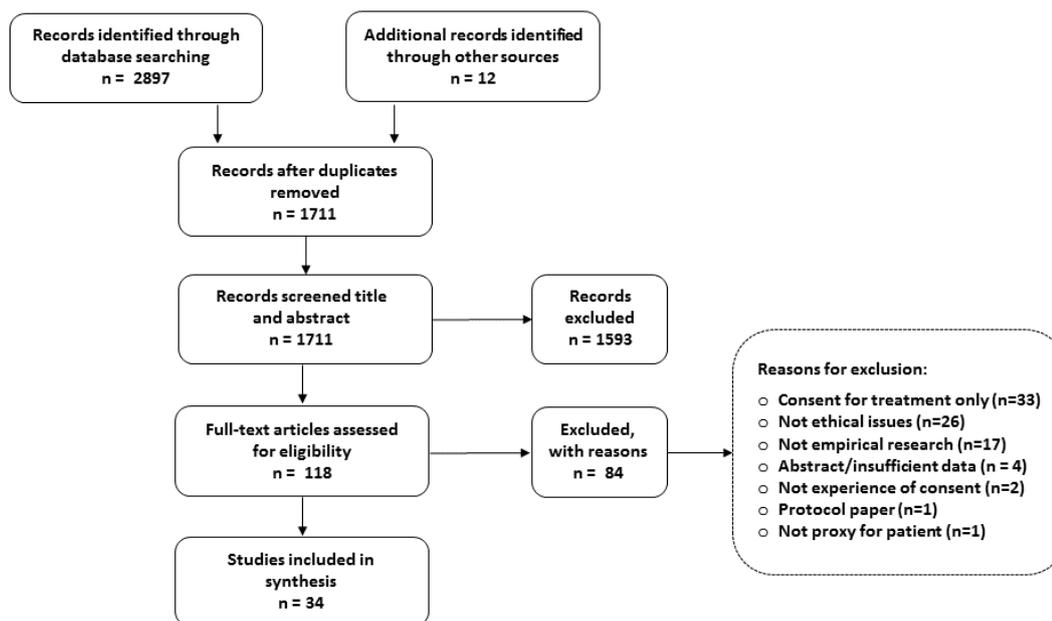
3.2.8 Development from the preliminary conceptual framework

Once the coding was complete, a revised framework was developed building on the earlier model, and the relative contribution of each study to the synthesis was summarised and tabulated under key themes of the framework. Where possible, all of the evidence was mapped onto the framework of proxy decision-making developed iteratively during the review.

3.3 Search results

The search identified 1711 unique papers, of which 118 were assessed as meeting the inclusion criteria following review of the title and abstract. Following full text review, 84 were excluded and 34 studies were included in the review (Figure 3-1 PRISMA flow diagram for systematic review of empirical studies).

Figure 3-1 PRISMA flow diagram for systematic review of empirical studies



Characteristics of the included studies are summarised in **Appendix 4. Summary of key characteristics of studies included in systematic review**. Included studies were published between 1986 and 2017. Almost all of the studies were conducted in North America ($n=32$) with one study conducted in Europe (99) and one study in Southeast Asia (183). No studies conducted in the UK were identified. The majority of the studies involved research into conditions characterized by progressive cognitive decline (dementia $n=19$, older people in long-term care $n=2$), or an acute event, which precipitated a sudden loss of capacity (critical care $n=11$, neurological emergencies $n=2$). No studies involved those with lifelong disabilities or impaired decision-making. No studies explored experiences of those acting as a proxy by virtue of their professional role, such as clinicians or researchers. Only five of the included studies explored experiences of proxy decision-making in real-life situations, while the majority examined hypothetical decisions. Sample sizes ranged from 10 to 1,515 participants. The studies generated both qualitative and quantitative data. Research methods used in the studies were evenly divided between structured or semi-structured

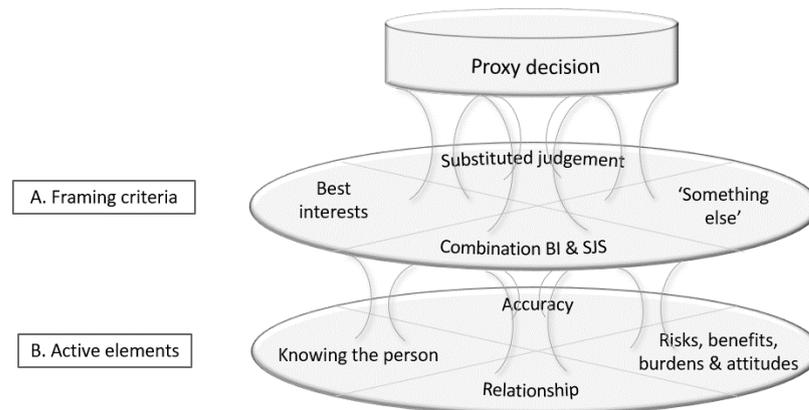
interviews and survey/questionnaire instruments, one study combined survey and interview methods (184), and one study combined survey and discussion group methods (185). Three studies evaluated interventions intended to improve proxies' deliberation or decision-making processes (185–187). All of the studies included met the quality assessment criteria.

3.4 Findings

Eight key themes were identified across two performative concepts. Four relate to the ethical framing criteria of decision-making: (1) the use of a substituted judgement approach, (2) use of a best interests standard, (3) a combination of substituted judgement and best interests standards, and (4) an alternative basis or “something else.” Four can be considered active elements of proxy decision-making: (1) knowing the person, (2) relationship, (3) accuracy of the decision, and (4) balancing the risks, benefits, and burdens and attitudes toward proxy decision-making. The codes and themes are summarised in a coding index (**Appendix 5. Coding index for studies included in systematic review**). The studies that generated data coded to each theme were tabulated (**Appendix 6. Tabulated findings from studies included in systematic review**).

A framework was developed which provides a synthesis of the concepts and perspectives that emerged from the empirical data, to describe the relationships between the framing criteria used by the proxy, and the active elements of decision-making (**Figure 3-2 Framework of proxy decision-making for research involving adults lacking capacity**).

Figure 3-2 Framework of proxy decision-making for research involving adults lacking capacity



3.4.1 Ethical framing criteria of proxy decision-making

Given the set of alternatives and possible consequences of each choice, both for the proxy and the patient, proxies' decision-making was characterised by uncertainty. The proxy's approach to decision-making emerged as a decision frame, which was dependent on their conception of the decision, potential outcomes, and consequences associated with each particular choice (188). Differences in the proxy's formulation of the decision, and factors such as the perceived risks and benefits of the research caused significant shifts in how the proxy was orientated to the decision. This provided a foundation for how the decision was made.

Six of the included 34 studies explicitly presented data on the framing criteria. Data on the framing intent of proxy decision-making were grouped into four domains: utilising substituted judgement, a best interests approach, a combination of both substituted judgement and best interests, and 'something else'. These domains were identified from the questionnaires, survey items, and qualitative themes reported in the included studies, and map onto the proxy decision-making 'standards' described in the bioethics literature (189). In order to meet these standards, decision-making would need to fulfil certain criteria, for example, decision-making centring on maximising the well-being of the patient would meet the best interests standard; or decision-making based on their views and preferences would meet the substituted judgement standard.

3.4.1.1 *Substituted judgement*

A substituted judgement was characterised by the proxy attempting to, or being directed to, make the decision that the person would themselves have made if they had capacity, as illustrated by one of the participants who was living with dementia.

'I would want her hopefully to make that decision on what she thought I would think. OK. Not what she thinks, not what somebody else thinks, but what I think...what she thinks I would have done' (190)

There were notably lower levels of support for the use of substituted judgement, in comparison to the use of best interests. 9% of proxies for people with dementia chose only substituted judgement as their preferred criterion of proxy decision-making for research (190), 15% of patients with dementia preferred substituted judgement alone (190), and 24% of proxies would base the decision on 'what the patient would want' (191). Despite this, when proxies were asked what criterion they had used for deciding about a proposed hypothetical study, around half stated they would decide primarily based on substituted judgement (32).

'Well I'd want to do what he would have want(ed). Whether I agree with it and he wouldn't agree with it is not an issue. He's the one that would be going through the study, so it has to be based on his feelings... I would want to do what he wanted, more than if it was something I thought I wanted and he didn't.' (32).

Proxies described using a 'substituted judgement' in other decisions they made for the person (32), although some distinguished decisions about research from other types of decision, and reported that they used a different ethical criterion for different types of decision.

'for research I would make it based on what I thought she would want. If it was treatment, I would probably make it based on what I thought was best for her, but for research, I'd probably go with what I thought she would want' (190)

3.4.1.2 *Best interests approach*

A best interests approach focussed on what would maximise the person's welfare or interests, as illustrated by this subject's views: *'what he thinks is best for me I would say. In that situation, I can't want or not want'* (190).

Proxies reported being used to making everyday decisions using a 'best interests' approach (32). Around half of proxies (32,190) and a third of patients with dementia (190) supported the use of a solely 'best interests' approach when deciding about research participation. These were in largely hypothetical scenarios. However, in a study involving actual research decisions the majority of proxies for people living with dementia responded that they would decide based on 'what would maximise the patient's well-being' (191). They reported the use of a 'best interests' approach to research decisions, even where this might override what the person's own decision might have been (32), perhaps perceiving benefits from the research that justified overriding the person's wishes in order to promote their well-being. Proxies clearly saw themselves as holding a protective role and so were concerned with protecting the person's interests (100,185,192). Some proxies did not appear to distinguish between the interests of the person and those close to them.

'Based on what would be best for him, not on what he would decide. I've made most of my decisions in life as to what would be best for him. What would be best for the family. There is no other way to decide (190)

3.4.1.3 Use of a combination, or another criterion – 'something else'

Moderate levels of support were given by proxies and patients for using a combination of substituted judgement and best interests for proxy decisions. 20% of proxies for people with dementia would use a combination of best interests and substituted judgement, and 18% of patients with dementia supported a combination of both criteria (190). Although some proxies reported that they would use a combination as that is what the person themselves would have used to decide.

'well the two might not be different. What's best for me and what I would do might be the same thing and I think that's what she would make the decision on. She would consider both' (190)

In one study, nearly half of the proxies agreed or strongly agreed with the use of both, and spoke about the desire to incorporate both criteria in considering research participation (32). Whilst most proxies in another study described a complex weighing process of their substituted judgement, with their preferences, and with the person's own current preferences (193).

In Black et al, proxies and people living with dementia were able to indicate that they supported 'something else' as an option which was neither best interests nor substituted judgement (190). 29% of proxies chose this third option, which often incorporated multiple concerns, such as considering whether it would be feasible for the person to co-operate with study procedures or to manage the travelling to study visits. The same proportion of people living with dementia chose the 'something else' option (29%), some wanting proxies to consider their own interests or those of family members, or following consultation with others (190). Proxies in Dunn et al described the need to weigh numerous factors concurrently, which would include the person's preferences and personality before becoming ill, potential societal benefits, and their current quality of life (32).

3.4.2 Active elements of proxy decision-making

Themes were identified that were considered to be characteristics or elements of decision-making. These functioned to a greater or lesser extent in the decision-making process depending on the context, the relationship between the patient and their proxy, and the attitude of the proxy themselves. They actively directed proxies to accept or reject the option of research participation by serving as factors to be weighed in the decision-making process, as indicators to the proxy for how they should frame the decision, and sometimes as justifying reasons for the decision itself.

3.4.2.1 *Relationship between the patient and the proxy*

Participants reported that the choice of who acted as their proxy was important, and participants commonly used aspects of their relationships when they reported their views or experiences of proxy decision-making for research. The choice of proxy was reported as relevant to proxy decision-making in three studies (194–196). One study that reported reasons for endorsing proxy consent centred on various aspects of trust, the closeness of their relationship and, in some cases, their previous experiences with decision-making for them (196). Similarly, another study cited trust and family closeness as reasons for choosing the individual identified as their proxy, with love and closeness also mentioned, with many reporting that their trust was based on the proxy's performance in a past crisis (194). Participants generally did not see a distinction between acting as a proxy for decisions about care or treatment and research, all participants presumed the same person would act as proxy for both types of decision (194). Notably, one study found there were low levels of support for a professional acting as their proxy, with only 7% allowing a healthcare provider

to provide consent on their behalf, compared to 88% who would allow a family member to provide consent (195).

Familiarity and similarity between the person and their proxy were often cited. Some participants discussed the reciprocal nature of family relationships that are built on mutual understanding and responsibilities. Older people in Berger et al's study reported that they had chosen a family member to act as proxy on a mutual and relational basis: *'She's most familiar with what I want, as I am with what she wants. She's really the one I trust the most'* (194).

Two studies reported that proxies consulted other people to gain consensus before making a decision about research participation. Black et al included some proxies who had made actual decisions on behalf of a person with dementia, some of whom consulted with other family members before deciding (190). Warren et al's study with proxies for nursing home residents found that 60% of proxies consulted others before making a decision, of these about half (27% of the total) consulted medical professionals (192).

3.4.2.2 Accuracy of the 'decision'

Many of the included studies focussed on whether proxies accurately predicted what the patient would decide about participating in a hypothetical research study (93,94,99,100,197–199). These studies use the patient's own prediction as the correct decision or the 'gold standard', against which the proxy's decision or prediction is measured as a form of 'diagnostic test' (198). This relies on the assumption that these predictions are conceptually the same as the patient's own decision. Proxies' decisions that are incongruent with the patients' own decisions were said to be either 'false positive' where the proxy would have enrolled the person when they would not have wanted to participate, or 'false negative' where the patient would have wanted to take part, but the proxy declined to enrol them.

The level of accuracy reported in the studies varied. Accuracy of 76% was reported in one study (197), whilst in Ciroldi et al the patient-proxy discrepancy rate varied between 32% - 42% (99), and Newman et al found that the overall percentage of discrepancy increased as the perceived risk associated with the study rose (93). Stocking et al found that 49.7% of patient-proxy dyads directly disagreed about patient enrolment in at least one of the five hypothetical research projects described (199). Of these disagreements, 47% involved the patient being willing to enrol and the proxy was unwilling to enrol them, and 52.2% of

disagreements reflected the reverse, proxy willingness and patient unwillingness (199). A study that examined the accuracy between patients who had been in critical care and their proxies, showed that most proxies would respond in accordance with patients' wishes, although patients were more likely to agree to participation in the genetic research than their proxies would have allowed (94). Muncie et al found that the agreement between proxies' decisions and the patients' decisions was no higher than the decisions of randomly assigned, unrelated, proxies would be (100).

3.4.2.3 Confidence and certainty

Three studies, all of which involved research in acute care settings, reported on levels of confidence in the proxy's ability to decide in accordance with the person's wishes or the certainty that the decision was in accordance with their wishes (94,197,198). Bryant et al's study with emergency department patients and their proxies found that both patients and proxies indicated relatively high degrees of confidence in the decisions they were making (197). Confidence was associated with accuracy in a study with critical care patients and their proxies, which found that 80% of proxies who were confident responded in agreement with patients' wishes (94). Both proxies and patients showed overwhelming confidence in the proxy's ability to make a decision based on the patient's wishes: 53.2% of proxies were very confident, 41.6% moderately confident, with only 5.2% not very or not at all confident (94). Patients also showed high levels of confidence in their proxy making a decision consistent with their wishes: 76.2% were very confident, 18.2% moderately confident, and only 5.1% not very or not at all confident (94). The only factor that influenced patients' confidence in their proxies was whether they had prior discussions with them, however having a prior discussion was not significantly associated with proxies' confidence in their own ability (94). Confidence was also associated with accuracy in Coppolino's study with elective cardiac surgery patients and their proxies, which found that agreement was higher between patients and proxies where proxies felt "absolutely certain" or "certain" about their predictions (198).

3.4.2.4 Leeway given to proxy

Eight of the included studies explored the amount of freedom or leeway the person would give their proxy when it came to making decisions about research on their behalf. The majority of participants were willing to give some or a complete amount of freedom or leeway to go against their currently stated preferences about future research participation, although it varied by scenario (200–203). Kim et al found that the leeway given to a close

family member by caregivers for people living with dementia varied little by study type, with 37% allowing no leeway, 57% some leeway, and 17% giving complete leeway (202). The main reasons given for granting leeway were that the proxies would have more or better information in the future, that the ratio of the risks/burdens vs. benefits may be different at the time of the study, or that the proxies may be able to better assess the risks at the time.

“There could be new info that needs to be factored into decision making process” and “They could have new information that wasn’t available when I gave instructions for the future” (202)

Whereas those who would not give any leeway to their proxy perceived leeway as violating their right to make decisions for themselves.

“I feel very strongly that the choices I make about my fate are mine and should not be changed” (202)

Participants who declined both research participation and allowing leeway frequently emphasized the risk/burden ratio or lack of direct benefit from the research as a reason for not allowing leeway.

“The brain inflammation [listed as a potential side-effect] is the showstopper for me. While probably severe at any age, I see it as life threatening for the elderly. It’s one thing going into this trial without knowing particular risks. It’s totally unacceptable to knowingly put people at risk” (202)

3.4.2.5 *Knowing the person*

Five studies reported that knowing the person’s wishes and values were relevant factors in proxy decision-making for research (32,184,185,194,204). Proxies described basing their decision-making as based primarily on their overall ‘knowledge’ of the person’s values, wishes, past behaviours and decisions, or some combination of these, by virtue of the relationship that exists between them (32).

‘You have to know what type of person your loved one is. Were they the type that did want to do other things for other people? Were they the type that would want to help other people? And then you just have to decide that through your talks with the other family members. You know, what they notice early on if they were that type of person and then ... I guess that would be your decision then. Because otherwise...it would be my thoughts and what my

morality and ethics are, not hers. So, I would have to talk to my daughter or my brother or mother and say, "What has she said in the past about stuff like that?" (185)

Fidelity to the person's wishes was achieved through representing their historical values, whether recalled from previous conversations, perceived in past behaviours, or embodied in patients' character traits (184).

'Since you couldn't ask him anymore what he thought or what he felt, you had to go by your recollections of things he'd done in his life and would he believe in doing this, would he believe in promoting science and moving forward with knowledge and things along those lines? Yes. Would he tolerate small amounts of discomfort for a greater benefit? Yes. So you....can only go on your perceptions of things he had done...' (184)

Other proxies cited the need to 'honour' the person's life, values, and wishes — even if they personally disagreed with the decision (32). However, in many cases, their explicit wishes were not known to proxies (204), and few proxies (30%) had previously discussed research preferences (198).

Many proxies felt that decisions about people with dementia taking part in research should be based on a written document or advance directive expressing their willingness to participate that had been made before they lost decisional capacity.

'I think the best thing would be to have a specific advanced directive for research that indicates what types of research you'd be willing to have yourself be a subject of and also who you indicate as the proxy to make those decisions for you when you're unable to before that has an opportunity to develop' (185)

One study reported that 88% of participants stated that their family could agree for them to participate in research in the absence of a research advance directive, and 80% stated that their families could enrol them in research that may potentially benefit them even if their advance directive opposed enrolment in research (205).

A commonly cited reason for participating was altruism (36,185,196,206,207), described as the desire to help research or to help others, to be a 'good citizen' (36), or the desire for future societal benefits [49]. However, proxies were acutely aware of the moral difference between deciding for oneself and deciding for others based on altruistic motives (207). Altruistic motives were a joint motivation for the person and proxy (207), where proxies may have experienced altruism 'by proxy', although it was sometimes considered to be a

secondary motivation, following the hope that the person themselves would benefit from the research (36).

'Well we knew that hey if this worked that it would be on the market and could conceivably help many other people, yes. But we were there primarily for very selfish reasons, seeing if could slow down the onslaught of the Alzheimer's.' (36)

Some proxies were aware that their own children or grandchildren may someday develop the same disease (Alzheimer's disease) and the trial might one day benefit them (36) – as a form of 'selfish altruism'.

'They had described to us at [major medical center] that they had nothing at the present time that would help. They were working on certain things and that probably there wouldn't be anything out in time to help him but certainly by the time our children, if they were ever to find out they had it, certainly by that time they should have help.' (36)

In one study, proxies for people with dementia reported that using the person's character as the basis of the decision was problematic, as the changes wrought by the disease made it impossible to use 'who' the person was in the past to make decisions today (185). Proxies contrasted the personality and decision-making preferences of the person prior to developing dementia versus their view of the person's current preferences (32). Proxies encountered difficulties with the complex ethical issues involved, such as reconciling the need for research in order to develop new therapies, with their values relating to autonomy, experiencing and inflicting pain, and their responsibilities as carers (185). Current preferences were frequently described by the proxies as taking precedence, regardless of prior preferences. Proxies believed that if the person currently would prefer not to participate, there was a certain point beyond which they would not be willing to 'force them' to participate (although the nature and extent of any such 'force' was not reported) (32).

3.4.2.6 Balancing risks, benefits and burdens, and attitudes towards proxy decision-making

Some studies addressed issues of perceived risks and benefits associated with participating in different type of studies, and study-related procedures that were considered burdensome. Ayalon et al's survey of community-dwelling people aged over 50 found that willingness to participate and to have a proxy to make decisions about research for them was associated with study type (200). Participants were more likely to endorse a moderate benefit and

minimal risk scenario, and less likely to endorse a minimal benefit and severe risk scenario, when compared to the minimal benefit and moderate risk scenario. Proxies for people living with dementia commonly cited concerns about potential risks when interviewed (32).

In one of the few studies that involved a real-life decision about a research study proxies for critical care patients perceived that where the risk of participation was too high, or felt patients may not benefit from participation, they did not consider participation any further (204).

3.4.2.7 Comfort with proxy decision-making

Four studies explored comfort with proxy decision-making. Dubois et al questioned five groups, including older people, informal caregivers, physicians, ethics board members, and researchers, using four scenarios (208). They found that as the study's risk-benefit profile becomes less favourable, the proportion of participants expressing comfort with proxy consent decreased in all groups (208). Where studies involved serious risks with greater potential benefits, their comfort with proxy consent was lower when the proxy was neither appointed nor designated, and higher when designated in a healthcare advance directive with instructions regarding research participation (208).

Stocking et al examined patients' own comfort with proxy decision-making for research for themselves and found this also varied by study type (199). Patients with dementia were presented with five hypothetical studies, 32.9% said they would not be comfortable with proxy enrolment decision-making in one or more of the hypothetical situations described, and their discomfort increased with the risk of the hypothetical study from 8.5% for a blood sample to 26.5% for intracranial stem cell implant (199). There was no statistically significant difference by age, sex, or education, between those who expressed comfort and discomfort, although they did differ by race; 44.9% of African-American participants reported discomfort compared with 27.0% of white participants (199).

Karlawish et al interviewed patients with Alzheimer's disease and their proxies and found high levels of comfort with proxy decision-making for research in both groups [28]. 85% of proxies thought that proxy consent was appropriate in general, and also for their relative if they were unable to provide their own informed consent (191). The proxies' reasons included their role in making other decisions for the patient such as finances and treatment, and the patient's wishes to contribute to research.

'Well because you have to make an awful lot of decisions for them. And if it seems something that is safe to do, I mean it is safe because they will be watching for the risks, and it might do some good.' (191)

86% of patients showed similar consensus as their proxy. Reasons commonly cited were that the proxy had their best interest in mind or knew of their intentions (191).

3.4.2.8 *Burden of proxy decision-making*

Six studies provided data on the burden of proxy decision-making for research. Proxies were acutely aware of the moral difference between deciding for oneself and deciding for others (185). Proxies for people living with dementia recognised that having the choice of whether or not to enrol the patient in research added to their burden.

'I guess what it all boils down to for me is that I'm just torn on this issue because intellectually I understand the need to have the research done and believe that this is the only way to find out more about the illness and to bring about some real progress. Okay. I support that; I really do. Emotionally speaking, I don't think I could bear to see my mother suffer.' (185)

Studies with proxies in critical care found that the burden varied by study type or level of risk. Barrett et al showed that few proxies reported it would be a burden to be involved in the consent process for the low risk (baseline) study or for the study involving two standard treatments (209). However, a greater proportion felt it would be a burden to participate in decision-making for the higher-risk treatment and for the scenario where a decision was needed quickly (209).

'I guess because a lot of time medication[s] have a lot of side effects, you know. I'd hate to hurt her. I think if she would take medicine then like have a heart attack from the decision I made...' (36)

Similarly, Mehta et al reported that 20% of proxies found the process very burdensome in the higher risk and shorter enrolment window scenarios, and up to 30% were very uncomfortable making the decision (206).

The perceived risk also affected the burden experienced by proxies for people with dementia (36). Burden could be decreased if the patient themselves was able to play a meaningful role in the decision, however some reported that, even when the person could be involved in the

decision, the burden was high because the decision to participate meant acknowledging the dementia.

'Well, it felt like . . . you was saying [sic] that you knew that he wasn't going to be capable of making his own decisions. You know that it hurts to know . . . that he's getting to that point that he can't even make decisions for himself.' (36)

One study reported that burden may be experienced as a result of feeling that other family members would not agree with their decision or would 'blame them' for enrolling the person (204).

3.4.2.9 *Acceptability of proxy decision-making for research*

Seven of the included studies explored acceptability of proxy decision-making, either from a societal perspective, for themselves at some future point, or as proxies on behalf of another person. A survey of 1469 community-dwelling people aged over 50 in the US showed high levels of support, with 70.7% agreeing to allow proxy-informed consent for themselves (200). A study with 240 survivors of a critical illness reported that, compared to alternative consent models, most (76%) selected "consent by surrogate decision-maker prior to enrolment" as their preferred framework, regardless of the level of study risk (210). In Sachs et al's study with different populations, those considered the 'well elderly' group reported a variation depending on the perceived risk of the study, with willingness to accept proxy consent declining from the blood sample study, to brain autopsy, to medication trial, to surgery/medication study (196). Comments about proxy consent from this group were very similar to those of the people with dementia, one participant who would refuse to allow a proxy to decide about the surgery/medication protocol said: *"It's too dangerous for someone else to decide"* (196). However, most (96%) community-dwelling older people were willing to designate a proxy for research decision-making (201).

Proxies overwhelmingly reported that they were keen to be involved. The majority (90%) of proxies for critical care patients wanted to be involved in decision-making about research on their behalf (209). Although, acceptability of involvement in the consent process was lower in the higher risk studies and those mandating less time to make a consent decision. Similarly, Kim found that 92-94% of proxies for dementia patients supported proxy consent for the less invasive study, compared to 53% - 62% for the most invasive of the hypothetical research studies (187). An earlier study led by Kim found that risk also influenced the older people

they surveyed (211). They found that acceptability of proxy consent-based research was strongly influenced by the level of perceived risk, resulting in an adjusted odds of finding a minimal risk study acceptable for proxy consent 60 times relative to that for high risk studies (211). However, in their 2009 study Kim et al found most of the 1515 community dwelling aged 50+ were supportive of allowing families to make proxy consent decisions for dementia research (67.5% to 82.5% by study type), even for a first-in-man gene transfer study nearly 68% stated that society should allow families to make such proxy decisions (203).

3.4.2.10 Willingness to participate

Seven studies examined participants' willingness to take part in research should they lose capacity. Kim et al found that, generally, older people's levels of acceptability for proxy consent for themselves were comparable to their willingness to participate in a research study, although for one hypothetical study (a vaccine study) a significantly greater proportion would allow proxy consent than would themselves want to participate (203). Patients in emergency departments and other members of the public reported a willingness to participate in a hypothetical SAH trial, with 34% definitely participate, 20% probably participate, 22% possibly participate, 5% probably not, and 10% would definitely not participate (9% could not decide) (195).

The vast majority of participants in Wendler et al's study were willing to participate in clinical research if they lost the ability to consent, ranging from 80% to 99% depending on study type and perceived level of risk or benefits (205). Exploratory analyses found no significant associations with characteristics such as sex, age, religion, and previous execution of a healthcare advance directive. Critical care patients were significantly less likely to participate in research as the perceived risk associated increased, with no associations found between their length of stay in critical care, age, race, or gender (93). Similarly, older people in one study were reluctant to consider research involving taking experimental drugs or those with serious known side-effects (194).

Proxies' willingness to enrol the patient as their proxy decision-maker was associated with their willingness to participate in research themselves. Clarridge found that the likelihood of the proxy for a critical care patient participating in research influenced the likelihood of that proxy permitting the patient to participate in research (212). Muncie found that proxies' decisions for their own participation were significantly associated with their 'guesses' of the patient's decision, and therefore with their decisions for the patient (100). Consequently, for

each hypothetical study, the proxies' decisions for the patient were significantly more frequently in agreement with the proxies' own decisions for themselves than with the patients' decisions to participate. Similarly, 80% of proxies for nursing home residents would be willing to participate in the hypothetical study, and proxies who would take part themselves were significantly more likely to give consent for the care home resident they represented (192).

Three studies found that proxies were more likely to enrol themselves, than would be willing to agree for the other person to take part. Both Sachs et al (196) and Kim et al (202) found that proxies as a whole were more willing to participate themselves than they were willing to give proxy consent for their relative, regardless of study type. Lim found that this did vary by study type, with proxies being five times more likely to have a favourable opinion for themselves as the patient in the lower risk studies, and six times more likely for the higher risk study (183).

3.5 Discussion

This systematic review suggests that proxy decision-making for research can be considered to comprise of two dimensions; the framing criteria used by the proxy to make a decision, and the active elements that feature in the decision-making process itself. The relationships between the framing criteria and the active elements are complex, operating on a number of different levels, as components interacting between themselves, with both explicit and implicit modes of interaction, and which may be context dependent.

The ethical framing criteria play a structural role, which forms the basis, or orientation, from which the proxy engages in decision-making, and shapes the nature of the decision. The decision frame used by the proxy was dependent on their formulation of the decision, the potential outcomes, and consequences. It directed the proxy's perspective on decision-making – whether they attempted to determine what the person's decision would have been through 'standing in their shoes' to meet the criteria of a substituted judgement, or whether they provided their own determination of what would derive the maximum benefit for the person and would therefore be in their best interests. Where proxies reported the use of a combination of both criteria, it was either expressed as hope that the decision they made would match the outcome of both, or that if they made a substituted judgement it wouldn't

be against the person's best interests. However, the low levels of support for both substituted judgement and best interests – substituted judgement in particular – and support for a combination of both or for a 'something else' option may reflect the complexity of proxy decisions in practice. This complexity was described as a complex weighing process of the proxy's substituted judgement, with their own preferences, and with the person's current preferences (193). In contrast to the rigid tripartite bioethical hierarchy of proxy decision-making standards (known wishes, substituted judgement and best interests), described as having become 'canonical' in the bioethics texts and professional codes (189), a picture emerges from the data of complex multifaceted decisions that often involve a weighing up of numerous factors.

3.5.1 Interplay between the dimensions of framing criteria and active elements

The four active elements influence how proxy decisions are made by modifying the framing criteria used by the proxy, and in turn, how or when the elements are drawn upon is influenced by the criteria used. Active elements have a varying functional role. They were frequently involved as factors considered by the proxy, as indicators to the proxy for how they should frame the decision, and sometimes as justification for the decision itself, it varied by context, patient-proxy relationship, and the attitude of the proxy themselves.

There are also associations between a number of the elements. The nature of the relationship between the person and their proxy is one such element that operates in both substituted judgement and best interests approaches and is also linked to the 'knowing the person' element. The relationship provides the proxy's authority to make decisions on behalf of adults lacking capacity (29) by enabling them to provide a substituted judgement, but the relationship can also enable to the proxy to be best placed to determine what is in the best interests of the person. The closeness of the relationship is the mechanism by which the proxy knows the person's wishes and preferences and is also the reason they are chosen by the person to represent them as proxy (194,196).

In contrast, the accuracy element appears to only be relevant when substituted judgement is utilised by the proxy where, unlike in best interest approaches, there could be considered a 'correct answer' to match. Studies that explored the accuracy of a proxy's substituted judgement generally demonstrated moderate levels of accuracy or agreement between

patients and their proxies. As a result, some authors noted that the variable predictive accuracy of proxy decision-makers raised questions about the ethics and validity of proxy decision-making (197,198), which threatened the ethical principle of autonomy for the patient (93). However, as described in Chapter 2 (2.3.2.4 Failure of proxy predictions) such studies have important limitations and methodological flaws (103), including that these studies are based on the assumption that there is similarity in decision-making patterns in hypothetical and actual treatment situations (97). Despite the use of the patient's own 'decision' as the gold standard, the patient is merely expressing a prediction (a preference or disposition (128)) rather than a consent decision, and in reality, proxies are being required to 'match a guess'.

A common theme across many of the studies was the relational authority that proxies hold. Patients and members of the community cited the bonds of love, care and trust when describing the proxy-patient relationship, as well as the reciprocal nature of family relationships and responsibilities. This is reflected in the data relating to who they would chose as their proxy, and the reasons for selecting that person are commonly that the proxy knows their wishes and values and may have been nominated for healthcare and/or research decisions in an advanced directive. Altruism is involved in the decision, both the altruistic tendencies of the person and also the proxy who at times consider themselves to be joint study participants. Their involvement in the decision-making process may engender feelings of a joint enterprise, although as research decisions do not occur in isolation, it may relate to wider complex power and responsibility issues within an interdependent relationship.

Individuals also reported granting leeway or a margin of flexibility to their proxy, even when an advanced directive was in place. This appears to reflect their understanding that these are future decisions, which means that factors and information will be involved that are not currently known, and therefore the decision outcome cannot be pre-determined. Leeway appears to be influenced by perceived risks and benefits. Factors such as leeway and knowledge of relevant advance directives may also be part of 'knowing the person' that a proxy would incorporate into their substituted judgement. Knowledge of the person's altruistic tendencies may function in a similar role but may also be affected by the proxy's own altruism, linked to selfish reasons or otherwise (213).

One element – the risks and benefits of participating and the nature and invasiveness of the study procedures – was identified as a characteristic that operated to influence proxy

decision-making in a number of different roles. It determined whether a substituted judgement or best interest determination was made by proxies, where if the burden was considered to be high then a substituted judgement was rejected, and best interests was used by some proxies (204) although not by all (32). It also served as a justifying reason for the decision itself, where it was the 'right' decision if the person could gain benefit from participating (200).

The attitudes of the proxy towards research involving people without capacity, and in particular their willingness to participate in research themselves, also operated at a number of levels and directions. The studies reported moderate to high levels of support for involving people who lack capacity in research, and acceptability of proxy consent models, although this too appeared to vary by perception of study risk and invasiveness of study procedures. Proxies who were willing to participate themselves were sometimes more likely to enrol the other person in two critical care studies (183,212), although this was not observed in other studies in dementia (196,202), which supports the contextualised nature of decision-making. Proxies' decisions for the others generally reflected what they would want done for themselves, suggesting that rather than the proxy 'standing in the shoes' of the patient, the proxy decides as though the patient were in their (the proxy's) own shoes (100). This may be because, when faced with uncertainty about what to decide when a person's wishes were not clear, the proxies considered themselves to be 'the reasonable person', and therefore decisions they would make for themselves should be applicable to the other person (100).

3.5.2 Gaps in the empirical evidence

The review identified important gaps in the empirical literature. The included studies were predominantly conducted in North America, for example no studies from the UK, or Africa were found, and only one from Europe and Asia respectively. None of the included studies involved people who had experienced head injury, mental illness, or those requiring palliative care, which make up a proportion of the population with impaired capacity. Additionally, proxies for individuals who have never possessed decision-making capacity, such as people with profound intellectual or developmental disabilities, were not included in any of the studies. Many of the studies involved hypothetical scenarios, and in some studies participants had little or no experience of making actual decisions about research or proxy decision-making. This may affect the generalisability of the findings from the included studies.

Both ‘false positive’ and some ‘false negative’ predictions were made by proxies, which the authors interpreted as meaning individuals would either be enrolled against their wishes or denied the opportunity to take part when they would have wished to do so, thereby threatening the ethical principle of autonomy for the patient (93). As a result, authors have noted that the variable predictive accuracy of proxy decision-makers may raise questions about the ethics and validity of proxy decision-making (197,198). Such studies have important limitations, including that these studies are based on the assumption that surrogates and patients have similar decision-making patterns in hypothetical and actual treatment situations (103). However, the greatest issue is that, despite the use of the patient’s own ‘decision’ as the gold standard, they are merely ‘predictions’ rather than decisions, and the studies in essence require proxies to match a ‘guess’. The indication for needing a proxy – that the person lacks capacity and there is a decision to be made – does not exist, therefore both the proxy and the patient are required to conjure up a parallel alternative reality. Inevitably, the realities they independently create result in different predictions. There are also significant issues with the methodology used in such studies (103) which limits their influence when examining proxy decision-making.

No studies reported the experiences of researchers or health or social care professionals acting as proxy decisions-maker by virtue of their professional role where no personal proxy was available – although this may reflect the legal position in the jurisdictions the studies were conducted in. The only study which included data on support for, or comfort with, professional or clinician involvement in decision-making showed low levels of support for professional decision-makers (195), although this is authorised in a number of jurisdictions including England and Wales (20,22,214).

Limitations of the studies reviewed include that the difficulty with search filters’ sensitivity and specificity in identifying ‘ethical’ issues may have resulted in relevant studies not being included in the review. The included studies were largely silent on the legal frameworks applicable to the research settings or populations under investigation, whether legally valid consent was being sought or given, or the concordance of participant responses with respect to the relevant guidance or legislation. The restricted populations and settings of the included studies may limit the transferability of the studies to other populations and jurisdictions. Patients who were included were, necessarily, those with less severe dementia, or survivors of critical illnesses who had regained decision-making capacity. Methodological flaws limit the generalisability of some studies that explored the accuracy of proxy

predictions, and caution must be used when interpreting the findings and drawing conclusions about the ethical validity of proxy decision-making as a result.

Quantitative methods using survey and questionnaire tools do not sufficiently capture the depth of the proxy experience, or the views of patients and members of the public. The views of others involved in decision-making, particularly researchers in the UK, were not included in the studies reviewed at all. Studies that explored the framing criteria for decision-making commonly asked proxies and patients to state whether they supported, or used, a substituted judgement or a best interests approach, or both. These terms were not necessarily explained to participants, nor did authors interpret participants' responses consistently, and studies may have been affected by participants providing socially acceptable responses. The low levels of support for both standards – substituted judgement in particular – and support for a combination of both or a 'something else' option may reflect the complexity of proxy decisions in practice. As one participant noted, in real life it is not a 'narrow framework' (190), and from the studies a picture emerges of complex multifaceted decisions that often involve a weighing up of numerous factors. Proxies clearly assume a protective role, and report using the person's current preferences, whilst honouring their past wishes as a form of extending their autonomy. Although, in studies involving proxies for people with dementia, questions about the 'present self' versus 'past self' are raised.

3.6 Summary

This Chapter sought to systematically review the empirical research on proxy decision-making for research involving adults who lack capacity, using a framework synthesis approach. The review had specific regard to: (a) how decisions were made through examining the views, experiences, and understanding of proxies and patients, (b) who was involved in the decision-making, (c) which factors were considered, and (d) what ethical principles underpin proxy decision-making. Decision-making on behalf of a person who lacks capacity is complex, ethically challenging, and highly contextualised and multifactorial in nature. The uncertainty about how decisions ought to be made by proxies, the weight of making a decision on behalf of another person, whilst balancing any potential risks or benefits, is burdensome for proxies.

The restricted populations and settings of the included studies may limit the transferability of the studies to other populations and jurisdictions. Methodological flaws limit the generalisability of some studies that explored the accuracy of proxy predictions, and caution must be used when interpreting the findings and drawing conclusions about the ethical validity of proxy decision-making as a result. The complexity of proxy decision-making for research and the myriad ethical issues involved are problematic to research using empirical methods, particularly quantitative methods.

The accounts of proxy decision-making given in normative ethical literature (and required by ethical frameworks) are not clearly or unequivocally supported by the empirical data on decision-making in practice, nor do they definitively reflect the views and preferences of those who are likely to require proxy decision-making. The findings from this review challenge the accepted reductive approach to proxy decision-making. They emphasise the differences between the standard interpretation of substituted judgement where the proxy is required to replicate the decision the person would have made, if they had capacity to do so, which studies using the 'gold standard and diagnostic test for accuracy' attempt to test empirically, and the reported experiences of proxies. Proxies tell a story of balancing a number of factors during the decision-making process, which seeks to honour the person's wishes while assessing the risks and benefits for the patient. The studies suggest that proxies use their close relationship to the person to guide them towards a decision that best achieves these aims, thus suggesting that proxies use substituted judgement as a tool to help determine ethically valid decisions, rather than a measure that can never be knowingly achieved. This uncertainty about how decisions should be made by proxies, and the weight of making a decision on behalf of a person who can be perceived as vulnerable through their lack of ability to protect themselves, whilst balancing any potential risks or benefits for the person, is burdensome for proxies.

The shortcomings of empirical research in medical ethics have been debated, including that a lack of normative analysis means that the empirical studies remain on a descriptive level (215). Attempting to draw (meaningful) normative conclusions from empirical studies has been widely criticised (49). Normative analysis of the findings from this review are considered to be beyond the scope of this thesis, however this systematic review does enable a broad view of the empirical literature in a form which is suitable for further normative analysis.

3.7 Learning points

This review systematically reviewed data from empirical studies exploring proxy decision-making for research in order to provide a rich and contextualised account. The approach enabled a novel conceptual framework to be developed which is informed by the empirical data and addresses the complexity of proxy decision-making.

The studies suggest that the relationship between the patient and the proxy has a fundamental role. The relationship is the justifying reason for being chosen or acting as a proxy, it provides the proxy's authority to act on the person's behalf, and influences the factors incorporated into the decision-making process through their knowledge of the person.

The empirically informed framework for proxy decision-making for research proposed here represents an initial attempt to take account of the contextual use of substituted judgement and best interests approaches, and the balancing of the active elements in the decision-making identified in this systematic review. This review indicates that this may more accurately reflect both decision-making in practice as reported by participants in the studies reviewed, and the reasons for having someone who knows the person well act as their proxy.

Further work to describe and develop the framework, together with empirically testing it with those involved in proxy decisions about research participation, may be more helpful than seeking ways to improve proxies' ability to 'match a guess' in a world of counterfactual wishes and hypothetical scenarios. This is the focus of the empirical study (the DECISION Study) reported in Chapter 6 of this thesis.

Chapter 4 Health and social care professionals' understanding of the legislation governing research involving adults lacking capacity – a cross-sectional survey

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4.1 Introduction

As discussed in previous chapters, England and Wales has a dual regulatory framework governing research involving adults who lack capacity to provide informed consent. The Mental Capacity Act 2005 (MCA) has provisions relating to research, where a relative or friend who is 'engaged in caring for the person or is interested in their welfare' is consulted as their personal consultee (20). Clinical trials of a medical product are regulated separately by the Clinical Trials Regulations (CTR), where a personal legal representative who is suitable 'by virtue of their relationship' provides informed consent (22). This is in contrast to other types of research where the consultee provides advice to the researcher, rather than consent (20). In circumstances where a person does not have a friend or relative to act in a personal capacity, there is provision for a professional involved in their care to act as a professional legal representative (22) or nominated consultee (20). Both the MCA and CTR require both those acting in a personal and professional capacity to provide consent or their advice based on what the person lacking capacity would have wanted, had they the capacity to choose for themselves, as their presumed will. The complexity of this dual legislation has been previously discussed in relation to its potential impact on conducting research in practice settings where individuals may lack capacity (33).

The complexity of the current legal framework, its legislative differences, and uncertainty surrounding their interpretation, has resulted in confusion both for researchers and Research Ethics Committees (217,218), as well as clinicians, relatives, and carers involved in decisions about adults lacking capacity participating in research (219). These differences

increase the burden on those involved in making decisions about research participation, and present barriers to conducting research with individuals with cognitive impairments (3,220). As a result, the exclusion of these groups from research is widespread, and concerns about their exclusion have been reported (221,222).

Healthcare professionals and social care practitioners are often involved in the identification, provision of information, and recruitment processes for research. As such, their role can be seen at that of gatekeeper, through which they can allow or deny access to research participation (223). A lack of knowledge and understanding by gatekeepers may act as an additional barrier to conducting research (223). There is evidence that healthcare professionals have limited knowledge of mental capacity legislation and the processes of informed consent for research. A study of UK care home managers' and practitioners' knowledge, understanding and use of the Mental Capacity Act 2005 (MCA) in practice, as opposed to a research context, found considerable variation in their understanding of the terms and principles of the MCA, with few participants aware of specific legislative points (224). A literature review of knowledge of consent for research into end of life care found that clinicians and researchers had poor knowledge of the ethics of consent and legislation governing adults lacking capacity, particularly the MCA (225).

A Canadian study assessed the knowledge of four groups (older adults, informal caregivers of cognitively impaired individuals, researchers in aging, and members of institutional review boards (IRB)) regarding who is legally authorised to consent to health care or research involving older patients (226). The study found that, while 80% of respondents correctly responded to questions about a person who was competent to consent or incompetent but legally represented, knowledge was worse (from 2% among older adults to 44% among REB members) for scenarios describing a research situation that involved an incompetent adult without a legal guardian (226). A survey of clinical researchers in Alzheimer's disease in the US showed that many participants were unaware of the states' laws or legislation governing research consent for incapacitated adults, including whether proxy consent is permissible and, if it is, who can serve as a proxy (227). This lack of knowledge may impact on their confidence and competence in enrolling those in their care in research studies. There have been calls for interventions to improve the understanding of informed consent and the use of the MCA amongst frontline support staff, clinicians, and researchers involved with people with a learning disability and their families in the UK (227,228).

No previous studies have examined UK healthcare and social care professionals' understanding or knowledge of the legal frameworks. The vignette-based cross-sectional survey reported in this chapter examined health and social care professionals' understanding of the legislation governing proxy consent for research participation by adults lacking capacity in England and Wales.

4.2 Methods

A cross-sectional online survey was conducted using a series of vignettes created specifically for the survey. Cross-sectional surveys have been described as snapshots of the populations about which they gather data as they are usually used to collect data from a population of interest at one time-point (229). Vignettes have been defined as 'short stories about hypothetical characters in specified circumstances, to whose situation the interviewee is invited to respond' (230). Vignette-based studies have been used in a wide range of scientific fields, including professional ethics (231), and have been used in studies examining professionals' attitudes and decision-making about medical treatment (232) and clinical trials (233).

4.2.1 Participants

Participants comprised of health and social care professionals whose role involved patients, service users or research participants from populations considered to be more likely to experience impaired decision-making capacity. This included medical and nursing professionals, Allied Health Professionals, and social care practitioners.

4.2.2 Sampling

The objective of the study was to obtain descriptive data; therefore, a formal sample size calculation was not performed. The target sample size of approximately 150 participants was informed by similar studies of Chief Investigators in the US (227) and researchers in ageing in Canada (226).

Health and social care professionals involved in caring for populations who are likely to include adults with cognitive impairments were identified through special interest and

professional groups such as the British Geriatrics Society and the Royal College of General Practitioners' Research Ready programme. These specialties were chosen, as they are likely to be involved in research involving adults with cognitive impairments who lack capacity to provide informed consent for themselves. Emails containing an invitation to take part and the link to the online survey were distributed by the groups/networks to their members or added to their newsletters. Social media platforms such as Twitter were also used to share details of the survey.

Prior to their participation the participants were required to confirm that they were a health or social care professional based in England or Wales, and that their role involved the care of patients/service users/research participants, some of whom may be unable to make decisions for themselves (i.e. people lacking capacity).

4.2.3 Data collection

The survey was conducted using an electronic survey instrument (Bristol Online Survey) using both fixed-choice and open-ended questions to explore participants' knowledge of the enrolment process for adults lacking capacity and their understanding of the legal frameworks through vignettes (see **Appendix 7. Vignettes used in cross-sectional survey**) describing five hypothetical situations. The vignettes were designed to explore the participants' knowledge and opinions regarding who should decide whether a person who lacks decision-making capacity will take part in a study. Each hypothetical study had varying levels of potential risk, with vignettes 1, 3, and 4 stating that there was no serious risk to participants; both clinical trials (vignette 2 and 5) and other types of research study were included. Sufficient detail was provided to allow identification of the appropriate proxy decision-maker.

Participants were required to indicate in each case who they considered to be legally authorised to decide whether the person should take part in the study or not by ticking all applicable answers from a list of carers and professionals involved with the person. Open text boxes were provided to allow respondents to provide explanations for their answers in response to the question 'What aspects of the case are relevant to your decision?' Sociodemographic information was also collected from the participant (gender, profession, length of time in professional role) and his/her prior experience of, or involvement in, research. Following their participation, participants were offered the opportunity to

download a summary of the legislation governing proxy consent for research participation by adults lacking capacity in the UK, which included the scenarios in the survey (**Appendix 8. Legal summary of research involving adults who lack capacity**).

The survey was piloted with seven health and social care professionals with similar characteristics to the sample population to test the survey acceptability, comprehensibility, and questionnaire content. Minor amendments were made to the survey design and content following the pilot.

4.2.4 Data analysis

Survey data were exported and analysed using IBM Statistical Package for the Social Sciences (SPSS software V.23) and qualitative data analysis software (NVivo 11)(180). Data were analysed to describe any associations between participant characteristics and responses that were concordant (or not) with the regulatory frameworks. Data were coded by themes identified both *a priori* and those identified during data analysis.

Concordance was assessed using the fixed choice answers and open-text responses. Responses were considered wholly concordant if the legally authorised decision-maker was selected (or included in the choice if multiple options were selected) and the text explicitly supported the reasoning behind the choice (or did not discredit the choice), and partially concordant if the text indicated an understanding of the legally authorised decision-maker or process. Responses were considered to show discord with the legal frameworks if the legally authorised individual was not selected and the text failed to support the true decision-making process or was directly opposed to it. Responses where the open text contained conflicting statements, or the selected option and text conflicted, were categorised as unclear or mixed. Where participants had selected a 'don't know' option or indicated in the text that they were unsure how to respond, responses were categorised as demonstrating uncertainty.

4.2.5 Ethics and research governance

A favourable opinion was obtained for the survey prior to its commencement from Cardiff University School of Medicine Ethics Committee following ethical review (SMREC reference: 16/63). Participants were provided with information about the study, including contact details for more information if required prior to participation. As the study was conducted

using an online survey tool a separate consent form was not required (234), however participants were required to agree with a statement confirming that, by completing the questionnaire, they were consenting to take part in the study.

4.3 Results

4.3.1 Survey results

The study commenced with an internal pilot in February 2017. Recruitment of participants, understanding and completion of survey, and provision of open text responses was assessed after 12 participants (approximately 10% of survey intended sample size). The decision was made to proceed with no amendments to the full survey, which opened in March 2017 for two months.

Including those in the internal pilot, 127 participants completed the survey (see **Table 4-1 Survey participant characteristics**). Participants were predominantly female (80%), worked in Wales (56%) and had a nursing background (34%). Medical professionals who provided details about their role included general practitioners (GPs) (n=13), and specialists in palliative medicine (n=2). Nursing professionals included Registered Mental Health nurses (n=9), research nurses or researchers (n=10), and those working in palliative care (n=5). Those identifying as allied health professionals were a diverse group that included midwives, clinical psychologists, paramedics, occupational therapists, speech and language therapists, and physiotherapists. Social care practitioners included care home managers or other staff (n=12), social workers (n=6), and those who had a role as an independent advocate or Best Interest Assessor (n=4).

Most participants were experienced professionals, having been in their role for more than 8 years (83%), and many were involved in research (63%) in a range of research roles but most commonly recruiting participants (31%).

Table 4-1 Survey participant characteristics

Characteristic	No. Participants n (%)
Country	
England	56 (44%)
Wales	71 (56%)
Gender	
Male	21 (17%)
Female	102 (80%)
Prefer not to say	4 (3%)
Professional background*	
Medical professional	28 (22%)
Nurse	44 (35%)
Allied health professional	29 (23%)
Social care practitioner	28 (22%)
Length of time in profession	
Less than 12 months	1 (1%)
1-2 years	6 (4%)
2-5 years	4 (3%)
5-8 years	11 (9%)
More than 8 years	105 (83%)
Involvement in research as part of role	
No	47 (37%)
Yes	80 (63%)
If yes: *	
<i>In a minor role (research being carried out where I work)</i>	33 (41%)
<i>Informing patients/service users about research studies</i>	37 (46%)
<i>Recruiting participants for research studies</i>	44 (55%)
<i>As a Principal Investigator at a research site</i>	18 (22%)
<i>As a Chief Investigator</i>	11 (14%)
Heard about the survey	
Invited through research/professional network or organisation	89 (70%)
Shared on social media	30 (24%)
Other	8 (6%)

*Participants could select more than one option if more than one applied

Responses indicated a broad spectrum of understanding about the legal frameworks, although responses were predominantly discordant with the law with low levels of understanding and some degree of uncertainty expressed. The number of options for the legally authorised decision-maker selected by participants was reasonably consistent across all five vignettes (**Table 4-2 Survey participant responses of decision-maker selected by**

vignette). For research studies where the MCA applies (Vignettes 1, 3, and 4) the family member may act as the personal consultee and provide advice about what the person’s wishes would be, if they had capacity in the matter; however, the decision about whether they take part in the study or not lies with the researcher (20,235). Where the research is a clinical trial of a medicinal product (vignettes 2 and 5) it is governed by the CTR (22). Under the provisions of the Regulations, the family member described in the vignette may act as personal legal representative and provide legally valid informed consent on the person’s behalf without any legal process such as a Lasting Power of Attorney for Health and Welfare (LPA) or court order (22).

Table 4-2 Survey participant responses of decision-maker selected by vignette

Decision-maker	Vignette 1 n (%)	Vignette 2 n (%)	Vignette 3 n (%)	Vignette 4 n (%)	Vignette 5 n (%)
No-one	14 (11%)	11 (9%)	7 (5%)	15 (12%)	6 (5%)
Person featured in the vignette (patient or care home resident)	49 (39%)	41 (32%)	30 (24%)	32 (25%)	46 (36%)
Family member described in vignette	46 (36%)	43 (39%)	57 (45%)	60 (47%)	48 (38%)
Medical professional described in the vignette	17 (13%)	28 (22%)	26 (20%)	38 (30%)	33 (26%)
Multi-disciplinary team following a Best Interests decision meeting	68 (53%)	75 (59%)	68 (53%)	44 (35%)	75 (59%)
The researcher	14 (11%)	10 (8%)	13 (10%)	16 (13%)	8 (6%)
I don't know	4 (3%)	7 (5%)	11 (9%)	8 (6%)	7 (5%)
Other	2 (2%)	6 (5%)	3 (2%)	2 (2%)	3 (2%)
Care home manager*	-	-	25 (20%)	-	13 (10%)

Participants were able to select more than one response in all vignettes

Shaded boxes indicate the option that was congruent with the legal frameworks in that vignette

*Option in Vignette 3 and 5 only

4.3.2 Concordance with the legal framework

Very few responses were wholly congruent with the legal frameworks. Most participants provided a mixture of responses across all five vignettes, including discordant, concordant, uncertain, and mixed or unclear responses (**Table 4-3 Survey participant response concordance by vignette**).

Table 4-3 Survey participant response concordance by vignette

Concordance	Vignette 1 n(%)	Vignette 2 n(%)	Vignette 3 n(%)	Vignette 4 n(%)	Vignette 5 n(%)
Discord	104 (82%)	96 (76%)	96 (76%)	104 (82%)	94 (74%)
Concord	12 (9%)	15 (12%)	10 (8%)	10 (8%)	23 (18%)
wholly	5	6	5	1	5
partially	7	9	5	9	18
Uncertain	5 (4%)	7 (5%)	12 (9%)	7 (5%)	4 (3%)
Unclear/mixed	6 (5%)	9 (7%)	9 (7%)	6 (5%)	7 (5%)

Half of the participants (46% 58/127) provided responses that were discordant with the legal frameworks in all five scenarios. Only 2 participants (2%) provided concordant responses across all five scenarios. Both were from a nursing background and actively involved in research, which included recruiting participants for studies. 24 participants provided either an 'I don't know' response or text that indicated an uncertain response to one or more scenarios, including one participant who responded that they were uncertain in all five vignettes. Vignette 3, which concerned a low risk study of a communication device being trialled in a nursing home, had the highest number of uncertain responses (9% 12/127).

Analysis of factors given as being relevant to the scenario revealed that the family member was selected as the decision-maker as they were considered to be the 'next of kin'. Where this response was provided, it was more common from participants from a healthcare professional background (93% 27/29) compared to those from social care practitioners (7% 2/29). Selection of the multi-disciplinary team (MDT) as decision-maker following a best interests meeting was common and was the predominant option in all the scenarios apart from vignette 4 which involved a study requiring access to medical notes and investigation results. Responses indicated that participants were unclear whether consent was required (or not) prior to access medical notes for research purposes.

'Best interests' was commonly reported as a factor relevant to the scenario (n=135) by both healthcare professionals (67% 90/135) and social care practitioners (33% 45/135). One participant (a senior social care practitioner) was concerned that the proposed intervention in Vignette 3 may be viewed as restrictive of the participant's liberty and questioned whether Deprivation of Liberty safeguards were in place. The same participant felt that the appropriate decision-maker was the nurse assessor from the NHS body that would commission his care in the nursing home. Another participant (a senior social care practitioner) stated that, as there was no person empowered to make the decision, the matter may need to be brought before a judge.

4.3.3 Relevant variables in decision-making

Neither the level of perceived risk, nor the study type, appeared to affect the level of knowledge or understanding. When comparing professional groups, nurses consistently had the highest proportion of responses concordant with the legal frameworks, between 30% and 50% depending on scenario, although they were also the largest professional group. Social care practitioners provided the highest proportion of responses that were discordant in all scenarios (71% 20/28), although there were much lower levels of involvement in research (36% 10/28) compared to other professional groups. GPs were commonly cited as the authorised decision-maker by other groups, as well as by GPs themselves, with the exception of a postoperative medication trial in a hospital setting (vignette 2). However, GPs own responses were no more concordant than other groups, with 54% (7/13) providing responses that were discordant across all five scenarios, and others expressing degrees of uncertainty. Prior involvement in research did not appear to affect the level of knowledge or understanding. Health and social care professionals who led research studies as either a Chief Investigator of a study or a Principal Investigator at a site did not provide responses that were more concordant than those who did not have a responsibility for leading studies; with 40% (10/25) providing discordant responses across all scenarios.

4.4 Discussion

The levels of knowledge of the legislation governing research involving adults lacking capacity found in this study were predominantly low, which raises concerns about the accessibility of research and the opportunity to participate for those who lack capacity, the

ability to conduct research involving such groups, and subsequently the impact on the evidence-base for their care.

4.4.1 Legally-authorized decision-maker

The findings demonstrated low levels of knowledge of the dual legislation governing research involving adults lacking capacity, which supports previous concerns about the complexity of the regulatory framework (33,236). Participants generally did not distinguish between research involving medicinal products and other types of research, nor between the processes of consultation and consent. Participants did not recognise that the researcher is the decision-maker under MCA (20), or that the MCA provisions enable recruitment without consent as there are additional legal safeguards in place such as stringent ethical review. For the two vignettes that involved a clinical trial of a medicinal product (vignettes 2 and 5) more participants identified the close family member as the decision-maker (22), although not necessarily recognising that they were providing legally valid informed consent on the person's behalf.

Of concern was the lack of understanding that a person who knew the person well in a personal capacity is legally authorised to provide consent under the Medicines for Human Use (Clinical Trials) Regulations (CTR) (22), or that a LPA or Court order is not required. This response was more frequently provided by social care practitioners, rather than health or allied health care professionals, and was reported by those considered to be senior practitioners (>8 years in their role). The role of the attorney in providing consent for medical research has been reported elsewhere to be unclear (237). However, an LPA for Health and Welfare is generally limited to health and care decisions, rather than medical research. The individual acting as personal consultee or legal representative does not need to be a legally appointed attorney or deputy, the MCA merely states that:

'The fact that a person is the donee of a lasting power of attorney given by P, or is P's deputy, does not prevent him from being the person consulted under this section.' s32(7)(20)

It may be considered good practice to consult the attorney as part of the requirement to seek the views of any carers and other relevant people before involving a person who lacks capacity in research (s7.57, s11.20 (235)). However, under existing law, the researcher (in accordance with the advice from the consultee) or the legal representative is the legally

authorised decision-maker. The role of LPA in research decisions is returned to later in the thesis.

4.4.2 Ethical basis for the decision

A second key finding was that participants widely reported the basis for the decision was what was considered to be in the person's best interests, regardless of who made the decision. Best interests is the dominant standard for treatment and care decisions, but not for research according to the legal framework in England and Wales (235) and beyond (66). It is considered an ethically weak basis for enrolling those without capacity into research, which is not intended (or likely) to benefit them. Whilst it is likely that a person acting as a consultee or legal representative will be concerned for the welfare and interests of the person who they are acting on behalf of, this is not necessarily what is in their best interests.

The source of this misunderstanding may be that the MCA is now firmly embedded in treatment and care decision-making for adults lacking capacity. This includes the fourth statutory principle which requires that an act done, or decision made, on behalf of a person who lacks capacity must be done, or made, in his best interests (s1(5)(20)). This is qualified by the MCA Code of Practice as:

'The only exceptions to this are around research and advance decisions to refuse treatment where other safeguards apply' (s2.12(235)).

However, the failure to emphasise the crucial difference between research decisions and all others and clarify the ambiguity regarding the degree to which best interests is involved in research decisions, appears to have led to confusion and uncertainty about the role of 'best interests' in research involving adults who lack capacity.

4.4.3 Comparison with existing research

The findings from this survey are consistent with similar studies in other jurisdictions and for decisions other than research. Uncertainty about how the mental capacity legislation should be interpreted has also been reported in a survey of care home managers and key informant interviews exploring research in care homes (238). Bravo et al surveyed Canadian researchers, and found that there was a lack of awareness about who can act as proxy decision-maker for research (239). They called for greater clarity and education about who

can act as proxy decision-maker (239). An earlier study led by the same author examined knowledge of the legislation governing proxy consent to both treatment and research of four Canadian groups (older adults, informal caregivers of cognitively impaired individuals, researchers in aging, and members of research ethics boards) (226). They found that knowledge of proxy consent for research was lower (from 2% among older adults, 36% among researchers, to 44% among ethics board members) for the scenario describing research involving an adult lacking capacity who did not have a legal guardian. They recommended that more education, including public awareness campaigns, were needed (226). A US survey of clinical investigators into Alzheimer's disease found that many of those surveyed either did not know or incorrectly thought no laws or regulations existed regarding who has the authority to provide proxy informed consent in their state (227). They also found that respondents who asserted that no one could provide proxy informed consent also reported that very high proportions of their patients were capable of providing adequate informed consent. They concluded that further training on regulations governing research involving adults lacking capacity may be needed, and interventions to improve informed consent which included all those involved (227).

Limitations of this study include that this was a self-completed survey, which may have resulted in selection and response biases. Although participants were required to confirm their status as a health or social care professional, it could not be independently verified that participants responding via social media platforms held positions in health and social care. The high proportion of participants from Wales, compared to England, reflected the geographical location of the research team and some networks that disseminated the survey. The wording 'legally authorised' in the question may have been interpreted as a specific legal process of a transfer of decision-making authority, rather than who is authorised according to the legal framework, although the phrase has been successfully used in a similar survey (226). Participants may have selected all those they thought should be included in the discussion, rather than the decision-maker as specified in the task.

The survey was not restricted to those already experienced in research as a range of views was sought, and there is an increasing expectation that research activity will become embedded across the whole health and social care system. Additionally, health and social care professionals may also be approached to act as a nominated consultee or professional legal representative for those in their care, if no family member or friend is willing or able to act as a personal consultee or legal representative. However, the inclusion of some health

and social care professionals who had limited, or no experience of research means they may not have understood the nature of research, conflating it with medical treatment which is intended to benefit the person directly.

4.5 Summary

Research involving adults lacking capacity is complex, and decision-making processes differ from usual care and treatment decisions, and between different types of research. This can result in confusion for researchers, patients and their families, clinicians and other professionals. This descriptive study has suggested that health and social care professionals have low levels of knowledge and understanding of the legislation governing proxy decision-making for research participation.

Participants demonstrated a lack of knowledge about the locus of authority; viewing multidisciplinary teams as the only authorised decision-makers, who were entitled to make decisions in accordance with the person's best interests, as is the case for medical treatment and care. Family members and researchers were consigned to information provider roles, although some responses indicated that they included family members in the MDT.

4.6 Learning points

The vast majority of participants did not recognise that the basis for enrolling an adult who lacks capacity in research is what the person themselves would have wanted if they had capacity to decide, their 'presumed will'. Participants did not understand or acknowledge that the family member was best placed to advise, or decide, what the person's wishes would have been. Whether participating was in the person's 'best interests' was overwhelmingly cited as the ethical basis for the decision. This suggests that the standard has become ubiquitous in decision-making for adults lacking capacity, regardless of the legal validity in situations such as research participation decisions. This conflict arises when what is in the person's best interests, as a form of beneficence, is given precedence over autonomy.

Appropriate mechanisms for involving adults lacking capacity in research is vital if such groups are to have an equal opportunity to participate as all other members of society. The low levels of health and social care professionals' knowledge and understanding described

in this study is a concern if legally and ethically legitimate enrolment processes are not adhered to. Health and social care professionals' experiences and application of the legal frameworks in practice, and attitudes towards the inclusion of those with incapacity in research, may warrant further in-depth exploration.

The findings from this survey suggest that there is a pressing need for interventions to improve levels of legal literacy, including enhanced education and training which focuses on the legal frameworks governing research involving adults who lack capacity to consent.

Chapter 5 Content analysis of Participant Information Sheets for consultees and legal representatives in England and Wales

A version of this chapter has been published as: Shepherd V, Wood F, Griffith R, Sheehan M, Hood K. Research involving adults lacking capacity to consent: a content analysis of participant information sheets for consultees and legal representatives in England and Wales. *Trials* 2019; 20:233 (240).

5.1 Introduction

As outlined in the previous chapters, the Mental Capacity Act 2005 (MCA) has provision for consulting an individual who knows the person with impaired capacity well to advise about research participation on the person's behalf (20). For Clinical trials of investigational medicinal products (CTIMPs), the Medicines for Human Use (Clinical Trials) Regulations 2004 (CTR) (22) requires a relative or friend acting as legal representative to provide consent on the basis of what they would have wanted had they the capacity to choose for themselves, their 'presumed will' (22). Should no appropriate relative or friend be available or willing to act as the person's proxy or surrogate, under both the MCA and CTR there are provisions for a professional to act as a nominated consultee (s32(2)) (20) or legal representative (Schedule 1, Part 1(2(a)(ii))) (22). Neither the MCA nor CTR have requirements regarding the information that should be given to the person acting as proxy about their role as proxy decision-maker, only concerning information that must be provided about the research project itself. A consultee is provided with information about the project, and asked what the potential participant's likely wishes and feelings would be about taking part in the project if he or she had capacity (20). For CTIMPs, the legal representative must be provided with the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted prior to giving consent (22). Written information about the study is tailored for proxies, usually in the form of an amended version of the information provided to participants themselves. If they are willing to act as proxy, they will then be asked to provide written confirmation of their advice regarding the person's wishes (20) or informed consent on their behalf (22). This is recorded using a consent form for clinical trials (22) or consultee declaration form for other types of research (20).

Proxy versions of Participant Information Sheets and consent or declaration forms are not standardised, and there is minimal guidance available for researchers when drafting documents for studies involving adults lacking capacity, although some templates are available (241). There is no guidance for proxies about how their decision should be made, or what to do if they are unable to determine what the person would have wanted. Many studies have empirically evaluated the readability and content of Participant Information Sheets and consent forms (242–245), and assessed participant comprehension (246). However, no previous studies have examined written information provided to proxies.

The study reported in this chapter aimed to understand the information context within which decisions about research are made by personal and professional consultees and legal representatives. Content analysis was used to explore the written information provided to proxies who have been approached to be involved in decision-making about research participation for an adult who lacks capacity to consent.

5.2 Methods

Documents can be considered as socially situated products that are produced, consumed and used in specific settings, where it is important to understanding how they function (247). Content analysis is an empirically grounded research method (248) which has been described as providing a ‘systematic and objective means to make valid inferences from verbal, visual, or written data in order to describe and quantify specific phenomena’ (248). Content analysis can take many forms (247,249). Content analysis has been used in a range of academic disciplines, including social and healthcare sciences, and has been applied to a variety of data and to various depths of interpretation (249). It allows for a much deeper understanding of the functioning of the document and exploration of the meaning and interpretation than merely examining the content empirically (247). This study was conducted using a pragmatic content analysis approach (247), incorporating both quantitative and qualitative analyses.

5.2.1 Sampling

Current or recently completed (i.e. within the preceding three years) studies were identified from the National Institute for Health Research (NIHR) co-ordinated UK Clinical Trials Gateway (UKCTG) public database (formerly the NIHR Portfolio database). Studies which

included participants aged 16+ years who may lack decision-making capacity, and therefore require proxy involvement, were eligible for inclusion. UKCTG primarily uses condition-specific search terms, in addition to filters such as trial status, therefore studies were identified by searching the database for appropriate medical conditions or populations. Studies that involved emergency research, and therefore a consent waiver where no proxy is involved at the time of recruitment were excluded.

Searches were conducted in June and July 2017. Eligible studies were divided between three groups of conditions that may be associated with:

- Progressive loss of capacity – search terms: dementia (all types) and Huntington’s disease
- Sudden loss of capacity – search terms: stroke, traumatic brain injury, and requiring critical care
- Life-long impaired decisional capacity – search terms: Down’s syndrome, learning disability.

All types of study designs were included. A sample of 30 studies was randomly selected from the list of eligible studies, stratified by the three populations. In content analysis, there are no established criteria for the number of sampling units or objects to study; the sample size is based on the informational needs and the ability to answer the research question with confidence (250). The sample size estimation for this analysis was derived from a similar study examining consent forms for clinical genetic content (245).

All study documents provided to the proxy were obtained through the UKCTG database links (funder or sponsor’s website, study website etc.) or were requested from the lead investigator, project co-ordinator, or sponsor as appropriate. Studies were only eligible if study documents were available. Where study documents could not be obtained, the study was considered to be ineligible and a replacement study was randomly selected from the same condition/group. Sampling continued until the target sample was reached.

The information that related specifically to the proxy’s role was reviewed, rather than information about the study *per se*. Attention was paid to the context in which the documents were used: the type of research and study population, information about why the proxy has been approached (including whether they were approached in a personal or

professional capacity), the proxy's role in the decision-making process, the required basis for the proxy's decision, and any information or guidance about how the proxy might approach the decision including any sources of guidance or support. The frame of reference was the legislation governing research involving adults lacking capacity in England and Wales.

5.2.2 Data collection

The sampling unit for inclusion was the study, the unit of analysis were the documents provided to proxies to provide information to help inform their decision-making for each study. These documents included proxy/participant information sheets (PIS), informed consent or declaration forms, or other relevant documents. Studies were allocated a unique reference number and anonymised to remove any identifiable information. Study documents were reviewed and analysed for content relating to the role of the proxy and the decision about research participation, and area of interest data extracted. The respective numbers and types of document were recorded by individual study and per group (progressive loss of capacity, acute loss of capacity, no prior capacity).

Content areas, defined as parts of the text that address a specific topic, were identified and extracted. Content was divided into that which informed the proxy why they had been approached; the basis for their decisions; how the proxy might approach making a decision; practical instructions to be followed; and information about withdrawal from the study. The analysis process followed that outlined by Bengsston (250) as a series of iterative steps, with the four main stages being: decontextualisation of the unit of analysis, recontextualisation, categorisation, and compilation. The meaning unit (or coding or content unit) was defined as words, sentences or paragraphs containing aspects related to each other through their content and context (249).

5.2.3 Data analysis

The documents were reviewed in order to ensure familiarity with the text, and the content areas from the study documents were extracted and entered into qualitative data analysis software (NVivo 11) (180). During the decontextualisation stage the meaning unit (the words or sentences that are intended to convey an item of information or instruction to the proxy about their role or decision) was coded using a coding framework agreed between three researchers. The data were coded iteratively with discussion with the research team to

increase the stability and reliability of the coding process. Sample data extracts were regularly reviewed by the group to ensure consistency of coding.

During the recontextualisation stage, the meaning units were re-read alongside the original data to ensure the content was adequately captured, with no extraneous data included that was not relevant to the aim of the study (250). For the categorisation stage, the themes and categories emerging from the meaning units were identified. There are no universally adopted concepts for the headings used in content analysis (250), however themes were the broader overall concepts, and the categories were the smaller sub-themes that brought together a number of related meaning units.

The compilation stage drew on a manifest level of analysis, which stays very close to the original text to describe *what was said* using the visible and obvious (251). Given the nature of data contained in this type of document, a manifest analysis which stays closer to the original meaning and context was considered to be appropriate. The data were summarised narratively according to each theme and category. A summary of themes and categories was tabulated, with illustrative meaning units presented. The themes and categories were quantified, to allow a greater representation of information (250).

5.3 Results

Of 1194 potentially eligible studies identified, 70 studies (6%) included adults lacking capacity. Study documents could not be obtained for 15 studies, either because there were no viable contact details for the study, or there was no response from the study team. There were no refusals. Sampling ceased when documents had been obtained for a total of 30 studies, which were subsequently included in the review (**Table 5-1 Characteristics of content analysis screened and included studies by population**). An additional file shows the study characteristics in more detail (**Appendix 9. Characteristics of studies included in content analysis**). Studies included both observational and interventional studies, of which 9 (30%) were classified as a clinical trial of a medicinal product. The majority of studies were sponsored either by a higher education institute (n=19, 63%), or by an NHS organisation (n=10, 33%). The NIHR were the funding body in 22 studies (73%), followed by charitable funders (n=7, 23%). Studies were either ongoing (n=14, 47%) or had been completed within the previous three years (n=16, 53%).

Table 5-1 Characteristics of content analysis screened and included studies by population

Population	Search term	No. studies identified	No. potentially eligible* studies	No. studies included	No. CTIMPs** included	Study IDs
Life-long impaired capacity	Down's Syndrome Intellectual disability Learning disability	181	9	4	1	01-04
Progressive loss of capacity	Alzheimer's disease Dementia Huntington's disease Care home(s)	505	33	12	1	05-16
Sudden/ acute loss of capacity	Critical care Acute stroke Traumatic brain injury	508	28	14	7	17-30
Total		1194	70	30	9	

* Eligible if study documents available (all other eligibility criteria having been met)

** Number of clinical trials of investigational medicinal products (CTIMPs) included

5.3.1 Quantitative data

Studies primarily combined information about the proxy's role with information about the study itself into one single document (n=28, 93%), although two studies had separate documents where a document that covered only the role of the proxy then referenced the study information contained in the standard Participant Information Sheet provided to all participants [study ID 04, ID 12]. Consequently, study information sheets ranged considerably in length (**Table 5-2 Content analysis quantitative data from study information sheets**). Where the information sheet combined information about the proxy's role and the study, the area of interest that related to the proxy's role comprised 7-67% of the total length of the document. Information sheets for professionals acting as proxy (median number of words 1610) were shorter than those for personal proxies (1698 words) and for professionals and personal proxies jointly (1788 words).

Table 5-2 Content analysis quantitative data from study information sheets

	Total no. of documents n = 42 (%)	Unit size by no. words range (<i>median</i>)
Total length of document	42	217 - 3997 (1665)
<i>CTIMP*</i>	14	217 – 2676 (2067)
<i>Non-CTIMP**</i>	28	230 – 3997 (1602)
Total area of interest	42	79 – 926 (344)
<i>Proportion of total length of document (area of interest/total length of document)</i>	42	79/1197–641/953 7–68%
<i>CTIMP</i>	14	79 -371 (232)
<i>Non-CTIMP</i>	28	155 – 926 (422)
Why the proxy is being approached	42 (100%)	22 - 494 (104)
<i>CTIMP</i>	14	22 – 217 (122)
<i>Non-CTIMP</i>	28	27 – 494 (98)
Basis for the decision	38 (90%)	8 - 267 (83)
<i>CTIMP</i>	10	14- 123 (51)
<i>Non-CTIMP</i>	28	8 – 267 (107)
How the proxy might approach deciding	13 (31%)	18 – 185 (67)
<i>CTIMP</i>	1	76
<i>Non-CTIMP</i>	12	18 – 185 (66)
Practical instructions for the proxy	38 (90%)	18 – 309 (80)
<i>CTIMP</i>	10	18 – 151 (75)
<i>Non-CTIMP</i>	28	28 – 309 (83)
Withdrawal from the study (including proxy's role)	34 (81%)	19 – 168 (44)
<i>CTIMP</i>	11	25 – 87 (49)
<i>Non-CTIMP</i>	23	19 – 168 (43)

* CTIMP: Clinical trial of an investigational medicinal product – governed by CTR

** Non-CTIMP: Research other than a clinical trial of an investigational medicinal product – governed by MCA

Studies were divided into those who provided separate documents for proxies acting in a personal capacity (relative or friend as a personal consultee or personal legal representative) and a professional capacity (nominated consultee or professional legal representative) (n=10, 33%), joint documents for both personal and professional proxies (n=9, 30%), where

studies had provision for personal proxies only (n=8, 27%), or where information sheets were not provided for professional proxies (n=3, 10%).

Content relating to why the proxy was being approached was found in all 42 study documents. Content relating to other categories of information varied considerably, with only 12 documents (29%) providing information about how the proxy might approach decision-making.

5.3.2 Key themes

5.3.2.1 *Representing the wishes, feelings and interests of the person with impaired capacity*

Almost all studies advised proxies to consider the wishes and feelings of the person they represented using standard phrases such as ‘You are being asked to advise the researchers about this person’s wishes and feelings’. Some extended this to advising on the person’s views about taking part in research in general, or the particular study in question using phrases such as ‘you may be aware of any views they may have about taking part in such a project’.

With the exception of two studies, the information sheets made no reference to the temporal aspects of the person’s wishes and feelings – whether the proxy should consider their past or presently expressed wishes – and the comparative weight that should be afforded to current and prior wishes should they conflict. The two study documents that did include temporal considerations stated that the proxy should base their advice on their knowledge of the person they represented and both, ‘their past and present views or feelings’ [ID 12, ID 14]. The MCA uses the future conditional tense to require the proxy to consider ‘what the person's wishes and feelings about taking part in the project *would be likely to be* if they had capacity in relation to the matter’ (s32(4b)) (20). The CTR provide less guidance, merely that the informed consent given ‘shall represent that adult’s presumed will’ (Schedule 1, Part 5, Principle 12) (22). Some study documents extended the proxy’s role to consider the interests of the person they represented as well as their wishes and feelings. This reflects the phrasing used in the template developed by the UK Health Research Authority (HRA) as part of their guidance (241). One study listed factors that the proxy should consider when making a decision, including: the aims of the research, previous thoughts and wishes, risks and benefits to them and others, how being involved with the research would

affect their routine, and any advance decisions about participating in research they may have made [ID 15]. One study advised the professional representative to ensure that there were no other known factors (e.g. cultural or religious beliefs), which may influence whether the patient would want to participate in medical research [ID 19].

Some study documents directed the proxy to disregard their own views when making a decision, through stating that 'it is important that you should set aside any of your own personal views about the project' or 'your views of research in general' [ID 02, ID 06, ID 12, ID 14, ID 22].

5.3.2.2 *Consulting with others*

Around half of the study documents (n=16) included advising or directing the proxy to consult with others during the decision-making process, phrased as either talking to others if wished, or if necessary. Some specified who might be consulted, including other relatives, friends, or healthcare professionals; while professional proxies were advised to restrict this to 'other colleagues who have an interest in the person's welfare, but who won't be involved in the research themselves' [ID 12]. Although there is no specific requirement to consult others under either the MCA or CTR, the MCA generally adopts a consultative approach to decision-making encouraging the involvement of others who are engaged in caring for the person or interested in the person's welfare when decisions are made (s4(7b)) (20). If the proxy was uncertain about taking on the role, eight studies advised that they could seek independent advice, although no information was provided about how or where that advice could be obtained. A small number advised the proxy to consult with the person him/herself, phrased as to 'attempt' or 'try to' seek the views of the person.

5.3.2.3 *Consultee's role*

Some of the non-CTIMP studies made it clear that the consultee was not being asked to provide consent on the person's behalf, as would be the case if they were a legal representative in a CTIMP. This was either through stating that their role was to give advice about the person's wishes [ID 04], or through formally stating it in the description of the proxy's role, such as 'A personal consultee is not asked to provide consent for or on behalf of their relative/friend' [ID 12]. In some documents where this statement was included, the wrong terminology was sometimes still used 'After appropriate consultation we would like you to complete the attached *consent form* indicating whether you feel the named person

would or would not have wished to participate' [ID 14], and 'The consultee does not give consent, only advice' was then followed by 'We would also like to seek your consent so that any remaining samples may be stored and used in possible future research' [ID 28] although this is not required (252). Only one study directly stated that the responsibility to decide whether the participant should be entered into the research lies ultimately with the researcher [ID 16].

5.3.2.4 *Extension of the proxy's role to include determining eligibility*

A small number of studies appeared to extend the scope of the proxy's role beyond that of representing the person's wishes or feelings about participation, or their presumed will. One information sheet provided to personal consultees had the option for the consultee to decline the study on behalf of the person if they didn't consider that their relative/friend was 'well enough to take part' [ID 12]. The role of professionals acting as legal representative was sometimes extended to determining the person's eligibility for the study, such as by asking for their 'written agreement to indicate you are satisfied the patient fulfils all inclusion criteria and none of the exclusion criteria (set out below)' [ID 19], or to 'make a decision about whether or not the patient is eligible to take part and whether it would be appropriate for them to be involved' [ID 27] or simply confirming that they understand 'what the study involves, including inclusion and exclusion criteria' [ID 30]. This was despite eligibility forming part of the investigator's role, as opposed to the role of the professional legal representative, which is to represent the person's wishes and feelings as someone who is unconnected to the study.

5.3.2.5 *Advance decisions*

Some studies asked proxies to inform the researchers about any advance decisions the person may have made, stating that these 'should take' or 'will take' precedence [ID 02, ID 25]. Others extended the scope to 'any advance decisions they may have made about participating in research' [ID 11, ID 13, ID 15, ID 22, ID 26]. This statement reflects the wording used in the HRA template (241). However, the MCA has provisions for Advance Decisions to Refuse Treatment which relate to *refusal* rather than a positive request, and refers to *medical treatment decisions* rather than those about research (20). The MCA Code of Practice states 'Researchers must not do anything the person who lacks capacity objects to. They must not do anything to go against any advance decision to refuse treatment or other statement the person has previously made expressing preferences about their care or

treatment' (s11.30) (235). This means the researcher has an obligation to respect the person's expression of refusal that may conflict with participation in a research study, i.e. where the care/treatment being refused is part of the intervention or associated requirements.

5.3.2.6 Inaccurate use of terminology

There were many instances of errors in the use of the terms for the proxy, where they were called a 'legal representative' when the study did not fall under the scope of the CTR, or the term 'consultee' was used when the MCA was not the governing legislation. A combination of terms was used for proxies in some studies ['professional consultee' ID 17], and alternative terms were introduced in some studies: 'independent physician' and 'proxy relative' [ID 27], and 'Registered Medical Practitioner' (ID 30). The term 'assent' was used in three studies [ID 12, ID 14, ID 22] either in the information sheet provided to the proxy, or in the title of document. Assent is not a recognised term in legislation governing research involving adults in England and Wales, although it is used in paediatric research and used in other jurisdictions.

The term 'consent' was used when the process was in fact consultation [ID 18, ID 22], or where the consultee declaration form required the 'Name of Person taking consent' [ID 03]. The opposite was also observed, where informed consent should have been obtained from the legal representative, but the documents referred to 'consultation' and 'consultee' [ID 26], or 'declaration' as illustrated by 'We will seek written informed consent from the patient, or declaration from a personal legal representative, as soon as possible after the patient's admission' [ID 19].

5.3.2.7 Disconnect between information provided to professional and personal proxies

Not all studies reviewed included the option of a professional acting as proxy. It was not clear in these studies whether the person could take part in the study if no personal proxy was able or willing to be involved. Despite the shared legal basis of personal and professional proxies, some studies appeared to differentiate between them. This extended to consent forms that differed significantly, both visually and in terms of content, from standard consent forms used in research. The appearance of these consent forms was more consistent with a consultation letter than a consent form. Unlike the personal legal representative consent

forms, they did not contain individual statements or boxes to be initialled, no counter signature was required from the person obtaining consent [ID 09, ID 23], they did not include similar statements about providing consent for access to medical notes by the research sponsor or other representatives [ID 09, ID 23], or consent to obtain a blood sample for analysis for the study and retention for future related studies [ID 09]. For one study there was no information sheet for professional legal representatives, and in place of a consent form there was a small section to be completed on the baseline case report form [ID 24]. In a second study there was also no information sheet for the nominated consultee, and the 'Registered Medical Practitioner form' did not mention 'consultee' or refer to advice regarding the person's wishes and feelings and had only two statements, one of which was that they had no objection and were not aware of any objections to the participant being enrolled in the study [ID 30]. One information sheet for professional legal representatives listed the inclusion and exclusion criteria, and details about the dose of the medicinal product being investigated, its preparation and administration, and trial unblinding procedures, whereas the equivalent for a personal legal representative did not [ID 19].

5.3.2.8 Inaccurate interpretation of the law

Some study documents appeared to inaccurately interpret the legislation. This included statements such as 'When determining who is able to provide such consent, the Medicines for Human Use Regulations state that the individuals' parents should always be approached first' for a trial involving adults with learning disabilities [ID 01]. The CTR do not specify which family members or friends, nor in what hierarchical order the researcher should approach family members to act as proxy (22). Another included the requirement that a mental capacity assessment be undertaken on all potential participants, during which specific details needed to be recalled by the person (a care home resident) as a form of test prior to being deemed to have capacity to provide informed consent for the study [ID 05]. The MCA clearly states that a person must be assumed to have capacity unless it is established that they lack capacity, and this presumption is a key principle underpinning the Act (s1(2)) (20). Other studies incorrectly stated the legal basis for the proxy's decision, such as they are required to 'assess whether study enrolment is in the patient's best interest' [ID 19]. Whilst the MCA has as one of the underlying principles that 'An act done, or decision made, under this Act for or on behalf of a person who lacks capacity must be done, or made, in his best interests' (s1(5)) (20), the exception to this is regarding decisions about research (s2.12) (235).

5.4 Discussion

The database search in this study confirmed findings from other sources that only very small numbers of studies include people who lack capacity (12,221,222). All included studies could recruit participants both with and without capacity and had study documents for the participant themselves if appropriate (these documents were not included in the study documents analysed). All studies had received Research Ethics Committee (REC) approval and were either currently recruiting participants or recruitment had been completed. Despite this, issues with incorrect terminology were common. This suggests that issues identified in a study which was conducted shortly after the introduction of the MCA, where the legal requirements for research involving incapacitated adults were not being consistently or correctly interpreted by researchers and RECs (218), are largely unchanged in the decade since. This lack of clarity may reinforce any confusion and lack of understanding about the legislation by health and social care professionals, leading to the exclusion from research of those who lack capacity (33). The discrepancy between the legislative requirements and their operationalisation in practice due to inaccurate interpretation of the law is also significant as it may affect the identification and involvement of the correct proxy in the decision-making process and interfere with the appropriate legal and ethical basis for that decision.

Study documents were relatively consistent in the information provided to proxies about why they were being approached (to provide advice as to whether the person who lacks capacity to decide for themselves should take part in the research), and the basis for their decision (what, in their opinion, the person's wishes and feelings about taking part in the study would be). Only a small number of information sheets advised the proxy to seek the views of the person themselves. These were all from studies involving care home residents [ID 12, ID 13, ID 14] whose lack of capacity may be associated with dementia and may be particularly subject to fluctuation and variation in decision-making capacity compared to the populations included in other studies. Although CTIMP information sheets were longer than those for non-CTIMP studies (median number of words 2067 compared to 1602), as found in other studies (253), the content that related to the role of the proxy in CTIMPs was nearly half that provided in non-CTIMPs (median number of words 232 compared to 422).

Information sheets varied considerably in the content relating to how the proxy should make a decision, with 21 studies not providing any such information across a total of 29 documents. Four of the information sheets did not provide information about withdrawing the person from participating; a further two provided it to the personal proxy only and not the professional acting as proxy [ID 19, ID 23]. These two studies involved the participant being followed up for 28 days and requesting withdrawal is a key part of the proxy's role throughout the whole duration of a participant's involvement in a study (s32(5)) (20), although it was included as a statement in the consent form for one of the two studies [ID 19]. Some studies did inform proxies that the researchers would seek consent from the participant once (or if) they regained capacity or from relatives/friends in the interim, but this approach risks leaving the participant without anyone to represent them in the intervening period.

Disparities were seen between documents for professionals acting as proxy and those for relatives/friends, particularly in acute and critical care studies. The role of the professional representative was distinguished from that of the personal proxy in several of the studies, both in the amount and content of the information provided to them, and how their consent or advice was sought and documented. This role was 'medicalised' in some settings (notably in critical care studies) where it was treated more like a consultation for a second medical opinion about the patient's suitability and eligibility for the study, rather than an attempt to represent the person's wishes and feelings about taking part. This may be due to the difficulty fulfilling the legal requirement for representing the 'presumed will' of a person who is unconscious or has significantly impaired capacity in an acute or critical care setting where no previous relationship exists between the healthcare professional and patient. This was in contrast to studies in care home settings where the professional acting as proxy is likely to have developed a close relationship with the person in their care, allowing them to more fully represent the person's current, if not past, wishes and feelings about being part of a research study. Studies consistently failed to address the complex issue of how the proxy would be able to represent the person's wishes and feelings if that had not been met while the person had capacity, or if such wishes had never been expressed, or if the person had never had decision-making capacity. These may be intractable questions under the requirements of the current legislation. There is currently no Health Research Authority (HRA) information sheet template for clinical trials which fall under the CTR in the UK (241).

There appeared to be a disconnect between the conceptualisation of advance decisions under the MCA as Advance Decisions to Refuse Treatment (ADRT) (20) and that used in the studies, which was based on the wording in the HRA template information sheet (241). This was seen both in terms of their scope being extended to cover decisions about research participation which is not included in the MCA, and the negative orientation towards treatment options under the MCA where an ADRT would be relevant only to studies involving the treatment that was being refused and not refusal of research in general. Only one study [ID 02] mentioned the role of a Lasting Power of Attorney (LPA) for health and welfare or a Court of Protection appointed Deputyship who would be involved in decisions about care and treatment on behalf of a person with impaired capacity. Although the role of an LPA or Deputy in decisions about research remains unclear (237). This topic is returned to in Chapter 6.

No previous studies have examined the information provided to proxies who are involved in decision-making about research participation by adults lacking capacity. The primary strength of this study is that it examined the content of a random sample of information sheets and consent/declaration forms provided to proxies in the UK. Studies from different populations were included in order to represent a range of contexts in which proxy decision-making occurs. Studies included clinical trials of medicinal products, and other types of research, both interventional and non-interventional studies. Content analysis allowed a comprehensive understanding of both the study documents' content and context.

The searches were conducted using one database, which is not necessarily intended for searches of this nature, therefore the search for eligible studies is by no means considered exhaustive. Studies could only be included where the documents were publicly available, or where the investigators were willing to share the documents, and therefore selection bias may have been introduced. There were no refusals to provide study documents. The difficulties with obtaining study documents meant that it was not possible to maintain the stratification of samples by the three groups of conditions (progressive loss of capacity, sudden loss, and no prior capacity), with a higher proportion of studies involving populations experiencing an acute or sudden loss of capacity.

A further limitation is that a relatively small sample of studies was reviewed, although this represented 43% of the potentially eligible studies identified during the searches, and the majority of studies were publicly funded by the UK Department of Health and Social Care

through the NIHR – the research arm of the National Health Service. Although study populations included those who had suddenly lost capacity, progressively lost capacity, and those who had never had capacity to make similar decisions, this did not include those participating in research involving end-of-life care or mental illness. The findings therefore may not be representative of all study populations where participants may have impaired capacity.

An important limitation is that only written information was analysed in this study, which forms only one ‘piece of the jigsaw’ of decision-making (243). In practice, information sheets are provided in addition to an interview with the research team, during which further information will be provided to proxies which may be tailored to their information and decision-making needs. Studies also used other forms of communicating with patients and proxies, such as providing brief or easy-read information to enhance the ability of the person with impaired capacity to understand study information and be supported to provide their own consent, or obtaining verbal consent where research was conducted following a medical emergency.

Whilst studies may have been designed to include adults who lack capacity, there are few data available on what proportion of participants did in fact lack capacity to provide consent, and who acted as proxy decision-maker on their behalf (in a personal versus professional/nominated role). Additional data that explored the numbers of participants who lacked capacity in a subset of completed studies, and who acted as their proxy, is not included in this thesis due to space constraints. However, a manuscript reporting the analysis of these data is currently ‘in press’ at a peer-reviewed journal.

5.5 Summary

This study examined the written information currently provided to family members, friends, and health and social care professionals involved in decisions about research on behalf of a person with impaired capacity. Existing study documents had ethical approval, yet many used inaccurate terms and lacked essential information, and some studies had incorrectly interpreted legal provisions. Particular issues were seen with the information provided to professionals acting as proxy in acute and critical care settings, where the clinical and representation roles were conflated.

To improve comprehension and reduce uncertainty for all those involved in research with adults lacking capacity, there is a need for accuracy in the use of terms for consultees and legal representatives by researchers in study documents. There needs to be greater clarity around the role of both personal and professional consultees and legal representatives, the basis for their decision, and whether they are being asked for consent or advice. Researchers may benefit from engaging with individuals or institutions with legal and ethical expertise when developing study documents involving populations where consent and recruitment may be complex. Consistency in the review of information sheets and consent/declaration forms by Research Ethics Committees could reduce the level of inaccuracy, and as a result may reduce the confusion and misunderstanding for those either seeking or providing informed consent or advice for research participation. These endeavours should focus on mechanisms for appropriate inclusion in research, and not be at the expense of further exclusion from research for these under-represented populations.

The findings suggest that an in-depth exploration of proxies' information needs and decision-making processes is needed which may enable a greater understanding of how proxies are prepared for, and undertake, decision-making in practice. Proxies' accounts of experiences of being consulted, including issues influencing their decisions, would add to the context of proxy decision-making for research, which is currently poorly understood. This may assist in developing a minimum standard of information provision that, if evaluated, would allow optimised written information to be provided by researchers. This would help ensure the proxy is fully informed about their role, enhance the consultation process with proxies, and support high quality decision-making and the provision of truly informed consent where appropriate. An exploration of family members acting as proxies is outlined in the following chapters. Further research to explore health and social care professionals' experiences of acting as nominated consultees and professional legal representatives is still required.

5.6 Learning points

Information sheets should include sufficient information to allow the proxy to understand why they are being approached and the basis on which they should make a decision. Orientating the proxy to make a decision based on what the person themselves would have decided, rather than their own personal views about research in general or the particular study in question, may be of benefit. Ensuring the proxy is informed about their role in

withdrawing the person from the study, should they feel the person would wish to withdraw from it, should be clearly stated and arrangements made to ensure the person remains represented at all times. It is important that this does not contribute to an increase in the length of study documents.

Further guidance for researchers when drafting documents for studies involving adults lacking capacity is recommended, particularly for clinical trials of medicinal products where template documents may be of benefit, and where professionals in acute and critical care settings are involved as consultees or legal representatives. The HRA may wish to consider producing a template for clinical trials involving adults who lack capacity to consent. Interventions to inform and support those that design and conduct research studies which include adults lacking capacity, as well as those responsible for the ethical review of such studies, may be warranted.

Further research is needed to explore the information and decision-making needs of those acting as proxies. There is a need to clarify the role of advance decisions and LPA in research, and to re-examine the legal basis for decisions for those for whom there is no evidence of their wishes and feelings about research participation.

Chapter 6 DECISION Study: qualitative exploration of family members' experiences of deciding about research participation on behalf of an adults who lacks capacity

A version of this chapter is in press as: Shepherd V, Hood K, Sheehan M, Griffith R, Wood F. 'It's a tough decision': A qualitative study of proxy decision-making for research involving adults who lack capacity to consent in England and Wales. *Age and Ageing* 2019

6.1 Introduction

As previously stated, decisions about participating in research, which is intended to generate new knowledge, are different to those about medical treatment or care where the aim is to choose the option that will most benefit the person themselves. The law requires the family member acting as a 'legal representative' (22) or 'consultee' (20) to provide consent (22) or advice to the researchers (20) based on what the person lacking capacity would have wanted, had they the capacity to choose for themselves. However, in many cases the person's explicit wishes are not known to proxies (204) and few have previously discussed their research preferences (198).

Previous studies identified that, whilst families were supportive of being involved in proxy decisions about research (191) it can be a difficult task (36). Family members carry the responsibility for making a decision with potentially far-reaching consequences for the health and welfare of another person. Reportedly, nearly all proxies experience some degree of burden in making decisions regarding research (36). The systematic review reported in Chapter 3 found that much of the existing research involves hypothetical scenarios and was conducted in North America (167), meaning little is known about how families negotiate these complex proxy decisions in practice, or under differing legal frameworks such as the UK. Another recent systematic review which examined how ethical challenges, including proxy consent, are operationalised in research with people who have dementia also found that there is a current paucity of evidence, and concluded that this is a key area for future research (45).

This chapter reports a qualitative interview study (titled the DECISION Study), which explored the experiences of family members of individuals who lack capacity and who have been

approached to participate in a research study. It builds on the questions raised in the literature review (Chapter 2) and the conceptual framework developed from the systematic review of existing research (Chapter 3), in order to address the gaps in empirical evidence identified during the systematic review. The objective was to gain an understanding of how proxy decisions about research participation are made in practice in order to develop and tailor future supportive interventions.

6.2 Methods

Qualitative research is a rich, diverse and complex field (254). It can provide a detailed description of events or experiences which are encountered in particular contextual conditions and seeks to gain an understanding or meaning of that phenomenon (254). Qualitative research relies on good research design in which the data analysis method is appropriate to the research question, and the data collection method is appropriate to that of analysis (255). Methods should be chosen and evaluated according to their appropriateness to the topic being researched, the research question, and the individuals whose experiences are sought (256).

Semi-structured interviews are designed to enable the participant's viewpoint to be expressed, particularly when compared to other methods of data collection such as structured interviews or questionnaires (256). The 'responsive' style of interviewing used in semi-structured interviews emphasizes the building of a relationship of trust between the interviewer and interviewee that leads to a more 'give and take' style of gentle and friendly conversation, and enables the generation of rich and nuanced data (257). A key element of a responsive interview is the development of an interview or topic guide which consists of questions and probes designed to elicit responses that have the depth and detail required and which can be used flexibly throughout the interview (256).

Thematic analysis is widely considered to be a foundational method for qualitative analysis that is not constrained to any one theory (258). This 'theoretical freedom' means that thematic analysis can be widely used across a range of epistemologies and research questions (259). It provides a highly flexible approach that can be modified to suit the needs of many studies to provide a rich and detailed, yet complex account of data (260). A rigorous thematic analysis can produce trustworthy and insightful findings (258), however, it is

important to establish how this 'trustworthiness' has been achieved (259). Lincoln and Guba (261) defined the concept of trustworthiness through a set of criteria including credibility, transferability, dependability, and confirmability. Procedures used to enhance the trustworthiness of this analysis included audit trails of data collection and analysis, documented analytical developments, and the use of reflexivity and discussion (259).

6.2.1 Design

Semi-structured interviews were conducted with family members who had acted as a proxy decision maker about research participation for a person who lacks capacity. The qualitative data were analysed using thematic analysis to identify and report patterns or themes within the data.

It was anticipated that approximately 20-25 interviews would be required to meet the study's aims, however defining sample sizes *a priori* in qualitative research is not straightforward. There are no rules for sample size in qualitative inquiry (262) as it relies on a number of ontological and epistemological assumptions and the analytical context of the research (263). Predetermining a sample size purely in terms of the number of individual informants, which is associated with a deductive approach to qualitative research relying wholly or predominantly on pre-identified themes rather than allowing these to emerge inductively, is viewed by some as problematic (264). Although this great ontological and epistemological debate is far beyond the scope of this thesis, a meaningful analysis will ultimately depend upon the nature and meaning of concepts expressed in the data, not their prevalence, frequency or typicality (263). Thus, adequacy of sample size can be thought of in terms of the number of events, incidents and experiences under exploration, rather than solely in terms of the number of participants (264). The focus is less on sample size and more on sample adequacy (265). The broadly inductive approach used in this study involved a more exploratory approach in which sampling decisions were guided by principles such as saturation (263) and 'information power' (266) although both concepts are themselves the subject of extensive debate (267). An inductive approach presupposes that themes are iteratively developed through the researcher's ongoing engagement with the data (263). Adaptive sampling decisions and concurrent data collection and analysis enabled an iterative approach to determine the adequacy of the sample size during the study.

6.2.2 Sampling and recruitment

Potential participants were identified through research networks, community interest groups, social media platforms, and research registries. Research networks, community groups, and research registries such as Join Dementia Research disseminated information about the study to their members, who then contacted the research team if they were eligible and interested in participating. Purposive sampling techniques were used to obtain a maximum variation sample. This included those who had experienced decision-making in different circumstances (such as following a progressive loss of capacity or a sudden loss of capacity), familial relationships (spousal, parent-child), types of study (clinical trials and other study designs), and decision outcomes (agreed or declined participation on behalf of the person). Participants were recruited in England and Wales only, rather than throughout the UK, due to the differences in legislation governing research involving adults who lack capacity between jurisdictions.

Contact with potential participants was usually initially by email to provide introductory information about the study and initiate communication to explore their circumstances and therefore eligibility. Many of those who got in contact were keen to participate but were not eligible for the study, either because the person they cared for was able to make their own decision about participating in research, or because they did not have experience of making research decisions. After initial contact by email, a telephone conversation was scheduled to enable the study to be explained in greater detail and to provide an opportunity for any questions to be asked. A Participant Information Sheet was also provided either by email or by post as preferred.

If the potential participant was eligible and agreed to participate in an interview, a mutually convenient date and venue was arranged, usually at the participant's own home. Interview location is considered to be a fundamental aspect of the interview process (268). Conducting the interview at their home meant that the burden of participating was reduced for the participant, who was often the main carer for the person they represented and interviewing in a home setting can foster a level of intimacy and reciprocity that is not easily replicated in other more alien settings (268). However, the benefits of interviewing participants in their own home or other locations unfamiliar to the researcher needed to be balanced against challenges such as unexpected interruptions and concerns around safety (254). Where a telephone interview was preferred, additional time and attention was paid to cultivating a

rapport with participants and ensuring responsiveness, which have been found to be important when seeking to obtain rich data from telephone interviews (269).

6.2.3 Data collection

A topic guide was developed which was informed by the critical literature review contained in Chapter 2, the findings from the systematic review reported in Chapter 3 (167), and in conjunction with a lay advisory panel. The topic guide (**Appendix 10. Interview topic guide for DECISION Study**) was further iteratively developed and refined during the data collection period (270). For example, questions about Power of Attorney were not included in the initial topic guide but emerged as an area of interest in the third interview and so were included and expanded on in the topic guide for subsequent interviews.

The topic guide proved a useful basis for prompting the interviewee to cover areas relevant to the research question, and to maintain the focus of the interview. This was relevant because participants often talked about their experiences of providing care for the person and making other decisions on their behalf. These additional areas provided a rich account of the context within which research decisions were situated, but it was important to ensure that data relating to the experience of decision-making for research was also obtained.

Interviews were digitally audio-recorded and transcribed verbatim by a professional transcription service provider. The transcripts were checked for accuracy and completeness against the source data and anonymised and allocated a Participant Identification Number. Participants were offered vouchers equivalent to £15 as a 'thank you' and in recognition of their time given to participate.

6.2.4 Data analysis

Data were analysed using thematic analysis which seeks to identify, analyse, and report patterns (or themes) within data (258). A theme captures an important conception about the data in relation to the research question, and represents some level of patterned response or meaning within the data set (258). A theme is said to capture and unify the nature of an experience into a meaningful whole, and so can bring meaning and identity to an experience and its various manifestations (270). Braun and Clarke's six stages of thematic analysis were used as the basis for the process: familiarisation with the data; generating initial codes; searching for themes; reviewing themes; defining and naming themes; and report

production (258). Data relating to the ethical concepts identified in the conceptual framework developed as part of the systematic review reported in Chapter 3 is described at length in Chapter 7 through a separate grounded theory analysis. It has been suggested that this pluralistic analytical approach can produce a multi-layered understanding of the phenomena through the use of different 'lenses' (271). The methodological challenges, benefits, and limitations of conducting pluralistic analyses are discussed in Chapter 7.

Data generation and analysis were undertaken concurrently to facilitate iterative coding and generation of themes, and exploration of candidate themes during subsequent interviews (254). The first 11 interview transcripts were initially coded and then reviewed independently by the research team to review and establish the validity of the coding framework, prior to complete coding of the remaining data (254). Data were coded at both the semantic and the latent level (258). Qualitative Data Analysis software (NVivo 11)(180) was used to assist with data management.

Reflexivity is key to the appropriate use of any qualitative method (272). Developments in the analytical process were recorded through field notes (273), analytic insights or 'noticings' that occurred during data collection (254), data analysis memos held in NVivo, and reflective discussions about the data. A method of analysis known as OSOP ('one sheet of paper') was used to organise emergent themes (274). This involves reading each section of data in turn and noting on a single sheet of paper the issues raised by the coded extracts, along with the relevant IDs, to create a summary of the coded data (274). Throughout the process every effort was made to optimise the quality and rigour of the analysis through following the quality steps outlined in the literature (275,276). Adequate information power (266) was assessed as being reached following complete coding of 17 interviews with no new themes being identified.

6.2.5 Ethics and research governance

Ethical approval for the study was provided by the School of Medicine Research Ethics Committee, Cardiff University (SMREC Reference Number 17/54). Written informed consent was sought and obtained prior to the interview. The consent form was completed by post where interviews were conducted by telephone. Explicit consent was given by participants for the interview to be audio-recorded and verbatim quotes used. Participants were assured that neither they nor the person they represented would be identifiable. Attention was also

paid to the potentially sensitive issues that may be raised during the interview, where there was the potential for the participant to become upset or distressed during the interview. In the event of a participant becoming upset or distressed, which did occur on one occasion, the interview was suspended or discontinued as appropriate. At the end of each interview, time was taken to ensure that participants did not feel distressed by their participation.

A comprehensive Risk Assessment (RA) for the study was undertaken, following Centre for Trials Research Standard Operating Procedures (SOP) for RA. This detailed any risks/potential risks of the study, including any potential risk/harm to participants and/or researcher. The RA contained a management plan for mitigating potential risks/harms and managing risks/harms should they have occurred, which included following the Lone Field Working SOP. Data were stored confidentially on password-protected servers maintained on the Cardiff University IT network.

6.3 Results

6.3.1 Participants

Interviews were conducted with 17 family members who had acted as a research proxy (either a consultee or legal representative) for a relative with impaired capacity (**Table 6-1 Characteristics of DECISION Study participants and interviews**). Participants were predominantly female (13/17, 76%), and were either an adult son or daughter (12/17, 71%), or spouse (3/17, 18%) of the person they represented, one person who was both a daughter of someone with impaired capacity and the spouse of someone with impaired capacity, and one daughter-in-law.

Table 6-1 Characteristics of DECISION Study participants and interviews

	Participants n (%)
Gender	
Male	4 (24%)
Female	13 (76%)
Relationship	
Adult son/daughter	12 (70%)
Spouse	3 (18%)
Other	2 (12%)
Daughter-in-law	1
Daughter and spouse	1
Interview	
Participant's home	8 (47%)
At another location	4 (24%)
Via telephone	5 (29%)

Participants were predominantly a proxy for someone living with a form of dementia who had developed impaired capacity gradually (n=16); one participant cared for someone who had suddenly experienced cognitive impairment following a stroke. Participants included those who had been approached by researchers to act as a consultee or legal representative on behalf of a family member, and those who had actively sought opportunities for their family member to take part in research, perhaps through research opportunities found online. The types of research that had been considered included clinical trials of investigational medicines and other interventional studies, as well as observational and questionnaire or interview-based studies. Proxies included those who had agreed to research participation on behalf of the person they care for, those who had declined, and those who agreed to and/or declined participation for multiple studies.

The majority of the interviews were conducted face-to-face, either at the participant's home (8/17, 47%) or another place that was convenient for the participant (4/17, 24%) such as the care home where their family member was being cared for. The remaining interviews were conducted by telephone (5/17, 29%). The duration of the interviews ranged between 19-90 minutes (mean 44 minutes).

6.3.2 Themes

Six themes were identified which captured the way proxies made decisions, viewed their role in relation to making decisions about research, saw their authority as decision-maker, and their experiences as research proxy for the person they cared for.

6.3.2.1 *Theme: taking all things into consideration*

A balancing act

Proxies balanced a range of different factors to construct a decision, including whether there were any advantages or benefits for their family member, which they balanced against any potential risks or harms. If the expected benefits outweighed any potential adverse effects then the proxy would agree to participation, or if there were no direct benefit then most proxies would agree to participation provided there was no detrimental effect.

“So then all these things you take into consideration you always have to weigh up everything” [03, adult daughter]

“Yeah and I think if the benefits outweigh the side effects we’d go for, go for it” [11, adult daughter]

Proxies understood that the purpose of research is primarily to generate future knowledge that will improve the care and treatment for people in the future. This meant that while expressing hope that the person they represented might benefit in some way from participation even if this was not the aim of the study, they were unlikely to agree to participation if there was any likelihood of harm.

“The purpose of doing it [research] is actually to potentially help other people in the future, not the subject that’s involved in the research. Therefore, there must be zero harm. It’s got, it’s not going to benefit them, but it’s also not got to disadvantage them in any significant way” [05, adult son]

Decisions could be influenced by previous negative experiences that the proxy or the person they represented had experienced in the past, particularly where the person had experienced harmful effects from prescribed medicines. This was the case even if the research was unrelated to that treatment and the risk of side-effects was very small.

“Medicine type trials worry me because of the experience that we had when they first diagnosed [her]...and I would not want to put her through that” [06, adult daughter]

Proxies often spoke of research as a joint enterprise, referring to ‘we’ or even ‘I’ when talking about participating in a study. Benefits and harms were viewed as relational, where both the person and their proxy would be affected as part of their intertwined caring relationship; therefore, the person’s interests could not be isolated from those of the proxy, particularly where the proxy was also the carer providing care for the person.

“If I thought that there was something that was going to improve her, her wellbeing tremendously, then I’d, I’d jump at it but I have to look at the risks of even a little ... even a little bit that she’s less than what she is now. That’s ... that is not going to be good for her, for her and us, you know, ultimately, it’s not going to be good for us” [06, adult daughter]

Weighing advantages and disadvantages of participating in research

The range of benefits or advantages considered by proxies went far beyond those that might arise from the intervention or medication under investigation, or any additional monitoring and access to specialist expertise that may form part of the research activity. Benefits identified as important included social engagement with others, such as the opportunity for the person to meet and talk to new people. This was particularly seen as beneficial for people who would otherwise be quite isolated and lonely and who would benefit from the stimulation that engagement with researchers would bring.

“Being able to talk to people, having different people to talk to.....lifts her mood you know..... and that’s why I like to keep going to as many things as I can, and why I take part in as much research as we can” [12, male spouse]

Some proxies described the additional health benefits of monitoring, investigations, and access to specialist expertise, which may form part of the research activity. These sometimes went beyond that which might be available as part of the person’s routine care. One daughter described how her mother, who had moderate-severe dementia benefitted from the sense of being ‘looked after’, which continued to enhance her sense of wellbeing even once the research had been concluded.

“One of the things she used to say about when we went down to [name of research centre] was oh I’m really looked after aren’t I. So even though she’s not been on the drug trial for a

while now she still uses that phrase, refrain, I'm really looked after aren't I and that gives her a sense of wellbeing and so that's good" [04, adult daughter]

Proxies described how this feeling of wellbeing and being looked after also came with a sense of making a bigger contribution beyond the person's own interests. It extended to the person feeling that they have value, have an opportunity to 'tell their story', and knowing at some level that they were helping others and contributing to society.

Many proxies reported that there were benefits to them as carers through the person they care for participating in research, which could better help them to support the person they care for. This included access to knowledge, as well as a source of emotional support.

"I'd be asked lots of questions about day-to-day care, day-to-day observations and it helped me, it really helped me. But I cried a lot especially in the initial stages because I was coming to terms with it and they were so good. I mean I know it helped me, but I didn't know that at the time that it would help me as much as it did come to terms with mum's Alzheimer's" [04, adult daughter]

These potential benefits were always considered alongside any potential harms or risks that might arise from participating in research. Proxies did not often cite risks that can result directly from participating in research, such as adverse effects from medication. Potential harms that proxies were concerned about commonly related to the risk of psychological harm to the person through becoming agitated or upset by the research procedures where they were not able to understand what they were participating in. The risk of upsetting or distressing the person was weighed up against the benefits of participating by proxies.

"Yes, he won't understand what you're saying. Well we could say you're having a scan and when you get there he wouldn't, and he would get quite agitated and ...it's just, can't even say it isn't worth it, it isn't worth it for dad" [10, adult daughter]

Attitudes towards risk varied; some would not consider any research where there might be risks to the person's health or wellbeing, others considered the person's own attitude to not being risk adverse and were prepared to make a decision that was in line with the person's character.

"I think she would think give it a go and see what the risk is. She's very much you know, the sort of, if my time's up, my time's up sort of person, but she would give something a try and if it doesn't work, then hey she's tried it, it didn't work [16, adult daughter]

Proxies also expressed concern that the person may not be able to provide 'accurate' responses to any questions asked of them as part of the research. They were worried that this may affect the quality of the findings, but also that the person's perception of reality would be accepted as the truth, and where this portrayed a negative image of the care being provided by the proxy as carer could potentially lead to problems.

Precarity and maintaining the status quo

Proxies saw their primary role as being to maintain the person's quality of life for as long as possible, whilst doing what they could to make the person's life better. The person was viewed as being in a precarious situation, where they could not afford to be any worse off than they already are. Many proxies also provided direct care for the person they represented, but these care arrangements were perceived to be fragile meaning proxies were reluctant to risk any complications that would jeopardise the status quo.

"So it's tough because ... I mean she's quite happy over there at the minute. And we are on a ... you know ... we're okay. Don't get me wrong. There are still issues but we manage and we muddle along okay" [06, adult daughter]

For many proxies, there was a realisation that the person's health will inevitably decline, perhaps as a result of progression of their condition or through advancing age, but they did not want to risk anything that might precipitate that decline.

"It worries me what she's going to be like as she deteriorates and I wouldn't want to speed that up so that would be my biggest concern that something might speed it up, um, the process because I know we're going to ... you know it's going to come at some time but I'd rather it didn't come that quickly really" [06, adult daughter]

Dual role as protector and advocate

In response to the person's vulnerability, proxies tried to do what they could to make the person's life as comfortable and safe as it could be and sought to protect them from harm. This sometimes included protecting them from the perceived threat of harm resulting from participating in research, and from the distress of being involved in making a decision that they were unable to make. Although research was also seen as an opportunity to make their lives better, which formed an equally important part of their aim. This dual role as both

protector and promoter of the person's interests could lead to a degree of uncertainty for proxies when deciding about research.

"You get this barrier with the carer because they try to protect them. I think the protective role is that you don't want to put them through. People, carers have this thing about research, that it's going to be invasive and it isn't always" [03, adult daughter]

"Actually am I, am I taking away an opportunity for her to be better than she is now?" [06, adult daughter]

Their protective role extended to fighting the person's corner when they needed to and speaking up for them when they were unable to do so – acting as an advocate for them to get access to services or treatment. For some proxies this meant them going further than just standing in for the person. Rather than attempting to place themselves 'in the person's shoes' in order to see things from their perspective, they inhabited the person's shoes and took over. One participant spoke about how she felt 'advocate' was not strong enough a word to describe her role in protecting her husband's interests.

"I see myself as a bulldog [laugh] or a bull terrier or whatever ... I mean I speak. I decide. I say no. I say yes. I say what goes" [09, female spouse]

The proxies' role as the person's advocate also extended to enabling them to fulfil their wishes to achieve what they really want to do – which may have been to help others and to contribute to society through participating in research.

"She said of course I want something that might help me, she said but you know me, don't you? You know that for me science is important, and it always was.... she said I do want to help people you know I want to help people, can you arrange it?" [04, adult daughter]

All decisions had the person's wellbeing at the forefront, but proxies drew on what the person would have wanted in greater or lesser amounts, balancing it against what they felt was best for the person. Some actively sought opportunities for the person to take part in research via the internet, including research registries and charity groups, others had been approached through organisations providing care or support such as dementia cafés or the person's care home. This may have been part of trying to maximise the person's wellbeing or enable the person to help others as they would have wished. This complex picture of balancing any advantages and disadvantages within the context of the proxy's role as carer is captured by this participant:

“If there was an indication of benefit to my mother, then it’s different, because then you’re seeing it as part of your caring role. Because if you can make somebody’s life better as a result of becoming involved in a research thing, then that’s obviously quite different, because there you see it as part and parcel of the providing care” [05, adult son]

6.3.2.2 Theme: Knowing the big and the little things

Knowing the person – familiarity and similarity

Generally, proxies had not had explicit discussions with the person about research participation or their preferences, but a lack of prior discussion did not affect the proxy feeling happy to make a decision as they used other things that they did know about the person. This included knowing the person’s character and previous interests, but also the core values that were important to the person – described as knowing what their ‘moral life’ has been. The closeness of their relationship may have meant that they had shared core values or held similar views about things, which helped the proxy to know what the person would decide or would want.

“I think of what my mum might have wanted when she was ... you know, what decisions she would have made prior to this disease taking over. My mum and I have always had a really very close relationship. You know we’ve always been close.... so I think pretty much we see things very similar” [06, adult daughter]

They may also have had a long-shared history with the person and had shared experiences that shaped their similar views. This was expressed both by those with parent-child relationships, and those with spousal relationships.

“There’s a trust between the two [of us], through experience as well as talking if you know what I mean” [14, female spouse]

Proxies felt well placed to know whether the person (and themselves as carer) could comply with the practicalities of the research and the logistics of making it happen. They expressed doubts about whether the person could participate, or should participate, even if they were sure that the person would have wanted to.

“I’m not sure he’d manage a scan in a machine, an MRI scan. I’m sure he would want to do it if he was able to, but it would be a question of making sure he understood” [07, female spouse]

Where proxies felt that the person they cared for would not have wanted to participate in research, they referred to the person's longstanding desire for privacy around health matters, their disinclination to engage socially with others, and the person having no particular desire to go out of their way to help others. This contrasted with those who did consider that the person they cared for would participate if they could, who cited the person's helpfulness to others, long standing interests in science or research, and being a part of society as reasons for their decision. Examples of the person's interests in science or furthering scientific knowledge included having previously worked in science or healthcare related fields, or an artist whose paintings included science-themed pieces.

Proxies sometimes discussed the issue with other family members and consulted them about the decision, but more often just informed them if the person was going to be participating as a way of keeping them up to date.

Temporality of relationships

Proxies spoke about knowing the person through seeing them day in and day out; they were sensitive to how the person reacted to situations where they may be unable to express their views or feelings. They also knew biographical aspects of the person's life such as their previous jobs and life-long interests, and what characteristics of the person were relevant to the particular decision context.

"Say the possibility was that she would want to feel, that she would want to be sick a lot of the time. She [always] hated that feeling of being sick. I would most probably not let her be in any research that would have that... knowing how mum hated feeling sick I would say no, don't do it whatever you know [laughter]... Knowing the person, you have to know the person don't you and silly little things like that you know" [04, adult daughter]

Proxies also recognised that preferences may change over time, and that those who are no longer able to express their views should not necessarily be held to those prior preferences.

"But at the same time, if anybody can change their mind over, you know, over years... they decide they no longer want to do x, y, or z and they've always done it. Then you'd, you can't turn round and say "Well because you've always done it, you've got to do it again". So you know, you have to be sensitive to everything that, whether it's concurrent because it's a part of the illness, or whether it's because he's just changed his mind you know [chuckling]" [14, female spouse]

Several proxies used examples from other types of decisions made for the person, such as food choices or financial investments, to show how they balanced the person's long-standing preferences against their current 'in the moment' wishes, and what the proxy themselves might consider to be the best option using their wider knowledge of the factors involved. One participant described how he has to do the food shopping for his father, and when choosing what to put in the shopping basket he considers what he knows his father always preferred to eat, and what he now likes to eat, with the fact that he is unable to chew food but needs a nutritious diet to maintain his health. Another used the example of making financial investments on behalf of the person, where their mother's previously voiced strong views about particular industries would guide the proxy towards alternative areas to invest in that were more in line with the person's wishes, whether or not they were still able to express those views.

6.3.2.3 *Theme: Trusted to do the right thing*

Relationships of trust

Proxies considered themselves to be trusted to make decisions in many of areas of the person's life, including decisions about the person's finances and medical treatment, either explicitly or implicitly. This might have been because they had a long history of being trusted to make decisions for the person, or because of the closeness of their relationship, which extended beyond close blood relatives. The proxies reported that, because they are trusted by the person the person also trusts the decisions made by the proxy – they are trusted not to make a 'bad decision'.

"Because she really trusted me bless her... and then I wouldn't have made a bad decision for her, I don't think I would have any way you know. If I thought it was a bad decision, if I had any doubt whatsoever, or anything, then I wouldn't have done it" [02, daughter-in-law]

The importance of trust relationships was also seen where the proxy felt that they could trust the researchers and get to know them, and where the opportunity to participate or introduction to the researcher came from a trusted source such as the care home who was caring for the person.

"You've got to be able to trust someone, yes... I mean it wasn't as if she {research nurse] sort of walked through the door, come up and you know, she was back and forward and you get

to know someone, even though you're not sort of speaking to someone, you see them on a regular basis, you know they're trusted by the home ..." [10, adult daughter]

Trust and reciprocity

Proxies described the reciprocal nature of trust within their relationships with those they represented. The person may have been the carer for the proxy previously, either as their parent or during their marriage during times of illness.

"You have to have the trust don't you, to make a decision for somebody. They have to trust you and you have to trust them, they know you're doing the right thing for them" [02, daughter-in-law]

"So within our family we are close enough to all trust each other...he would trust me with anything and I would trust him with anything. If only one of you trust the other, there's something wrong" [14, female spouse]

However, not all family members were trusted equally by the person. One family member was usually closer to the person or had been consistently present in the person's life. Proxies universally reported that they were the one family member that was closest to, and most trusted by, the person.

"Yeah, she does [trust me to make those decisions]. She wouldn't trust my sister or brother, but you know they've been on and off the scene for a number of years, I suppose. But I've been the constant, you know?" [06, adult daughter]

Where a Lasting Power of Attorney (LPA) had been created, a part of the LPA was choosing who the person wished to make decisions for them. Where an LPA was in place, all of the proxies had been chosen by those they cared for to act as attorney, usually alone rather than jointly with others. An LPA was not generally seen as bestowing authority on the proxy or as a source of authority itself but could be seen as a concrete example of the person's trust.

"I suppose I think lasting Power of Attorney for me is mum saying, "You make the decisions for me. No matter what," I suppose" [06, adult daughter]

The importance and relevance of holding Lasting Power of Attorney (LPA) on the decision-making process or actual decision itself varied between proxies. For some, it was regarded as something in the background of their daily lives, other proxies considered it to be merely

'rubber-stamping' what was already there. Proxies often spoke in terms of their relationship, and that an LPA meant they were being trusted by the person to act on their behalf.

"I think it feels more than just a simple document, when I think about the responsibility that's attached to it, I think of it in relation to the trust that they put into me" [17, adult son]

All proxies reported that they hadn't previously considered the role of LPA for health and welfare in decisions about research participation, even though they had been involved in decisions about research and all but one of them held some form of Power of Attorney. Proxies did not see decisions about research as being separate from those about the person's health and welfare, but as intrinsically linked or related. Although proxies recognised that there were differences between decisions about research participation and those about care or treatment.

"So in that regard I would see, yeah, it would fall under it. It's probably not necessarily there but, cos it comes under wellbeing, doesn't it? So, yeah, I think ... well I've certainly acted in that, it's my decision to make for her" [06, adult daughter]

Some proxies thought that the same person who made decisions about the person's health and welfare should be the same person who would make decisions about research participation, as this would be the person who knows them and their wishes best. For some, this included knowing the person's views about participating in research. They may also be acting as the person's carer and therefore may consider themselves to have responsibility for the person's welfare generally, or because they would be best placed to understand the implications of participating on the person and their quality of life.

Some proxies considered the practicalities of including the designation of Power of Attorney for research participation under the existing arrangements for LPA for health and welfare issues. Proxies weighed up the potential benefits of having decisions about research under the umbrella of a LPA for health and welfare, recognising that there are differences, but that it might offer a practical compromise in comparison to the likelihood of creating an additional LPA and the legislative processes that would involve.

"I think there should be effectively a kind of LPA that relates to research. In that sense, I'm just not sure whether it's better to have it under the health one, or in an ideal world it would be a separate LPA ... I mean the prospect of their creating a new one to cover research seems quite kind of dim and distant, so amending the health one to put, put that research into it

might be the more practical thing to do and if that was the case, I can't see why and it is a bit different, but I still think you could do it there" [17, adult son]

Some proxies considered the practicalities of including the designation of Power of Attorney for research participation under the existing arrangements for LPA for health and welfare issues. One proxy considered the value of an opportunity for meaningful discussions about the person's wishes and preferences with their attorney who would have the responsibility to interpret their wishes that would occur through the process of creating a LPA for research participation.

"Well, I think anything that can awaken conversations is important ... it just makes us stop and think" [15, adult daughter]

Different ethics?

Several proxies reported that, as a result of the impairing condition, the person they cared for was unable to accept or fully comprehend the diagnosis they have been given. This made it difficult to have a conversation about research into the condition because the person became defensive or got upset. Broaching this subject was therefore sometimes seen as a breach of the person's trust.

"It upsets her that I've mentioned it because I'm the person that she trusts most of all. And, and I can't do that to her. So it's not worth it" [06, adult daughter]

Maintaining a relationship was considered to be more important than the person participating in research, and so the proxy was not willing to risk upsetting the status quo of their relationship. For some proxies this meant it was impossible to engage the person in discussions about research, even if their known previous wishes would be to participate.

"There's absolutely no way that I would be talking to her about things that might upset her. So if something, research-wise, came along and asked about, you know, you've got to talk to her about how dementia impacts her on this. There's no chance that I'm talking to her about that because that's going to upset her" [06, adult daughter]

"from where I see it, my relationship with her and keeping things kind of on an even keel is worth so much more for us both, than I think the additional benefit of her being a single participant in a multi-person study, that I, I just, I suppose I would just weigh that up and say, for us at this point, it's not, it's not something we could do together. Um, and keep a kind of cordial relationship and I don't think it's worth risking that" [17, adult son]

The difficulties of engaging the person meant that a small number of proxies would consider not explicitly telling the person that they were being involved in research if they felt it was justifiable. Hypothetically, this might be by deliberately telling the person that the intervention or investigation was part of their routine medical treatment, or by omitting to make clear that they were participating in a study. They justified this as ‘ethics being different for someone with dementia’, although others would not consider anything but complete honesty and openness.

“If I was making the decision for her and it was available, I would potentially do it, I know it’s a bit tricky, but without her necessarily knowing exactly what was going on. I would still be prepared to do that, if I thought it was an important study” [17, adult son]

There were instances where proxies would hypothetically agree to participation even if the person themselves wouldn’t derive any benefit and may experience some harm.

“Because her fate’s sealed so it makes no difference in my view and you’ve just got to be practical about it, if she can be useful in that sense, then I would definitely put her up to it.” [17, adult son]

6.3.2.4 Theme: Enriching lives

Doing good things

The value of participating in research was seen as something more than just a route to getting better care or treatment that could benefit the person, but as something more enriching – an opportunity to make a positive contribution and to ‘do some good’.

“There might be something that came along and you thought, “Oh yeah, that, that would really make a difference,” but more for how it could help other people” [06, adult daughter]

“If it helps her, great. If it helps other people probably even better because there’d be more than one person helped” [08, adult daughter]

A motivation to participate in research generally was in order to benefit society at large, as well as those with the same condition, and sometimes thinking about younger generations of their families who may be affected by the same condition.

Being good people

Proxies considered whether the person themselves would wish to help others or had altruistic character traits, described as being *'good people... in the depths of their real being'* [14, adult daughter]. Some proxies described how their closeness to the person also included knowing their core or moral values. Proxies used examples of the person's previous willingness to help in other ways as indications of their altruistic nature, such as donating blood, volunteering, or registering as an organ donor.

"He's quite altruistic, so I think he probably would help people if he could. I don't think he'd worry about it for himself, he wouldn't say "Oh I'll benefit from this"" [14, female spouse]

Although it was recognised that such altruism was not universal to all, and in some cases the person would only really have been interested if they themselves would benefit.

"I have to say that she's quite selfish like that, I think if she thought it was of benefit to her, she would take part in it" [16, adult daughter]

Proxies viewed these characteristic traits or personal values as still relevant, even where the person was no longer able to express or understand such altruism. Some proxies saw participating in research as a moral obligation, others considered that the potential familial risk of the condition meant that there was a duty to participate. As well as attributing it to the person they represented, some proxies expressed this view for themselves, revealing the complex intermingling of 'self' and 'other' attributes.

"I see it as a moral obligation on people generally, to do what's right for, for the future. And I've always seen research like that" [14, female spouse]

6.3.2.5 Theme: I wouldn't want to make a bad decision

Decisional authority - it's for me to decide

Proxies viewed themselves as having ownership of decision-making, with proxies referring to themselves as the decision-maker, regardless of whether they were providing consent for a clinical trial or advice as a consultee. Proxies generally saw themselves as being comfortable with having the responsibility to make decisions about research on the person's behalf, seeing it as a natural extension of their role because it formed part of their wider obligation or responsibility to look after them.

"I just see, I see research as my responsibility because I'm looking after [name of husband] and hopefully I would make decisions that were appropriate" [07, female spouse]

Other proxies acknowledged that being the decision-maker comes with a feeling of responsibility and can also bring uncertainty for the proxy.

"It's a responsibility, and I suppose with all responsibility comes ..., oh I don't know how to express this, comes that sense of ..., self-doubt on occasions I suppose" [15, adult daughter]

Whilst some proxies reported that making a decision about research was straightforward, others described it as a difficult decision. These views were reported both by proxies who had agreed to research participation on the person's behalf, as well as those who had declined.

"Once I said yes it was then forgotten about, it wasn't something, I sort of woke up the next morning thinking, oh, have I done the right thing ... because no, I thought at the time I had" [10, adult daughter]

Making right and wrong decisions

Some proxies described knowing what to decide as a dilemma, as they were unsure what the 'right' decision was – which was usually linked to the decision outcome. They expressed concern about making a 'wrong' decision that they would later regret, which made it difficult to make a decision at times.

"I thought well perhaps, I don't know, have I done the right thing. It's very, very difficult" [03, adult daughter]

"I think it is difficult. And it's difficult because you're scared of what they could ... scared might not be the right word, but you're, you're worried that you make the wrong decision" [06, adult daughter]

A small number of proxies recognised that there might not be a 'right' or 'wrong' decision or felt that it would not matter if they did get it wrong as it was just part of life to get things wrong from time to time. However, in comparison to other decisions that proxies had been involved in, or were responsible for, decisions about research were not the most problematic that the proxy had faced. Other decisions about medical treatment or whether the person could no longer be cared for in their own home were comparably harder.

"I mean I'm currently making a decision about whether to have him put in a home and I'd say that's in the nine, ten level ... but the decision about that particular bit of research was a three" [13, adult son]

Comfort appeared to be increased when there was expected to be no negative impact on the person, when they felt supported by the researchers, or if the proxy knew the person's views about research or that they had participated prior to losing capacity.

"...and that's the way my mother has always thought, felt. Yeah, so it was easy, didn't worry us at all" [11, adult daughter]

Proxies also described how they felt more comfortable about making decisions about research when they felt supported by the researchers or felt reassured that the research was being conducted ethically.

"I think if somebody's coming from you know... big organisations that fund a lot of research ... that to me in itself is a lot more comfortable. I know that it's as ethical as it could be and funded properly, you know, so that sort of research I think I'd be quite comfortable in going for" [09, female spouse]

Most proxies felt reassured by knowing that, if the person did participate, the proxy could withdraw them from the study at any time. This was illustrated by one participant who did not appear to be concerned about her deciding that her mother should participate in a clinical trial of a new medicine, describing it as 'only a study':

"No, I didn't feel ... I didn't think that was difficult. Because it is only a study, and you can ... I can change my mind at any time. So it wasn't a sort of all or nothing type thing" [01, adult daughter]

Accuracy vs authenticity

Where the person had given any indication of their wishes, either explicitly or not, then the proxy was guided by that, however most proxies did not have any clear directions and so used what they knew about the person as the basis for the decision.

"Knowing what she's done before and her views on things before and just recognising that it's a good thing to do research" [08, adult daughter]

Others had had explicit conversations about participating in research, which may have extended to written instructions, as the wife of a man with severe dementia who had passionately campaigned and spoken in the media about his condition described:

“I mean the thing is he may not now make his decision what to do but I know from what he's said in the past that he would do anything to help..., and I'm not sure he didn't write it down” [07, female spouse]

Whilst proxies couldn't be certain it was the decision the person would have made themselves, some proxies reported using what they thought the person would decide in combination with what they themselves as proxy thought was the 'right' decision. Proxies were generally satisfied it would at least be 'in line' with what the person would have wanted (or not wanted) and so authentic to the person, if not what they would actually have decided for them self. The proxies were trying to do what they thought the person would want them to do, which was to protect their interests.

“I would very much make a decision on well what I thought, really. What I thought she'd want, or she wouldn't want me to put her through” [12, male spouse]

In the absence of any indication of the person's wishes, a small number of proxies reported that the decision falls to them alone to decide what is best for the person, even if they were not sure that the person would have agreed with their decision.

“I think, I think if my dad had a full capacity and had at any time discussed it or given any indication then maybe my decision would have been different. But he didn't, it felt that well it's my decision I am doing it because I think that's the best. I do think it's the best that he takes part in the trial and if he is ... if it will help in the future, I think it's a good thing. Whether it's the right decision or not I don't know, only time will tell I suppose” [01, adult daughter]

Different research contexts

Proxies' views about the relevance of the type of research study involved were mixed. Some expressed concern about potential side effects of new medicines or interaction with the person's existing medication, however some proxies did not view the type of research as a particularly relevant factor in their decision-making. Others considered the risks associated with a clinical trial, where side effects would be monitored and stopped if necessary, to be less concerning.

"I think it might have been different for a different type of study. And I think it would be different if it was, I suppose if you were talking about, I don't know, a more serious illness" [01, adult daughter]

"... because it's unlikely it's going to be any sort of permanent harm and if anything's really going disastrously wrong and the researcher's finding that it is harming lots of people well it's going to be stopped isn't it?" [08, adult daughter]

Talking about their main concerns about the person participating in a research study, the type of study was less of a consideration for proxies than the impact on the person, such as the potential distress caused to the person from being asked questions they couldn't answer, and the practicalities of being involved.

"I didn't want him to be distressed. If I could answer the questions rather than dad actually be put you know, and answering ..." [10, adult daughter]

"I think also you think how long is the research going to last, she may be okay now, but is she going to be able to cope with it all the way through ..." [03, adult daughter]

A nice bit of research

Proxies were influenced by their own attitudes towards research, or views about the particular study in question. The research needed to be viewed as important and worthwhile by the proxy, who frequently referred to the study under consideration as being a 'good' piece of research, because otherwise they did not feel able to agree to their participation.

"...and I said, "This is quite an easy decision", because it was just, I thought it was quite a nice bit of research" [02, daughter-in-law]

"If you're responsible for somebody who can't make those decisions themselves, then you need to be damn sure that the thing that they're getting involved with is worthwhile. And I think it's the worthwhileness, which is the important thing. If the carer doesn't feel that the work is worthwhile, then I don't see how you can make a decision to put somebody in for it" [05, adult son]

But proxies recognised it was easy to consider the research from their own perspective – would they want to participate themselves? – and agree to participation because they wanted to do it, rather than deciding for the person. Some proxies recognised this tendency to take their own views, feelings and life into consideration, and that this was not the intended basis for the decision.

“If it’s actually doing it for me it’d be very different. So you have to sometimes keep reminding yourself this isn’t about me, this is about them and actually trying to remember to come back to that and sometimes reminding yourself to do that and that’s, it’s very easy to get carried away sometimes and think you’re doing it because you want to do it. That doesn’t count”. [08, adult daughter]

Seeking assent and respecting dissent

Once the proxy had made a decision that the research might be ‘a goer’ they would involve the person. Usually this was to gauge their feelings about it or to check it was ‘OK’ rather than seeking any meaningful involvement in the decision itself. This was because the person was not currently capable of understanding the impact of their decisions or weighing up the competing arguments. However, if the person said ‘no’ and if there was enough feeling behind a ‘no’ then the proxy would respect it.

“If she’d have said “no” to all of them, even if I would have thought, well you’re being silly, and if she, but she’d have said “no”, I would have just said, “well I’m sorry, [name of mother-in-law] doesn’t want to take part in this” [02, daughter-in-law]

Because the proxy was familiar with the person, they felt that they would be able gauge whether they objected or not, or if they had understood. Proxies considered themselves able to tell from the way the person said ‘no’ – they know them well enough to ‘see it in the person’s face’ or just get a sense or feeling from them ‘in the moment’.

“...it would depend how she said it, I think, because I know her, if there was enough feeling in it, no I wouldn’t want to do that, no, then I’d be like well you know, she doesn’t want to do that, it’s just judging her at that, at that time” [16, adult daughter]

6.3.2.6 Theme: It’s a tough job

The proxy as caregiver

Decisions about research were not made in isolation and were influenced by the family member’s dual role as both carer and proxy. Proxies described being a carer as hard work, both mentally and physically, and so the proxy took that into consideration when it came to the person participating in research. Participating in research can involve research visits and assessments that are in addition to the person’s usual care and treatment activities, which the person was unable to access without the support of the carer.

“And then obviously I do all the care. As soon as I’m home, I’m doing all the caring for mum. So it’s like, actually, I need to also think about if things go wrong my ability to be able to continue to do, and, you know, not go off the rails myself sort of thing” [06, adult daughter]

Whilst most proxies accepted that they were responsible for the person, some described ‘running someone’s life for them’ as a weight or a responsibility, but, as this daughter described, it was also an honour to be entrusted with the authority to make decisions for the person.

“I mean it’s, it is quite a thing to make somebody else’s decisions for them a lot of the time isn’t it? But it’s, I suppose it’s an honour that somebody actually wants to do that for you isn’t it, to actually give you that ...” [08, adult daughter]

Dyadic relationships and role reversal

Their caring relationship meant that proxies wanted to continue sharing their life with the person they represented and to have them ‘around for as long as possible’. They felt a strong sense of responsibility towards the person, and often described a change in the dynamics of their relationship where the parent-child roles were now reversed, sometimes a change that has occurred gradually over time. For some proxies, their caring relationship was seen as the source of their responsibility to care for the person and make decisions on their behalf, as a parent does for their child, rather than any legal source or process.

“You change. You become the parent. And I think that’s what it is. Forget the Powers of Attorney and all that sort of stuff. When you have somebody, they might not, you know with mum’s condition as she is... I’ve just become the parent. So I’ve assumed that parental role. So you don’t think about it. You just do it. Yeah” [06, adult daughter]

Like caring for a dependent child, their new ‘parental role’ involved continuously making everyday decisions such as what the person was going to wear and what they were going to eat, which could be difficult for the carer to sustain over time and was sometimes described as wearing the carer down.

“I mean who decides what coat he wears when we go out and it’s like this you know, it’s what they call the wearing down which you don’t really take into account unless you think about it” [07, female spouse]

Acting as a carer and proxy for someone who was no longer able to make their own decisions also had an emotional impact on the proxy. This was particularly felt by a participant whose

wife had always been the primary carer for their whole family, and who had previously been a successful businesswoman, but now needed her family's help and support:

"But it's one of those things, you've just got to, from being a very capable woman ... and now, because I have to do it all. She can't make decisions anymore. So it's seeing the change is err, it can be a bit upsetting if I dwelled on it". [12, male spouse]

The need for support for proxies

Whilst some proxies reported that making a decision about research was straightforward which didn't require great deliberation, others described it as a difficult and challenging decision. Improving the decision-making process was recognised as being much more than just ensuring the proxy had received adequate information. Proxies thought that greater decision support when considering research decisions would help in the future. This included orientating them towards considering the person's own views and preferences.

"Actually trying to write it in very simple English and saying if you're making a decision for your loved one what [you] would be thinking about is what would they like to do ... and prompting people so it helps them think actually it isn't about me it's about them and what they'd like" [08, adult daughter]

Proxies suggested that this support could take the form of a different sort of information sheet, which covered their role as proxy decision-maker, or other sources of advice and guidance.

"... and actually just raising awareness about how difficult it is for people to make, actually make decisions for other people too, supporting people saying you don't need to decide here and now, you've got time, all these, your cooling off type periods" [08, adult daughter]

Some proxies reported that simply having an opportunity to discuss what they thought the person's views and wishes would be and reflect on whether they were making decision based on the person's preferences or their own, could have an impact on improving understanding about their role as proxy.

"I looked at it, you know, whether mum should, I just thought, just said, no, you know, it was an instant thing, it wasn't really then, until after speaking to you, I actually thought about it and I was thinking well was that the right thing to do? I don't, you know, and it just starts you thinking about it doesn't it?" [16, adult daughter]

6.4 Discussion

The study findings have demonstrated that proxy decisions about research are complex, contextually dependent, and emotional and relational in nature. Proxies were guided by their responsibilities and obligations to do what is best for the person they care for and viewed decisions about research as part of their wider caring responsibility. Proxies did not necessarily seek to replicate the decision the person would have made, even if it had been possible to do so. Instead, they constructed a decision using what they thought the person would have decided, accessed through their knowledge of both the person's life and their moral values, whilst balancing the relational harms and benefits of participating, in order to make a decision that was in line with what they thought the proxy would want them to do. Thus, seeking a decision that was authentic to the person they represented, rather than attempting to accurately predict their preferences.

6.4.1 The relational and constructivist nature of proxy decision-making

Decisions were made within the context of a dyadic relationship between the proxy and the person they represent, where dyadic refers to an existing close relationship (277). The relational and constructivist nature of proxy decision-making identified in this study is supported by previous research which describes how choosing family members to act as a proxy is not solely based on their ability to predict the person's wishes (202). Instead, Brock suggests, it is because strong family feelings of love, trust, and responsibility towards one another brings relational obligations and responsibilities, and with these comes some discretion about how these are fulfilled (114). The constructivist nature of proxy decision-making identified in this study is supported by Yarborough's discussion around constructed judgements, where the proxy's familiarity with the life narratives of the person they represent is the most salient ethical consideration in research, not the degree of risk or the nature of the health condition being studied (278).

A recent Australian study explored how health proxies make decisions about treatment on behalf of a person living with dementia (279). The DECISION Study extends this by showing that research proxies also use the person's expressed wishes where available and, where these were not known, their in-depth knowledge of the person's values and preferences facilitated decision-making on their behalf. Another theme identified in both studies was

proxies 'striking a balance' between respecting the wishes of the person and looking after their interests, although protecting the person's 'best interests' was a stronger theme in the Australian study due to the nature of the decisions under investigation, which often centred around end-of-life care and Advance Care Planning (279). As reported by proxies in the DECISION Study, the difficult balance between honouring the person's wishes and protecting their interests is more complex in practice. A theme from Fetherstonhaugh's study that was not identified in this study was consulting other family members (279). Participants in this study reported making the decision themselves, unusually without consultation with others, although they informed other family members once they had made the decision. The Fetherstonhaugh study didn't identify the importance of relationality and trust between the person and their proxy, which was a central theme in this study, nor the concept of temporality of relationships that was identified here. Time can be said to consist of three dimensions: the past, present, and future. Proxies in this study considered all three dimensions when making decisions, even though the legal frameworks appear to focus on the single temporal aspect of the person's past wishes.

6.4.2 The context of the proxy as carer

A previous study which explored experiences of proxy decision-making for treatment and care decisions found that it can be a difficult role, and the uncertainty of decision-making can take its toll on proxies (280). Similarly, the participants in the DECISION Study also identified the 'tough job' of being a proxy, which often involved acting as an advocate for the person, and where sometimes there was an emotional and decisional burden, particularly when combined with day-to-day care for the person. There have been calls for future research to be directed towards understanding the difficulties people actually experience when serving in the proxy role by approaching the question of how surrogates contribute to the care of their loved ones in terms of the complexity and 'muddiness' observed in practice (24). This study aimed to contribute to the evidence by exploring how decision-making for those with impaired capacity is contextualised within the wider care and decision-making paradigm. It identified for the first time that there is a need for decision-making support for those who experience difficulty when facing a decision about research participation on behalf of someone who lacks capacity to consent.

6.4.3 Decision-making about research participation

Proxies' reasons for agreeing to participation in research on the person's behalf in our study closely matched self-reported reasons for participating in research. Decisions about participating in clinical trials made by patients themselves are known to be complex. Patients attempt to make sense of the trial itself, of the rationale for the trial, of the trial interventions and of the randomisation process, and they try to make the decision that is right for them (281). In a study with patients approached to participate in a clinical trial, reasons for taking part were complex and wide-ranging including personal benefit through access to new treatment or enhanced monitoring as 'inclusion benefit' (282), and enriching their personal life, in addition to benefiting others through exercising their moral duty and to benefit future generations (283). A study of patients' reasons for participating in a clinical cancer trial also included themes identified in the DECISION Study, particularly hoping for help while helping others, and that the decision to participate was guided by emotions, and based on a trusting relationship with healthcare personnel rather than on careful reading of written information (284).

The findings were also consistent with a previous study that explored how proxies made decisions about treatment and care (as opposed to research) which found that, while surrogates considered many factors, they focused more often on the person's well-being than simply on their preferences (285). Similarly, both the previous research about treatment decisions and our study about research decisions found that prior conversations with the person about their preferences was not a significant factor in whether proxies prioritised well-being or preferences (285).

6.4.4 The importance of knowing preferences and values

Similarly, in this study, many proxies referred to altruistic characteristics or acts by the person they represented as an example of knowing they would want to help others through participating in research, in addition to considering any benefits to the person and the proxy themselves. It has been suggested that access to the person's life narrative would allow the proxy to know their altruistic nature (or not) as those willing to participate in research are generally motivated throughout their lives by the welfare and needs of others and not just themselves (278). There is no reason that diminished decisional capacity must rob people of their ability to continue such a legacy (278). Although there are concerns that unlike acting

altruistically in this case the person is cast in an altruistic role by others (17) or motivated by the proxy's desire for 'altruism by proxy'. One participant also highlighted that acting as proxy or research partner is itself an altruistic act [04, adult daughter] and so proxies may themselves also be orientated towards an altruistic disposition. This may be a characteristic or value shared with the person they represent as an example of the shared values (similarity) that several proxies referred to when describing their close relationship as the basis for 'knowing the person' (familiarity). The importance of knowing the person and the centrality of relationships are common themes in the wider literature about caring for those with conditions characterised by dependency and vulnerability (286,287).

Family members did not view decisions about research as being separate to those about the person's health or welfare but being intrinsically linked, although they recognised that there were differences between the types of decision. When making decisions about research participation they had made a decision as someone who knew the person best and had not considered their role in relation to being designated their attorney (or not). However, many proxies spoke about the potential benefits of extending an LPA to include decisions about research, which many had not considered previously but all assumed to already be the case. Additional data, which explored the role of Power of Attorney in decisions about research, and participants views about extending current legal arrangements to optionally include research, is not included in this thesis due to space constraints. However, a manuscript reporting the analysis of these data has been submitted to a peer-reviewed journal.

Participants' views about LPA and research contrasted with those of health and social care professionals who care for those who lack capacity to consent who, when surveyed, commonly assumed a LPA was needed in order to act as a research proxy (Chapter 4) (216). Participants described how the 'power' aspect of a Power of Attorney brought clarity to some situations, where individuals and organisations knew who was authorised to make proxy decisions and to what extent. A comprehensive report into the ethical issues surrounding dementia, including dementia research, (288) recommended that that serious consideration be given to enable the role of the welfare attorney in England and Wales to be explicitly extended to include decisions over research, both within the Mental Capacity Act (20) and the Clinical Trials Regulations (22). Extending the role of LPA to include decisions about research may help address the current uncertainty and concern of health and social care professionals about where the locus of authority lies in decisions about research (216).

6.4.5 Application of the legal frameworks in practice

The threshold for involvement in the decision-making process did not reflect the legal dichotomy of capacity/incapacity. Proxies generally sought the involvement of the person in the decision, regardless of the extent that they were able to participate. Often this was to seek their assent to participate, that they were 'OK' with it, or indicated any dissent or objection to taking part. Proxies generally felt that they were able to get an indication of the person's willingness or not, and whilst the absence of any assent did not change their decision, any sign of dissent, no matter how uninformed, was considered binding by most proxies. The ability to express a preference about the 'reasonableness' of an option has been described elsewhere as a faculty that may be retained by those affected by dementia (289).

Notably, proxies didn't distinguish between whether they were providing consent (for a clinical trial (22)) or advice to researchers (20) but still viewed themselves as having the authority to make decisions about participation (or not) without reference to their legal position as a consultee or legal representative. Those who had acted as consultee, for example, saw themselves as the decision-maker despite the role of consultee being to provide advice to the researcher who makes the decision regarding participation (20). The consultee effectively having the power of veto (17). A comparison between the legal and ethical requirements and empirical evidence about how proxy decisions are made in practice forms the basis of Chapter 8.

6.4.6 Conceptual and theoretical frameworks

The relationship between the interview data and the ethical concepts identified in the conceptual framework from the systematic review (Chapter 3) is described at length in Chapter 7 through a grounded theory analysis. When viewed through a decision-making lens, as described in this thematic analysis, a number of theoretical links can be identified.

A growing number of theories of proxy (or surrogate) decision-making have been proposed (290). Many explore the psychology of making decisions on behalf of another person using hypothetical scenarios, where decisions are assessed by how close they are to the stated wishes of the person (131). However, proxy decision-makers are not necessarily aiming to match the wishes of the recipient, but instead to make what they perceive to be an optimal decision – in other words what they think is best for the person irrespective of the person's

actual or simulated goals or desires (131). Tunney and Ziegler suggest that in order to achieve this, proxies simulate their own preferences and the perceived preferences of the other person, and this computation of alternative perspectives is affected by factors including the significance of the outcome, future accountability, and degree of empathy. Construal Level Theory suggests that risk preferences are affected by psychological distance, therefore greater emotional involvement between the person and their proxy reduces psychological distance and so closes the empathy gap between them (129). Lowenstein's 'risk-as-feelings' hypothesis suggests that preferences and choices are affected by emotional reactions to risk, rather than a purely cognitive evaluation (291).

Many of these concepts feature in proxies' own accounts of decision-making reported here. The findings from this study indicate that research proxies balance both what they think is optimal (or best) for the person, alongside what they think the person would have wanted them to decide (what is the 'right' decision) within the specific decision context. As there is a close personal relationship between the person and their proxy, with significant emotional involvement, the proxy's emotional attitude towards risk invokes their protective role. This is particularly relevant where there is a relational aspect to the benefits and harms which will also affect them as the person's carer. The risk aversion and fear of uncertainty expressed by proxies may have resulted in them exhibiting a status quo bias (292) intensified by their emotional response to the person's vulnerability. However, proxies are also seeking to advocate for the person and respect their known wishes and feel a responsibility to continue to act altruistically on their behalf. It is when there is conflict or uncertainty surrounding these factors that proxies experience the burden of decision-making.

Further development of these conceptual and theoretical links with the data is the subject of Chapter 11, where the theory underpinning proxy decision-making for research is discussed in more detail in relation to the development of a complex intervention to support proxy decision-making.

6.4.7 Reflections on the study and qualitative research methods

This study has explored research proxy decision-making in a variety of real-life situations with a range of family members who had acted as proxies. It was generally easy to establish rapport and trust with participants both in person and by telephone, and a responsive approach provided rich first-hand accounts of proxies' experiences. This has enabled an

understanding of proxy decision-making from the perspective of family carers for the first time in the UK. Limitations included the selection of proxies who all agreed to participate in the study and therefore necessarily had a positive attitude towards research generally. The recruitment methods used attempted to include proxies for those who have had lifelong impaired decision-making ability or an acute loss of capacity in order to incorporate a wider range of experiences, but it proved difficult to recruit these individuals. However, participants did include those who had made the decision for the person to participate, as well as those who declined, and a range of study types that included clinical trials of medicines, which have different legal provisions from other types of research (33).

The majority of participants represented someone whose cognitive impairment was associated with dementia, as a result the findings may not be transferable to proxies representing people with different impairing conditions or in different situations. The challenges experienced around involving people experiencing anosognosia, in which the person is unaware of or in denial about their impairment due to their condition (293), are specifically associated with dementia-related pathologies and may not be experienced by proxies making decisions on behalf of individuals with other impairing conditions. Seeking assent, or at least any indication of 'non-dissent', was considered a way of involving the person in the decision and increased the proxies' comfort as decision-maker, would not be relevant to patients who are unconscious in ICU. The decision context, where proxies considered previous wishes and preferences, and where the person was unlikely to regain capacity and hold the proxy to account for their decision, should be borne in mind when considering the transferability of the findings to populations with life-long impairments or with a temporary loss of capacity.

Throughout the study attention was paid to ensuring the quality of the qualitative research, incorporating the characteristics of good qualitative research that have been proposed (276). These are considered to include elements such as: sensitivity to context (attention to participants' perspectives); commitment and rigour (in-depth engagement with topic); transparency and coherence (transparent methods and data presentation); and impact and importance (enriching understanding) (275). Situating the qualitative interview study within a larger programme of doctoral work enabled a deeper engagement with the topic through the literature and systematic reviews that preceded it, and greater sensitivity to the ethical and legal context through the prior development of a conceptual framework. Adopting a reflexive approach enabled consideration of how prior clinical experience has impacted on

subjectivity when conducting the research, and also how the research methods used has influenced the research (254). Attention has been paid to rigour throughout the study, and the findings, together with the additional analysis reported in Chapter 7, hopefully provide a much richer understanding of families' experiences as proxy decision-maker for research as a result.

6.5 Summary

Proxy decision-making for research is a complex process with inter-woven layers of decision-making. Family members acting as proxies balance a number of different factors related to the person they care for and their values, preferences and interests, within the specific decision context of the potential harms and benefits of the study and the practicalities of being involved. They use these factors to construct a decision that is authentic to the person and their life and that would be in line with what the person themselves would choose if they were able. They use the person's biographical narrative and their own views about research, alongside the information about the specific study in question as 'building blocks' to form a decision that they think will lead to the best outcome for the person as well as themselves as the person's carer. Decisions about research participation are also influenced by proxies' prior experiences, their emotional attitude to risk, and perceptions about the value of the research. Currently, decisions about research are not included in Lasting Power of Attorney arrangements, despite previous recommendations from the Nuffield Council on Bioethics (288).

Proxies viewed research as being inevitably linked with all other aspects of the person's life and so felt that decisions about research weren't isolated from their role in maintaining the person's health and wellbeing more generally. Proxies are guided by their responsibilities and obligations to do what is best for the person they care for and see decisions about research as part of their relational responsibility as the one who is trusted to care for the person and protect their interests. Decisions can be problematic for some proxies who are concerned about making the 'right' decision, and some proxies may benefit from decision support to make an informed decision about research participation on behalf of the person.

6.6 Learning points

Proxy decisions about research are complex, contextualised, and guided by proxies' hope for benefit for the person they represent whilst seeking to protect them from any further harm. They are not necessarily hoping for the person to benefit directly from the intervention, but they also consider the 'benefit of giving' that comes from contributing to science or helping other people in the future.

The close relationship between the person and their proxy means that the potential benefits and harms of participating are seen as relational, and the research itself is perceived as a joint venture, particularly when the proxy is also an informal caregiver.

Knowing the person means knowing their past preferences and values, as well as their current wishes and ability to cope with the practicalities of research activities and procedures. Proxies make authentic decisions which are constructed within the context of their temporal relationship with the person they represent. This relationship of trust, which is characterised by relationality, similarity and familiarity, is seen as both the source of the authority to make decisions, and also guides the content of those decisions.

However, decision-making can be burdensome for some proxies who are attempting to make a decision that will provide the best outcome for both their family member and themselves, balanced against uncertainty and precarity. Proxies may benefit from support when making decisions about research, which may be through acknowledging that decisions can be difficult and to orientate them towards considering the person's views and preferences about participation.

Chapter 7 DECISION Study: an empirical analysis of ethical aspects of proxy decision-making for research using a modified Grounded Theory

7.1 Introduction

As discussed in the literature review in Chapter 2, normative accounts of proxy decision-making have historically been based on an ethical framework that proposes a ‘step-wise’ approach which starts by first turning to the person’s advanced directives or statements about their wishes or, in the absence of any such directive, a substituted judgement, then asking what the patient would have wanted, and lastly relying on the standard of best interests (28). However, a number of flaws with this theoretical bioethical hierarchy have been identified, not least that it rests upon false assumptions (28) and is far removed from proxy decision-making for research in practice as reported in Chapter 3 (167). This criticism of ‘abstractedness’ is illustrative of the perceived shortcomings of traditional philosophical approaches to ethical issues, where reflections and even proposed solutions are too far removed from everyday practice in healthcare (294). There is a need to develop new understandings about ethical practices, such as proxy decisions regarding research participation, that take account of the complex and morally pluralistic world in which they are situated.

As part of the systematic review of empirical studies reported in Chapter 3, a framework was developed (**Figure 3-2 Framework of proxy decision-making for research involving adults lacking capacity**). However, as the studies included in the review were predominantly hypothetical or scenario-based studies, further work to empirically explore proxy decisions about research participation in practice was required. The aim of the DECISION Study interviews was to explore proxies’ views and experiences of decision-making for research, as reported in Chapter 6, and to interrogate the ethical conceptual framework with the potential to revise it, which is the focus of this chapter.

In order to analyse the interview data within the context of proxy decision-making from both a sociological and ethical perspective, a pluralistic analytical approach was used to examine the data through multiple lenses. Methodological pluralism includes bringing together

multiple methods, data collections, theories, analyses, or disciplines within the same research project (295). The use of mixed qualitative analytical methods in single studies has been termed 'analytical pluralism' (295) and has seen a recent growth in popularity (271). Analytic pluralism does not necessarily seek one definitive 'truth' about a particular dataset but tries to uncover a multidimensional understanding of the various elements at play within it (296). Pluralistic qualitative analyses have been found to be valuable in providing a multi-layered understanding of phenomena which possess ontological and epistemological multiplicity and multidimensionality (297). They also have the potential advantages of balancing the strengths and limitations of individual methods against each other and being easier to disseminate to a wider range of audiences (296).

Grounded Theory (GT) methods have been widely used by empirical researchers in bioethics (298) and legal research (299) and to explore decision-making processes about research participation (300). As distinct from the thematic analysis (TA) reported in Chapter 6 which seeks to understand events or experiences of a phenomenon (254), GT focuses on building theory that is grounded in the data, with an emphasis on understanding processes and actions (254). Developing a model in GT involves interpretation to work out how the different codes, concepts, and categories, in the analysis 'fit together' to create a theoretically informed explanation of the social and psychological processes underlying the phenomenon of interest (254) and generate substantive theory as a 'mid-range' theory, which consists of elements – conceptual categories and their properties, and hypotheses or relations between the categories and their properties (301). However, while the application of the GT can result in a theory, in many cases it amounts to a new or better conceptualization or a framework that links concepts but falls short of a fully elaborated theory that covers all aspects, stages, consequences, and likelihood of a process or a phenomenon (302). There are many definitions of theory, but the meaning used here is that a theory is 'a particular kind of representation of some phenomena . . . it comprises constructs, relationships among constructs, and a boundary within which the relationships among constructs hold' (303). Theory as described here also has modifiability, and so can be altered when existing data are compared with new relevant data (304).

It has been suggested that ethical concepts are amenable to an analysis of their functions, where functions are understood as goals set by moral agents and ethical principles are shorthand for obligations and duties which reflect what is valued in a given concept (305). This analysis used the participants' accounts of proxy decision-making about research

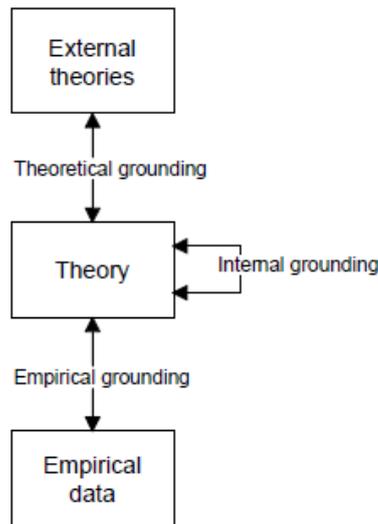
participation in order to develop an understanding of the ethical concepts involved, to analyse their respective functions, and to explore the interactions between those concepts.

7.2 Methods

Semi-structured interviews were conducted with family members who had acted as a research proxy for a person who lacks capacity. In addition to exploring proxies' experience of decision-making about research participation reported in Chapter 6, the aim of the interviews was to critically examine the framework developed during the systematic review, and further refine it based on updated concepts that were identified from the interview data. A full description of the methods used for participant recruitment and data collection has been provided in Chapter 6. Following completion of the thematic analysis reported in Chapter 6, the original uncoded interview transcripts were revisited to undertake an additional analysis using a modified version of GT. GT was selected as, while some tensions exist when it is applied in the context of ethics, it is considered to stand in a "harmonic relationship" with most ethical theories (51). It can be used in conjunction with numerous qualitative approaches such as TA, and in varied mixed forms of qualitative analysis (306).

The GT approach emerged out of the empirically based sociological theorizing by Glaser and Strauss (301), however, GT has since developed and diverged into different 'dialects' (307). One of the areas of division is over the strictly inductive approach favoured by orthodox GT where categories are generated from the data without prior engagement with the literature, as contrasted with an abductive approach which may incorporate pre-existing theory or theories to discover new concepts, ideas or explanations of the data (308). Other variants have also been proposed (308). One modified or extended version, multi-grounded theory (MGT), seeks to combine aspects from both inductivism and deductivism. MGT involves three complementary types of grounding processes: empirical grounding, theoretical grounding, and internal grounding (**Figure 7-1 Three complementary grounding sources for a developed theory in Modified Grounded Theory** (from Goldkuhl and Cronholm 2010)) (307). It therefore not only provides an empirical data-ground for the emerging theory, but also proposes that other knowledge sources are needed for justification (307).

Figure 7-1 Three complementary grounding sources for a developed theory in Modified Grounded Theory



MGT has been increasingly adopted in recent years as it allows for other resources — theories, conceptual frameworks, and other data — to be used to inform the research (309), although its use in empirical ethics has not previously been reported. As this analysis built on the findings from the systematic review and the ethical framework previously developed, the MGT method was selected as it embraces the use of existing theories and research questions as a fundamental aspect of the analytic approach to theory development. This has enabled the development of a richer account of proxy decision-making that is grounded both empirically and theoretically (307).

7.2.1 Sampling

Rather than using the number of participants or quantity of data to determine sample size, grounded theorists focus on the richness and ability of the data to illuminate the concepts being investigated (310). It is generally accepted in GT that the aim is to achieve theoretical saturation, with categories considered to be saturated when gathering additional data no longer generates new theoretical insights or new properties of the core theoretical categories (310). This is achieved through theoretical sampling of multiple incidents in multiple groups and maximising the differences among groups, paying attention to a diversity of concepts and relationships from different vantage points (301).

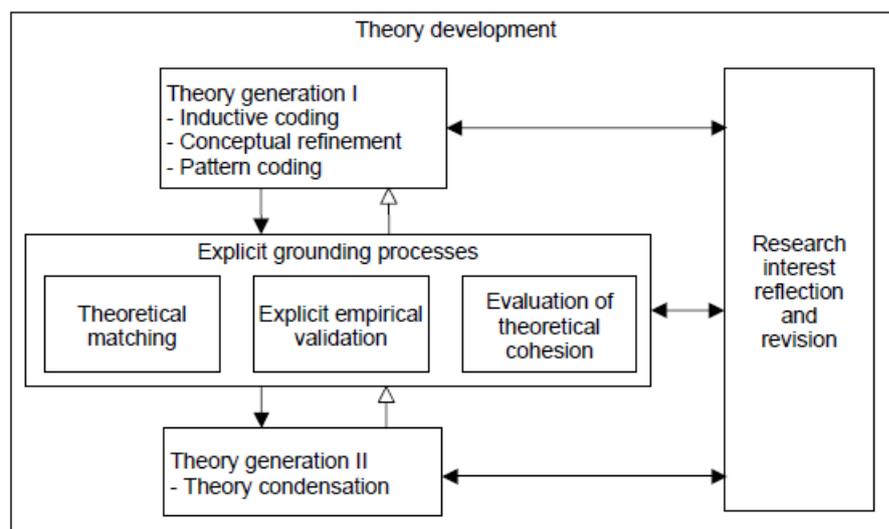
Theoretical sampling is an iterative process, where the evolving data analysis and theory development shapes the selection of subsequent participants to help further develop the

theory and so sampling is driven by theoretical considerations (254). Whilst the data used for this study was collected primarily for a thematic analysis of the proxies' experiences of decision-making (Chapter 6), the interviews were also intended to develop an ethical model of proxy decision-making building on a framework previously developed (167). Despite GT not being explicitly selected at the outset as the method used to address the research question exploring the ethical issues, attention was paid to the developing ethical concepts throughout the data collection period, and a range of proxies and a variety of incidents were sampled as a result.

7.2.2 Data analysis

Many variations of GT, including MGT, share the same set of key methodological strategies, including: moving from initial coding to focused coding; memo-writing to record the analytic processes; to identify and refine categories; and develop initial theory (311). The multi-grounded theory (MGT) process (see **Figure 7-2 Working structure of the Modified Grounded Theory approach** (from Goldkuhl and Cronholm 2010)) is divided into three stages of theory development: theory generation, explicit grounding, and research interest reflection and revision. Theory generation consists of inductive coding of the data, conceptual refinement, pattern coding, followed by theory condensation (307).

Figure 7-2 Working structure of the Modified Grounded Theory approach



The transcripts were initially coded using inductive coding – a process of letting the data ‘speak’ which corresponds to open coding in GT. Coding in GT methods has a particular focus on actions and processes, rather than topics. Therefore, the initial analysis purposefully involved the use of gerunds (verbs ending in -ing such as asking or deciding) as much as possible (312) which allowed for a reconstruction of actions and which subsequently facilitated the development of the theoretical framework (310). The higher-level codes and initial categories were identified inductively through grouping or clustering of similar codes, and then reviewed alongside the coded data to ensure they accurately captured the action or process. The conceptual refinement stage required working with the categories in a critical and constructive way to identify the content, context, and function of each concept (307). Rather than a one-off event, it was an intensive and iterative process throughout the whole data analysis phase, in which a key task was creating a comprehensive definition of the categories. Refinements in the categories’ definitions, and developments in the analytical process generally, were recorded through extensive data analysis memos (254) held in NVivo. Discussions during the various stages of data analysis were documented throughout the process.

Following on from this, pattern coding was undertaken, which is said to correspond to axial coding in GT (307). This stage involved the conceptualizing of action patterns from the categories identified, in which the categories were combined into theoretical statements. The proposed conceptual relationships between the categories were then identified to begin linking the categories into a coherent theoretical model (301). The concluding stage in MGT is theory condensation which corresponds to selective coding in GT (307). In order for theory condensation to take place, three types of explicit grounding processes must occur which help to analyse and control the validity of the developing theory through internal and external grounding. These are: theoretical matching, explicit empirical validation, and evaluation of theoretical cohesion (313). This stage largely consisted of discussions around the congruence of the findings with empirical data from the systematic review, and the relevant normative concepts, in order to evaluate the cohesiveness of the theory being developed.

The resulting conceptualisation is represented in the following sections in the form of an ethical framework. Reflections on the use of MGT, and conducting pluralistic analyses, are described in the discussion section of this chapter.

7.3 Results

7.3.1 Participants

As reported in Chapter 6, interviews were conducted with 17 family members who had acted as a research proxy for a relative who had impaired or absent capacity. Participants were predominantly female (13/17, 76%), and were either an adult son or daughter (12/17, 71%) or spouse (3/17, 18%) of the person they represented. One person was both a daughter of someone with impaired capacity and the spouse of someone with impaired capacity, and one person was a daughter-in-law. Participants were predominantly a proxy for someone living with a form of dementia who had developed impaired capacity gradually; one participant cared for someone who had suddenly experienced cognitive impairment following a stroke.

7.3.2 Categories

Six categories capturing the ethical practice of proxy decision-making for research were identified. These categories are inter-related, and reveal concepts operating in different roles within proxy decision-making. The concepts take the form of characteristics of the proxy-patient relationship, decision processes or 'following principles', and standards of ethical decision-making, all set within the context of how research is viewed and valued.

7.3.2.1 Reflecting on research – its value, and difference from treatment or care

Proxies recognised that decisions about research were different to those about medical treatment. They viewed participating in research as having value, beyond any potential benefits to the person, which influenced their decisions about whether the person they cared for should participate.

“And just recognising that it’s a good thing to do research” [08, adult daughter]

Participants recognised that this value judgement was an important requirement for the proxy to make a decision about participation on behalf of another person.

“If you’re responsible for somebody who can’t make those decisions themselves, then you need to be sure that the thing that they’re getting involved with is worthwhile. And I think it’s the worthwhileness, which is the important thing. If the carer doesn’t feel that the work

is worthwhile, then I don't see how you can make a decision to put somebody in for it." [05, adult son]

Underpinning the proxy decision is an assumption that the person would share the proxy's own view about the value of taking part in research. This may also mean the proxy 'projects' their views onto the person.

"For the whole of society, because my mother, if research, if she were eligible, could assist people in the future, then that has got to be good hasn't it?" [15, adult daughter]

7.3.2.2 *Relationality, trustworthiness, and being trusted*

Trust and having a trusting relationship were fundamental values underpinning proxy decision-making for research. Trust featured through both the trustworthiness of the proxy and the functions or roles it played in decision-making. Trustworthiness determined who is chosen to act as proxy. Trust provided the authority to make decisions on the person's behalf – where the proxy was trusted and so their decision was trusted by the person – and it also provided the conditions for making the proxy decision as it required the proxy decision-maker to make the right (or good) choice for the person.

"You have to have the trust don't you, to make a decision for somebody, you, they have to trust you and you have to trust them, they know you're doing the right thing for them" [02, daughter-in-law]

Trusting an individual was not necessarily task-specific, it may apply to trusting them in all areas of the person's welfare. However, trust was relationship-specific and so not all family members are trusted equally. Being trusted was linked to the nature of the relationship between the person and their proxy, drawing on principles of mutuality and reciprocity and elements of similarity of worldview. Mutual trust also featured between family members who act as proxies jointly or severally.

"I actually signed here, but we're of the same frame of mind anyway and I like just told her [referring to her sister]. Yeah, fine. We've both got the same thoughts on these little things. Yeah, we just trust one another" [11, adult daughter]

Trust was considered to have moral weight by proxies, where proxies felt the responsibility of having trust bestowed upon them. It was viewed as a heavy burden at times, but it was also considered an honour.

"It's quite onerous sometimes ...I mean it is quite a thing to make somebody else's decisions for them a lot of the time isn't it?" [08, adult daughter]

Trust was generally implicit within the relationships between the proxy and the person they cared for. However, there were examples of trust being explicitly stated, or being demonstrated or made manifest, such as through the process of appointing the proxy to be their welfare or financial attorney, which was effectively saying 'I trust you to make decisions for me'.

Trust was considered to have organic properties. Trust grew over time as the person has increasingly been trusted to look after the person's affairs and so was increasingly viewed by the person as trustworthy. It was transitive in nature as it flowed or was transferred from one person to another. This transitivity had particular relevance when those involved in approaching the proxy regarding participation were known and trusted by them, or in cases where trusted care home staff introduced researchers they trusted to the proxies.

"It was well going down the lines and if the person you trust trusts that other person you trust that person as well. Yes, and I trust this home completely ...and they trust [name of researcher] ...so I trust [name of researcher]." [10, adult daughter]

7.3.2.3 *Respecting known wishes*

Proxies used what they knew about the person and their wishes and preferences about taking part in research as part of their decision, sometimes using the person's biographical narrative as the primary source for knowing what they would wish. Some proxies had had specific conversations with the person they represented, or they were aware of written statements about the person's wishes to take part in research. Some proxies knew about the person's previous participation in research and used this as a guide to knowing their likely wishes about taking part in the particular research study under consideration.

"He may not now make his decision what to do but I know from what he's said in the past that he would do anything to help. Knowing what his previous thoughts were, and knowing that he actually said, and I'm not sure he didn't write it down" [07, female spouse]

Where there had not been previous discussions or statements that the proxy could use to determine what the person would decide, they used other factors as the basis for their decision. These were based on knowing the person's previous occupations and interests, which indicates to the proxy whether they would have wanted to participate or not. The

weight given to these interests was dependent on how committed to them the person was, for example they may have had a lifelong interest in science or medicine. Proxies used these examples to provide justification for their decision.

“For her science is important and it always was, though she was an artist she studied science and she did a lot of abstract paintings about science.” [04, adult daughter]

Proxies also used what they knew about the person’s values and virtues when deciding on their behalf, particularly whether the person was altruistic or willing to help others. They knew whether the person would wish to 'do good' generally, even if they did not know their specific wishes about research participation.

“I think knowing my mum and [name of husband], they would both be helpful to everybody. You know, they’ve not led lives where they’ve been set away from society, they’ve always joined in with society if you see what I mean. I see it as a moral issue. Um that sort of being a good citizen.” [14, female spouse]

Some proxies acted intuitively when making a decision, rather than deliberating over the relative factors. In these cases, decisions were considered easy and were made quickly or automatically, perhaps because they knew the person well and so could come to a decision relatively effortlessly.

“I think that because I know him so well, we’ve been married for thirty years. Because I know him really well, we know each other really well.” [14, female spouse]

7.3.2.4 *Integrating preferences and interests*

The proxy considered a number of factors when making a decision about research participation, which may involve integrating the person’s known wishes and preferences and what is in their current and future interests, whilst seeking to respect both. Some proxies viewed this entirely from the person’s perspective, where they tried to consider what the person’s assessment about their own interests would be.

“I think they sort of go hand in hand really because if you put yourself in their shoes then you know what they think would be best for them, so you’re sort of reading what they’re going to be doing themselves and you can more or less sort of read what they’re thinking and I think it goes hand in hand. Knowing what he would want and what he would think is best for him.” [10, adult daughter]

The process of weighing up and deciding necessarily takes into account new information that wasn't available at the time of any expressed wishes, particularly where the significance has changed given the change in situation and therefore context. Examples of this included where a procedure that the person previously tolerated and would have been happy to undergo as part of a research study would now make them fearful and cause distress.

“The only issue I would have with those is these days giving blood tends to hurt her a little bit. I don’t know why, it never did before, but it does now. So, yeah. Whether pain is a different thing. She usually doesn’t tell you if she’s in pain but giving blood does hurt.” [11, adult daughter]

Respecting the person's values or preferences, even if they were strongly committed to them, could be overridden if the proxy considered it would be against their interests to participate. A proxy whose husband had provided clear instructions that he ‘would do anything for research’ would find it difficult to agree to research that involved an MRI scan that he would not be able to understand and so would now find it distressing. Another proxy whose husband similarly would always have wanted to participate described how his change in circumstances meant that some of his preferences before his cognitive impairment were now considered in light of the need to protect his welfare.

“He’s always been a bit of a risk taker. But at this stage, where before it would’ve been risk-taking, now I see it as not risk-taking. I would see it as ... not really having capacity to think in depth as to outcomes. Yes, it is. I mean it’s all ... with [name of husband] it’s all about his welfare now, you know.” [09, female spouse]

Proxies recognised that considering either interests or preferences may direct them to a decision that directly conflicts with the other. They used a process of balancing or integrating both preferences and interests to a greater or lesser extent, although concern for one aspect may emerge as a priority.

“The primary thing that I have to look at is quality of life for mum. A secondary thing is the benefits to other people, you know, [that is why she would want] to do it in the first place... But undoubtedly on anything it’s got to be the quality of life for her” [06, adult daughter]

7.3.2.5 *Aiming for the best and protecting from harm*

Proxies sought to make decisions that were the ‘best’ for the person involved, understood in its broadest sense rather than viewed as making a decision that was in their ‘best interests’.

This might be in terms of achieving the best outcome, where their health or welfare could be improved through participation or where there was no detriment to the person but they may have a positive experience, or best in terms of being a standard to achieve the best possible decision, which may be heavily influenced by the proxy's perception about the value of participating in research. Proxies aimed to make a good (as opposed to a bad) decision. The aim to make a good decision also rested on a value judgement by the proxy that contributing to research is a good thing, and so the proxy having a positive disposition or attitude towards research alters how the proxy views research participation for the person and whether it is for the 'best'.

"I am doing it because I think that's the best. I do think it's the best that he takes part in the trial and if it will help in the future, I think it's a good thing." [01, adult daughter]

While proxies understood that the research was not necessarily intended to benefit the person directly in terms of the intervention mediating the progress of their condition or improving the person's health, they still hoped that there would be benefit. This may be distinguished from the *expectation* that the person may benefit indirectly, such as from the social benefits of taking part. This instilling of hope may be a benefit of research participation in itself, as it may provide a positive coping strategy for the proxy at what could be a difficult time.

"It was a selfish thought [that] they [the tablets being trialled] might help mum be more like mum was" [04, adult daughter]

While the proxy might have anticipated some benefit from research participation, or at least a neutral impact, when it came to the possibility of any harm or risk or a negative experience, they put the person's welfare as uppermost. This same approach was used when making all decisions on the person's behalf.

"With [name of husband] it's all about his welfare now, you know. Hopefully I can just make his life a little bit better from the miserable existence he's been landed with really. So, it is definitely on a basis of his welfare first and foremost" [09, female spouse]

The proxy acts as a substitute for protecting the person's interests, where the need for protection was viewed as arising out of their perceived vulnerability. Caring for the person involved protecting them from 'threats' which could be from a number of directions, including: protecting them from invasion of bodily integrity (where research may be seen as

potentially invasive); protecting them from any burden or negative impact from research; protecting them from the effects of the illness; and protecting the integrity or continuity of the person's self through upholding their previous wishes or the values they previously held.

"I mean obviously I don't want to put him at any further risk. He's got limited time now, I don't mean free time, I mean limited time alive ... because he's quite frail, and so I wouldn't want to put him into any form of danger. Lumbar puncture does carry a risk. I'd probably say no; it would be because he could do without the complications of anything going wrong." [13, adult son]

"It's protection of his being, you know, that's how I see it. But he is what he is still." [14, female spouse]

However, a protective role may also have harms associated with it, perhaps by harming their interests through denying them the benefit that comes from participating in research both in terms of directly improving their health and wellbeing, as well as from 'doing good'.

"It's difficult because you're scared of what they could ... scared might not be the right word, but you're worried that you make the wrong decision ... and actually am I taking away an opportunity for her to be better than she is now?" [06, adult daughter]

The responsibility for decision-making, and the obligation to make good decisions, is viewed by proxies as part of their role, arising out of their responsibility to care for the person. The proxy's role as carer meant that they were looking after them (rather than just acting as their proxy) so for some proxies considering if the person would benefit from research fell under their aim of looking after the person and maximising their health and welfare.

"If there was an indication of benefit to my mother, then it's different, because then you're seeing it as part of your caring role. Because if you can make somebody's life better as a result of becoming involved in a research thing, then that's obviously quite different, because there you see it as part and parcel of providing care" [05, adult son]

There were three instances where proxies talked about 'serving the purpose' or 'using' the person if they don't benefit directly, or whether they would still agree to participation even if there was some harm or risk involved. One proxy raised concerns about whether, in the absence of any kind of assent or dissent from the person they cared for, if they agreed to participation then they were agreeing for the person to be 'used' as part of the research. Other proxies felt that they would be willing to agree to research participation if there was a

purpose to the study, even if the person themselves wouldn't derive any benefit and may experience some harm.

"Again, this sounds very callous, but because my mother is ninety-three, if it was causing her some distress, but I was convinced that it would serve the purpose, then I would go along with it." [15, adult son]

7.3.2.6 Seeking authenticity – getting it 'right'

Proxies also aimed for the decision to be the right decision, which meant one that would be consistent with what the person would want or would have decided, rather than seeing it as being a replica of the person's decision.

"I would be pretty sure that the decision that I made, would be in line with what she would have wanted." [15, adult daughter]

For some, this was a process of making a decision for the person and *then* comparing the person's decision with it; others used what they thought would be the person's decision and tried to approximate it. All proxies appeared to use what they knew about the person and the values, wishes, and goals that were important to them, as a way of making sure the decision was authentic to the person.

"I think of what my mum might of wanted when she was ... you know, what decisions she would have made prior to this disease taking over. And you know if I really thought, actually you know, she would want to do this then I would do it. But you know with the head that she had prior to this she'd look at this and ... I'm sure she would make the same decisions that I'm making on her behalf about that research" [06, adult daughter]

In order to make a decision, some proxies described a process of consciously trying to stand in the person's shoes and attempting to make the decision that they think the person would have wanted to make or wanted them to make.

"So you have to sometimes keep reminding yourself this isn't about me, this is about them and actually trying to remember to come back to that and sometimes reminding yourself to do that. It's very easy to get carried away sometimes and think you're doing it because you want to do it. That doesn't count." [08, adult daughter]

As part of seeking authenticity, some proxies consulted with other people who also knew the person well and who may have knowledge that they didn't have, although more often it was

just informing them rather than involving them in the decision itself. Another form of seeking authenticity was proxies involving the person themselves in the decision, irrespective of their ability to comprehend. Proxies respected their personhood and actively sought their participation in the decision and to incorporate their views. However, their assent, or any sign that they objected, was only sought if the proxy was inclined to agree to their participation. Proxies considered that they were able to read the person’s reaction as they knew the meaning of their responses and expressions, with proxies appearing to seek an emotional rather than necessarily a cognitive response.

“So, but I kind of get a feeling from her I think, but it would depend how she said it, I think, because I know her, if there was enough feeling in it, ‘no I wouldn’t want to do that, no’, then I’d be like well you know, she doesn’t want to do that, it’s just judging her at that, at that time.” [15, adult daughter]

7.3.3 Ethical framework

A framework was developed which depicts the categories identified, and the role or functions that the categories hold within the ethical practice of proxy decision-making for research. (Figure 7-3 Ethical framework of proxy decision-making for research).

Figure 7-3 Ethical framework of proxy decision-making for research



Within this framework, a fundamental underlying concept is the proxy's belief and attitude towards research, which includes the value that the proxy places on the study in question (whether it is a 'nice bit of research' or not) and whether they believe that participating in research is a 'good' thing or not. The proxy's appreciation that research is different to treatment or care, with different aims, is also fundamental to proxy decision-making. If the proxy does not attach particular value to participating in research or does not consider the particular study to be worthwhile, this impacts on their view as to whether the person's participation would be a good thing or the best thing for them. If the proxy does not appreciate the significance of the decision in terms of distinguishing it from treatment or care, and subsequently not consider the person's own wishes and preferences about research, their consideration of the relevant advantages and disadvantages may be void. The characteristics of the relationship between the proxy and the person they represent also plays fundamental role in decision-making. The proxy feels trusted by the person they represent, and so feel that the person would also trust the decision they make. This of course rests on the proxy's own self-reported account of their trustworthiness and that they are trusted by the person.

There are two key elements to the decision-making process itself, which operate as a kind of following principle. Proxies follow the principle of respecting the person's known wishes and values, which is affected by their belief that wishes and preferences should continue to be respected when making a decision on a person's behalf. Proxies also consider these preferences in the light of their assessment of how participating or not in the research study would impact on the person's interests and their own mutual interests. They consider that that their role as proxy cannot be isolated from their caring relationship, and so preferences cannot be isolated from interests. They therefore attempt to integrate these preferences and interests when making a decision about research participation.

The final part of the framework is the standard that the proxy is aiming for, or the outcome they hope to achieve. Proxies' dual role as both the person's representative and their close family member means they feel a dual moral obligation to protect the person's welfare and maximise their wellbeing whilst promoting their previous and current preferences, and so they seek a decision that is both best and right for the person. The proxy aims for a decision that is a balance between what is the 'best' outcome for the person they represent through maintaining their welfare (which might be broadly conceived as a form of beneficence) in both medical and non-medical terms, whilst seeking to protect them from harm (broadly

conceived as non-maleficence). Additionally, the aim for the proxy is to come to a decision that is authentic to the person they represent and would be in accordance with what they would want if they were able to choose for themselves. They viewed this as being the right decision and doing what is 'right' forms a critical element of proxy decision-making.

7.4 Discussion

This analysis reveals how proxies' decision-making for research is ethically complex in terms of the underpinning concepts, the processes and principles followed by proxies, and the outcomes the proxies are aiming to achieve. The findings showed that, rather than the type of research involved or nature of the decision being made (providing consent for a clinical trial or advice for other types of research), of greater significance was whether participating would advance or harm the interests of the person they represented, and whether the decision would be authentic to the person and their values. Where the 'best' outcome is the one bringing the most good to the person (29). Proxy decision-making in practice does not reflect the normative accounts of a hierarchical or 'step wise' approach, a finding which is supported by previous studies (204). However, these previous studies suggested that proxies use a combination of best interests and substituted judgement (193) or an approach that also considers the interests of others (190), or that there is a continuum between substituted judgement and known wishes (81), and these findings are not reflected in the multiconceptual approach identified in this study.

7.4.1 Overview of the ethical framework

Proxies described a process of integrating both their family member's preferences and interests into a decision about research participation, that took account of what would be best for the person and would be in line with what they themselves would have wanted. In some instances, the proxy considered that they would agree to participation in a study that might result in some harm if that is what the person would have decided, and in other circumstances the proxy would reject a proposal that might lead to any negative impact on the person despite knowing that the person's decision would have been to proceed. This varied according to a number of contextual features, or it changed over time where the proxy considered the person to have been in an increasing precarious condition. These findings suggest that proxy decision-making may be affected by a magnetism that draws the proxy to

consider one or more factors, which have a decisive influence on the determination of the decision-making process. The concept of a 'magnetic factor' appears in a number of court judgements (314,315) where, rather than meaning that an element is given particular weight in the 'balance sheet' of options, a magnetic factor pulls the evaluation of all elements in a specific direction and thus determines the outcome of the case (150).

Proxies attempted to make a decision that was authentic to the person they represented and was congruent with their wishes, rather than attempting to determine what would be in their best interests or attempting to make a substituted judgement. Authenticity has been described as considering what the person *would want* done in the current circumstances, or deciding what the person *would choose*, based on having lived a life that expressed their individuality (118). An authentic decision is one that the person would identify with (316). It is recognised that this is a hypothetical choice, made in the absence of autonomous decision-making capacity and any sufficiently clear expression of the person's actual choice (118). Authenticity has been described as a sustained achievement that is exercised over time, in comparison to agency which is considered a momentary one (118), and as a concept of 'consistency' is given legal recognition in the Mental Capacity Act 2005 in England and Wales (20). Proxies took a number of routes to seek an authentic decision, including using the person's biographical narrative to access details about their past values and preferences, and seeking their agreement or any signs of assent or dissent to indicate their current views or feelings about participation.

Seeking authenticity, rather than making a substituted judgement, underlines that the proxy is not morally neutral, and is not merely acting as an empty 'conduit' passing on the person's known wishes (317). Acting as the decision-maker involves some transfer of responsibility to the proxy as a moral agent (60). This concept is supported by proxies' views about having responsibility for decision-making that arises out of their caring relationship with the person they represent and care for. The legal frameworks reflect that the person is selected to act as proxy by virtue of their relationship with the person (22) as they are engaged in caring for them and interested in their welfare (20). Their dual role as both a proxy and carer results in a dual moral responsibility to represent the person's preferences whilst promoting their interests. An authentic decision is one which is informed by knowledge of the person's values and is motivated by respect for the person (318). These moral responsibilities, and proxies' own reports of both respecting the person's values and promoting their interests, are

consistent with the intention of informed consent, which seeks to both respect an individuals' autonomy and advance their welfare or well-being (319).

Participants spoke about trust as being a fundamental element in a number of different forms, including the nature of the relationship between them and the person they represent, and their qualities of trustworthiness as being the reason they were trusted to act as proxy. Proxies often cited examples of being trusted by the person, perhaps using these qualities of trustworthiness as a justification for being trusted to act as proxy, although this level of trust can inevitably only be presented from the proxy's perspective. The proxy's reporting of trust may have been a form of justification, both justifying why they feel they have been given the responsibility to make a decision as well as justifying their decision. Many of the proxies had however been nominated by the person as their attorney for health and welfare and/or financial matters, and so may have felt that that was a tangible sign that the person had trusted them to make decisions generally on their behalf.

The functions of trust relationships in the context of informed consent and research have previously been analysed, including awareness of entrustment being an important component in decision-making (320). Similarly, characteristics of trustworthiness play a role in decision-making, where a person can be characterised as trustworthy when she 'acknowledges the value of the trust that is invested in [her, and] uses that to help [her] rationally decide how to act' (321). In this study proxies also spoke about the transitive properties of trust between themselves, the organisation or individuals caring for their family member, and the research team. Other studies have previously highlighted the role of trust between the proxy and the investigators, although they did not identify the trust between the person and their proxy (193). However, the relationship between the proxy and the person they represent is fundamentally different in nature to that between the person, their professional carers, and researchers. Alternatively the concept of reliance, which can be understood as a form of dependence that does not necessarily feature the emotive relationship necessary for trust between parties, or obligations of professional integrity, may differentiate these particular relationships (320).

Fundamentally, proxies needed to consider that participating in the study in question is a worthwhile endeavour, which in part was based on their belief that participating in research had value, and that the person they represented had a contribution to make that was

valuable which may rest upon their epistemic and testimonial beliefs of the person they represent as having 'knowledge' to contribute to the world (322).

7.4.2 Framework development from the initial conceptual framework

This ethical conceptual framework builds on the initial framework developed following the systematic review reported in Chapter 3. Many of the core concepts identified in the initial framework are present in the revised framework, such as the importance of the relationship between the proxy and the person they represent, although some terms have been amended such as welfare and interests rather than 'best interests'. This is in part because, unlike in the studies included in the systematic review, this study explored actual decision-making in practice and participants were neither prompted to use terms such as best interests or substituted judgement, nor were these concepts identified in the data. Additionally, some of the original concepts have been updated, including that accuracy is now represented in the form of authenticity.

The changes are reflective of the differences between the systematic review and this study in terms of: the participants (generally milder cognitive impairment in the previous studies), study design (previously largely hypothetical scenarios or regarding a single clinical trial), and methodology (predominantly questionnaire-based quantitative data in the systematic review). This study used qualitative inquiry and multi-grounded theory methods (MGT) to explore the experiences of proxies in a range of contexts, including across different types of studies, thus providing a richer account of the concepts identified in the initial framework. The differences may also reflect the legal frameworks governing research and incapacity in England and Wales, and pertinent jurisdictions in the systematic review (predominantly North America). In particular, the application of the Mental Capacity Act 2005 (20), which has its origins in a 'best interests' paradigm, and provides for a model of substitute decision-making in England and Wales that differs markedly from the frameworks adopted in many other jurisdictions (323).

7.4.3 Reflections on the study and use of pluralistic qualitative analyses

Although there are many differing opinions, there is a belief that sociology has a role to play in bioethics (324) and social science can help empirical bioethics to connect bioethics with the 'real world' (294). Grounded Theory, which is based on the concept of interaction, is considered to be in a 'harmonic relationship' with many ethical theories particularly those which focus on the actions of rational actors (51). However, its understanding of reality as a social interaction with shared interpretative process is in contrast with ethical theories which alternatively focus on an individualistic account of human agency (51). The assumption made in this study that proxies are actors who make their choices on the basis of preferences and information is in line with a non-individualistic account of autonomy, which stresses the importance of social structures and interaction. Therefore, the relational account of proxy decision-making serves as a linking element between the sociological analysis in Chapter 6 and the ethical analysis described in this chapter.

Qualitative data tend to be complex, and so a single dataset may benefit from a range of analytic approaches to 'unpack' different possible meanings within it (295). This additional analysis of the qualitative data through an ethical lens has added an understanding of the ethical dimension of proxy decision-making to that gained through the sociological lens, adding meaning to something that would otherwise have appeared a thinner, less multi-dimensional phenomenon. However, conducting pluralistic analyses using the same dataset is not without its critics and its challenges. Much of the criticism is based on the accusation that it is impossible to mix conflicting underlying philosophical paradigms (325). However rather than mixing paradigms, alternatively Floersch describes a process of concatenating analytic techniques in order to produce a hybrid multidimensional understanding of the phenomenon being studied (326). Thematic analysis (TA) enabled a description of proxies' experiences, whilst using multi-grounded theory (MGT) methods has enabled a deeper understanding of the actions and processes; therefore, this dual analysis has demonstrated how TA offers breadth while MGT offers depth. This is reflected in Wertheimer's work on 'widening the lens' regarding ethics in relation to conducting research where he proposes that, in order to examine a particular area, we need a wide angle lens as well as a microscope (15).

On a practical level, many of the challenges arise from one researcher using multiple analytic techniques. There is a widespread idea that in GT research the researcher should delay the literature review until the end of the analysis to avoid contamination (308), as described in the original work of Glaser and Strauss (301). However, this view of the researcher as a blank slate (or *tabula rasa*) who adopts a 'naïve empiricism' approach has since been rejected by many grounded theorists (310). Instead, a more critical and reflective approach to existing literature has been proposed, in which informed grounded theorists use the theoretical and empirical base both as a source of inspiration and in order to situate their work, whilst extending, challenging, and refining the field (308). As this analysis followed on from the previous theoretical and empirical research, a multi-grounded theory approach (MGT) was used which allowed me to critically and reflexively engage with the existing theory and empirical research. This enabled comparisons to be drawn between the concepts and relationships identified during the study and those previously described, in order to generate a stronger account of the ethical concepts that are active in proxy decision-making for research. Nonetheless, adopting a different analytic perspective was not easy, and at first it was challenging to discard the echoes of the previous thematic analysis. It has been suggested that having separate researchers conducting the two analyses is preferable, since it may have led to more distinct findings (271). However, adopting a technique similar to that described by Ashworth as phenomenological bracketing was helpful, where presuppositions are purposefully suspended (327). This required a conscious re-orientating towards analysing actions and processes, and away from experiences and views, when analysing the data using modified GT methods, and being observant for 'seeing' familiar patterns and themes in the data. Distinguishing between coding towards theme generation in the previous TA, and coding towards action patterns and theory construction in this MGT analysis was aided by the use of gerunds when coding the data (312).

7.5 Summary

Following analysis of family members' experiences regarding making decisions about research participation on behalf of someone who lacked capacity to provide consent, an ethical conceptual framework of proxy decision-making for research has been further refined. This analysis using grounded theory methods has provided an additional dimension to understanding proxy decision-making that provides a richer account than the use of a

single analytic method alone could. Pluralistic analyses have previously been likened to the concept of someone experiencing a song though listening mainly to the lyrics on one occasion, whereas at another time it may be by focusing on the baseline, and hence bringing something new to how the song is perceived thereby allowing for a fuller appreciation. The analyses presented in Chapters 6 and 7 are intended to provide a hybrid account of proxy decision-making, where both the tuneful melody and the meaningful lyrics can be heard.

7.6 Learning points

An illustrated account has been provided of the way in which proxies' attitudes and beliefs about the value of research, together with their trust relationship with the person they represent, play a fundamental role in their decision-making. Proxies make decisions that pay attention to the person's preferences and interests, whilst seeking to achieve a decision that is authentic to the person. Thus, they seek to make a decision that is 'best' for the person, whilst making the 'right' decision. This is in contrast with the normative accounts of proxy decision-making and the hierarchy of ethical principles identified in the literature.

This empirical account of 'real world' practice has enabled the framework, which was developed from the previous largely hypothetical studies, to be further refined. Understanding how proxies translate ethical principles into practice may open up the space for future exploration of whether the legal frameworks and research governance processes reflect the ethical practice of proxy decision-making, as well as the normative accounts previously described.

Chapter 8 Triangulation of the ethical and legal requirements and empirical research in proxy decision-making for research

8.1 Introduction

Previous chapters have explored the existing normative and legal accounts of proxy decision-making, reviewed the wider body of empirical research examining proxy decision-making in practice and the addition of new empirical research, and lastly considered the development of an intervention to support future decision-making. The challenge yet to be addressed is to consider how the normative and empirical accounts can be used such that a richer account of proxy decision-making, which is both informed by empirical data and ethical theory, can emerge. Whilst the normative and theoretical dimensions described in Chapter 2 are essential for making moral judgements (30), the 'empirical turn' in bioethics has led to growing recognition that empirical methods can (and should) open ethics' windows to the real-life world (48). Empirical findings, such as those reported in Chapters 3 and 7, contribute more than just descriptive information to which ethical theories are applied (30). Socio-empirical methodologies generate data which capture the lived moral experience of events, practices, and attitudes, and seek to make sense of the social world and how those within it make sense of it (49). However, a number of shortcomings of empirical ethics studies have been identified, including the lack of reflection or normative analysis, and the attempt to draw normative conclusions from empirical findings (215). Conversely, normative ethics has been criticised as being too abstract and disconnected from the lived experience to be capable of making truly authoritative 'ought' statements (328). The epistemological challenges (and controversies) involved in integrating the two very different perspectives have been widely reported (49,329). An analogous debate surrounds the conceptual and empirical relationship between ethics and the law – it is suggested that the law should (at least) be compatible with and supported by plausible ethical theory (29). Huxtable (330) contends that law is inherently empirical in nature, doing 'ethics work in the real world' and that its edicts must have purchase in that real world. Unlike other areas of mental capacity law, no case law relating to decisions about research (as opposed to innovative treatment) has been identified that could help resolve ambiguities or interpret the legal frameworks.

Making the relationship between the normative-empirical elements more explicit is important when conducting good quality empirical research in medical ethics (49). Therefore, this chapter seeks to draw together and examine the existing normative, empirical, and legal accounts in order to identify some common ground and problematic areas, as well as highlighting unresolved questions, in order to start sketching out a new approach to proxy decision-making that is attentive to existing practice and the legal context within which it is situated. The overarching framework of this thesis first described in the introduction can be used to position this chapter in relation to those previously presented.

The first level of inquiry was '*Lay of the Land*' research, which defined current practices or beliefs (Chapters 2 to 7). This chapter (Chapter 8) presents the second level '*Ideal versus Reality*', which explores how well actual practices described in the preceding chapters matches our ethical and legal 'ideals'. This chapter aims to explore the tensions between the empirical research and normative arguments in order to mutually inform understanding about proxy decision-making for research, with the additional perspective of the legal requirements, as a first step towards addressing the epistemological gap between the dimensions.

8.2 Methods

Three domains: socio-empirical research (Chapters 3, 6 and 7), normative-philosophical analysis (Chapter 2), and a previous review of the legal frameworks (33), were triangulated to determine instances of convergence, disjuncture, and 'silence' – where a theme or finding arises from one source and not another (331) – in order to provide a broader understanding of the ethical issues. Applied ethics methodologies (52,332) have described a two-way relationship between empirical data and normative theories that allows a social practice to be examined from both 'poles', with both serving to establish a mutually critical and clarifying perspective where one pole is not subservient to the other. The approach was extended here to additionally consider the requirements of the legal frameworks' provisions for research involving adults lacking capacity as a third 'pole', in order to highlight tensions between the three competing positions and generate an account that reflects the legal, normative and empirical ethical landscape.

Triangulation was first used in the health and social sciences to measure particular constructs using multiple tests to look for 'convergent validity' (333) and later developed by, amongst other, Denzin who described different forms of triangulation (data, investigator, theoretical and methodological) (334). Data triangulation, as used in this chapter, looks for dissonance or disjuncture between two or more sources to generate unexplainable divergences (335). Dissonant findings can serve as a point of departure for the creation of a new hypothesis, or a more nuanced understanding of the problem under investigation (336). Rather than seeing triangulation as a method for validation or verification, the intention here is to deepen and widen one's understanding of an issue (337), to ensure that an account is rich, robust, comprehensive and well-developed. The triangulation method used in this study was adapted from the protocol proposed by Farmer et al (338) which followed three stages: construction of a matrix to allow comparison of key issues against those represented in the three data sources, comparison of themes to create a single list of issues, and coding of individual themes for convergence, disjuncture, and silence. The categories identified in the conceptual framework in Chapter 7 were used as the organising categories to help examine how (and if) these categories are reflected in normative and legal accounts of proxy decision-making in order to allow comparison.

8.3 Results

A number of significant areas of convergence, disjuncture, and silence were identified between the domains of empirical research, normative analysis, and the legal provisions for proxy consent. Six key concepts are discussed in this paper: 1) research and its value and difference from medical treatment, 2) relationships, relationality and trust, 3) respecting known wishes, 4) integrating preferences and interests, 5) aiming for 'the best' and protecting from harm, and 6) seeking authenticity and getting it 'right'.

8.3.1 Research – its value and differences to treatment

In order for proxy decision-making to have sufficient moral authority for research participation, there is an assumption that it is morally acceptable to conduct research involving adults who lack capacity to consent. Several empirical studies have examined the acceptability of proxy decision-making, either from a societal perspective, or from a personal perspective either through the acceptability of acting as a proxy on behalf of another person

or as requiring a proxy for themselves at some future point (196,200,201). The studies generally found high levels of support for proxy decision-making for research, with participants reporting both comfort with, and acceptability of, proxies. Some participants reported a variation in comfort and acceptability depending on the perceived risk of the study and potential benefits, with willingness to accept proxy consent declining as the perceived risk increased. This was seen in one study where more than 90% of participants were comfortable with proxy consent by a family member for studies involving little or no risk and potential personal benefits, which lowered to 80% for studies involving serious risks with greater potential personal benefits (208). Studies found high levels of participants' willingness to take part in research should they lose capacity. Overwhelmingly, proxies reported that they were keen to be involved in decision-making. In one study, the majority (90 %) of proxies for critical care patients wanted to be involved in decision-making about research on their behalf (209). Participants generally saw no distinction between acting as a proxy for decisions about care or treatment and acting as a proxy for research – they presumed the same person would act as proxy for both types of decision (194).

The proliferation of national and international legal and bioethics frameworks with provisions for proxy decision-making for research indicates widespread societal acceptability, although the universality of their respective fundamental values has been questioned (339). Disjuncture can be seen between the two separate regulatory regimes that govern clinical trials of medicines and other types of research involving adults lacking capacity in England and Wales. Significant differences exist between the level of risk permitted (with a greater requirement for justification for participation in a clinical trial than other types of research), who may act as proxy decision maker, how much information is provided to the person lacking capacity, and whether they retain the power of veto (33). Significant differences also exist in the legal frameworks between decisions about research to those about treatment and care. Under the Mental Capacity Act 2005 (MCA), any act done or decision made must be done, or made, in their best interests (20). However, decisions about research are exceptions to this principle [s2.12](235). The Medicines for Human Use (Clinical Trials) Regulations 2004 (CTR) relate only to clinical trials of medicinal products (22); all medical treatment decisions are bound by common law.

Decisions about research for those who lack capacity to consent are subject to competing normative demands, including requirements both for the protection from harm and ensuring their inclusion in order to address forms of injustice that flow from their exclusion. Society's

obligation includes protecting the 'vulnerable' from exploitation (although vulnerability is a contested concept) however, obligations also extend to principles of equality, including equitable access to participate in research. Appropriate inclusion of the individual with impaired capacity in research which they would have agreed to if capable of exercising their own autonomy appeals to upholding justice in a variety of forms, including distributive justice, where no one group receives disproportionate benefits or bears disproportionate burdens of research (340).

8.3.2 Relationships, relationality, and being trusted

Decisions about research and consultations seeking informed consent occur within socially contextualised situations, and those involved are regarded as situated embodied agents (341). Shared relational bonds create a concept of shared agency, where what matters most is not what is decided, but who does the deciding. The fundamentally relational nature of the patient-proxy relationship means that it is not only informed by autonomy but also by concepts of mutuality, inter-dependence, and reciprocity. Normatively, this sharing of bonds allows the proxy to express something of the person's own agency, which provides the proxy's moral authority as decision-maker. This concept of relationality is founded upon persons being conceived as socially embedded, where social identities are formed and expressed through relationships.

The legislation echoes this focus on the relationship between the patient and proxy, and the decision-making authority arising as a result. Under the MCA a proxy is a person who is 'engaged in caring for P or is interested in P's welfare' [Part 1, s32(2)](20). The CTR states a person who 'by virtue of their relationship with that adult, is suitable to act as their legal representative for the purposes of that trial' [Schedule 1, Part 1, 1(a)(i)(aa)](22). This situates the legal authority for decision-making within a relationship characterised by care and attentiveness to the needs of the person, as well as attending to their wishes and feelings. The authority for a professional acting as proxy may also arise from a relationship, that between patients and healthcare professionals, where trust includes the belief that healthcare professionals in general are benevolent, and the relationship is interpersonal and emotional in nature (342). Although any potential conflict arising from the person's relationship with the clinician both as the provider of their healthcare and as researcher warrants further consideration. Notably, in one study there were very low levels of support

for a professional acting as their proxy, only 7% would allow a healthcare provider to provide consent on their behalf compared to 88% for a family member (195).

Empirical studies considered that the proxy's authority to make decisions on their behalf arose by virtue of their relationship with the person. Patients reported that the choice of who acted as their proxy was important, and both patients and proxies commonly used aspects of their relationships such as family ties, mutual trust, love and care, when they reported their views or experiences of proxy decision-making for research (194–196). Whilst proxies may be designated by the person to act on their behalf, either formally or informally, or they may fulfil the role as a family member or close friend who comes forward at the appropriate time, no studies explored the difference between bestowal of authority and assumed authority. None of the empirical studies examined the basis for healthcare professionals acting as proxy in the absence of a family member or friend who was available and willing to act as proxy. Similarly, the normative accounts are largely silent on professionals acting as proxy decision-maker and representing the person's presumed will.

There is currently no formal process for prospectively nominating a research proxy under a Lasting Power of Attorney, unlike for matters relating to health and welfare or finance and property (20). Recommendations have been made to consider extending the role of welfare attorney to include decisions about research in England and Wales (288). The empirical findings reported in Chapter 6 suggested that nominating a proxy to make decisions about research in the event of a loss of capacity was supported by proxies and may facilitate discussion about someone's wishes and preferences about future research participation in the event that they lose capacity. The donation of a Lasting Power of Attorney to a family member or friend may also be a form of trust made visible.

8.3.2.1 Individual versus family decision-making

Two empirical studies in the systematic review reported that proxies consulted other people including the wider family group for consensus or validation before making a decision about research participation. Warren et al's study with proxies for nursing home residents found that 60% of proxies consulted others before making a decision (192). One study reported that burden may be experienced as a result of feeling that other family members may not agree with their decision or would 'blame them' for enrolling the person (204). Similar views about the helpfulness of consulting other family members, and the difficulties when they did not agree, has also been reported in studies exploring decisions such as end of life care with

families of people living with dementia (343). In one study investigating the reasons for proxies accepting or declining research participation on behalf of a person with dementia, disagreement among family members accounted for 10% of decisions to decline. However, as reported in Chapter 6, some proxies describe a process of merely informing or updating other family members, rather than involving them in the decision itself.

Normative ethics is largely silent on the concept of joint or shared family decision-making, preferring an individualistic account of the role of proxy, despite evidence of its use in practice (167). The proxy decision-maker is described in the normative literature in singular not plural nouns. This discrete approach may be reflective of an individualised conception of autonomy (344). Under this individualistic approach to autonomy, the proxy can be thought of as being in possession of a fully formed, precisely focused decision tucked neatly away, which they would be able to access and provide on command via a substituted judgement (104), whilst a contrasting relational approach to autonomy utilises relational and social dimensions of selfhood and identity (345).

Broadly speaking, the law's approach to autonomy in the UK (and other comparable jurisdictions) can be considered as individualistic (346). The legal frameworks offer two ways to provide meaningful protection for autonomy in the event of a loss of capacity: through mechanisms to respect precedent autonomy either through formal statements of wishes or by taking account of past views, or by supporting those with impaired capacity to maintain involvement in decisions thus enabling participative decision-making (347). The former is reflected in provisions for decisions about research in both the MCA and CTR, the latter is the focus of CRPD. The challenges of capacity and decision-making in practice within a predominantly autonomy-based legal framework in England and Wales have been reported, particularly where autonomy is conceived as non-interference and fails to take account of the social context of decision-making in practice (347). An autonomy-based legal-framework fails to recognise other values such as trust and responsibility and does not represent the reality of proxy decision-making, which is situated within families or other social networks that are built on relationships of care.

This divergence between consultative and atomistic approaches to proxy decision-making is most notable under the dual legislation framework relating to provisions for research. Under the provisions of the MCA, the research team must make arrangements to obtain the views of any carers and other relevant people before involving a person who lacks capacity in

research [s11.20](20). This reflects the wider consultative approach to decision-making under the mental capacity legislation; however, the CTR has no equivalent provision or requirement to consult others beyond seeking consent from a single legal representative.

8.3.3 Respecting known wishes

Normative accounts of proxy decision-making for individuals who are unable to make decisions for themselves relies on the ethical standard of substituted judgement, presuming that proxy decision-makers have the ability and knowledge to accurately represent that individual and their known wishes and preferences or 'presumed will'. Substituted judgement is intended to support an individual's autonomy by leading the proxy to the decision the person would have wanted. Substituted judgement has been widely endorsed, however a number of commentators have argued it is problematic (115). It raises normative issues about whether the right to self-determination can be applied to those who lack capacity and therefore lack the fundamental elements of autonomy, those of agency, independence and rationality; or indeed to those who have never had capacity to conceive of themselves as autonomous agents. This results in an ethical paradox where the required standard can never truly be achieved in practice and may be so problematic that the validity of all proxy consent is questionable.

Empirical studies reported that knowing the person's wishes and values were highly relevant factors in proxy decision-making for research (32,184,185,194,204). Proxies described primarily basing their decision on their overall 'knowledge' of the person's values, wishes, past behaviours and decisions, or some combination of these, by virtue of the relationship that exists between them. However, few people communicate their preferences about research (348) and many proxies do not know the explicit wishes of those they represent, or have previously discussed research preferences (198). This may be interpreted as a counterfactual task, where proxies are required to extrapolate from the person's prior preferences, values, and character traits to determine what the person would choose if they were competent to do so. However, as reported in Chapter 6, in reality proxies' use of their knowledge of the person, their values, the details of their previous life, and past and current preferences formed the basis for the process of proxy decision-making for research participation. The conditional nature of substituted judgement relies on counterfactuals which is problematic when considering its validity, particularly so for those who for whom there is no satisfactory evidence regarding their wishes. According to Wierenga (349), the

interpretation of the counterfactual reasoning required in proxy decision-making is so problematic that in many cases no proxy consent would ever be valid.

Empirical studies that elicited proxies and patients' attitudes towards the use of substituted judgement found low levels of support compared to other decision-making standards such as a determination of what would be in the person's best interests (190), although just under half of proxies reported the use of primarily a substituted judgement when asked to make a decision about a hypothetical research study, in comparison to slightly more who used best interests (32). Some proxies were able to distinguish between decisions about medical treatment or care and those about research, using different ethical standards for different types of decisions (190). The proxies' ability to apply a substituted judgement, and the 'accuracy' of their decisions is discussed later.

The legal frameworks have a divergent approach to the use of substituted judgement. The CTR require the proxy to provide informed consent on behalf of the patient based on their presumed will regardless of whether the person previously had capacity or not. Presumed will may be taken to mean 'substituted judgement' although there is no guidance available from regulatory bodies nor any interpretive discussion from commentators about what constitutes presumed will, nor how it can be ascertained. Under MCA the proxy provides advice to the researcher as to what in their opinion the person's wishes and feelings about taking part would be if they had capacity; the researcher then makes the decision about whether to include the person in the study. It is not apparent if the MCA is asking for a substituted judgement – or if the decision is merely informed by the proxy's advice based on their own judgement of the person's wishes, which would appear to have less conviction than their presumed will. There is similarly a lack of guidance or discussion as to understanding and representing a person's wishes and feelings about research participation under the MCA. Given that under the MCA the legal basis for all other decisions made on behalf of adults lacking capacity is 'best interests', this partitioning of research decisions from non-research decisions can be problematic to comprehend for those involved (216).

From a legal perspective, the MCA does not provide any temporal framing of advice as to the person's wishes and feelings to guide proxies; although through its use of the future conditional tense proxies may take account of their previously expressed wishes as well as any current preferences. The legal basis for both personal and (in the absence of a personal representative) professionals acting as proxies remains the same – that the proxy is able to

represent the person's wishes and feelings about the project and therefore their presumed will. It is likely that most healthcare professionals will have had little or no contact with the person prior to the event that led to the loss of capacity, although they will be in a position to determine how the research might impact on the person's (medical) interests. However, there are no alternative provisions or basis for those acting in a professional, as opposed to personal, capacity.

8.3.4 Integrating preferences and interests

The normative account of proxy decision-making described in the bioethical literature is a sequential hierarchy of known wishes, substituted judgement, and best interests (21). Under this model, the substituted judgement draws on the value of autonomy and responds with respect and best interests draws on the value of welfare and responds with beneficence (126), although there have been attempts to recast these sequential standards as a continuum (81). Decisions guided by a substituted judgement are meaningfully shaped by the person's values and preferences, and as these influences become less clear, weighty, or specific to the individual, decisions migrate along the continuum towards decisions governed by the person's immediately discernible interests (81). A number of alternatives to this tripartite model have been proposed, some of which are discussed in Chapter 2, such as an integrated 'substituted interests' model which emphasizes authenticity and asks proxies to provide knowledge of the person's authentic values and interests rather than attempting to guess what the patient would have decided (82). Another proposal is 'best judgement' which takes a more holistic view of a person in which love has a normativity that has relevance in the decision-making context, where decision-making draws on the values incorporated in each of the traditional standards through being responsive to the specific person's weighting of relevant values (126). This comes closer to the empirical account of proxy decision-making where both preferences and interests are considered because that balancing or integration is what the proxy is substituting for.

In the event of a loss of capacity, a person's autonomy can be expressed not only through enacting their preferences as a form of precedent autonomy (120), but also in the choice of a designated surrogate (350). The act of being chosen as proxy may be at least as important as the proxy's articulation of the person's preferences. As a result, the proxy has two sources of moral authority: one is substantive, what he or she knows of the patient's wishes, the other is procedural, which stems from the act of being chosen. Both the articulation of

preferences and the choice of a proxy are exercises in self-determination, which may reflect 'the social nexus' considered by some to be necessary for autonomy' (351). The proxy's role can be thought of as being on a continuum having both contractual and covenantal dimensions – where the proxy is bound by a literal interpretation of patient wishes with limited discretionary authority, whilst part of a covenantal relationship founded on mutual obligation and trust which bestows a discretionary authority that stems from being designated as a surrogate (350). Under this view, deviation from prior instructions would not be seen as a violation of the person's autonomy, instead proxies would be viewed as making nuanced and contextually informed moral judgements (350). This context would include the relevant impact on the person's interests, and a consideration of how these interests and known wishes should be balanced or integrated.

Proxies participating in the DECISION Study described a process of integrating both what they considered would be the person's preferences wishes and feelings about research participation, as well as considering any positive and negative impact on the person's wellbeing. The findings were in line with that of a previous study undertaken in the US which found that nearly half of the participants (49%) agreed or strongly agreed that that they would base their decision on what their loved one would choose as well as what would be in the best interests of their loved one (32). Some proxies spoke explicitly about the desire to incorporate both standards in the decision, which the authors described as honouring preferences while weighing burdens and benefits (32). Unlike Berger's account of a continuum where best interests become more relevant as preferences become less clear, the DECISION Study proxies incorporated a weighing of interests in decisions regardless of the strength of known wishes.

The legal frameworks contain disparate provisions for who is suitable to act as personal consultee (someone anyone engaged in caring for the person or interested in his welfare [Part 1 s32(2(a))] (20), whilst their role is to provide advice based on what, in their opinion, the person's wishes and feelings about taking part in the project would be likely to be if they had capacity in relation to the matter [Part 1 s32(4(b))] (20). The same individual also has a dual role as both the person's proxy and as someone who loves and cares for the person, and all other decisions they are involved in would be made on the basis of what was considered to be in the person's best interests. A nominated consultee is someone who is 'prepared to be consulted' [Part 1 s32(3(a))] (20) but still provides advice on the same basis. The CTR specifies that someone is suitable to act as either their personal or professional legal

representative 'by virtue of their relationship' and their informed consent represents that person's presumed will [Part 5(12)](22). This may well be a relative or health or social care practitioner and so is likely to have existing relationships and/or a duty of care towards the person outside of their role as representative. Thus, different proxies may have different relationships and obligations towards the person and have differing levels of knowledge about the person's wishes and feelings, requiring a balancing of interest-protecting and preference-promoting concerns.

8.3.5 Aiming for the best – protecting from harm

The empirical data suggests that family members acting as proxies have a dual role in representing the person's wishes and feelings but also acting as a substitute for protecting the person's interests. The latter stems from their role as protector of the person they see as vulnerable, where proxies described a desire to protect the person's quality of life when considering participation in research (32). Proxies, many of whom are (or had previously been) the person's direct caregiver, are accustomed to making everyday decisions using a 'best interests' approach or at least one that considers their interests (32). In the DECISION Study, proxies sought to make decisions that were the 'best' for the person involved, understood in its broadest sense rather than viewed as making a decision that was in their 'best interests'. Their aim was to achieve the best outcome for the person they represented and cared for, which included weighing the advantages and disadvantages of participating, and protecting them from any perceived burden or negative impact from research. This consideration of the advantages and disadvantages went beyond merely biological risks and benefits to the person. Decisions were made in the context of a caring dyadic relationship; they were viewed as relational and included any psychosocial impact as well as the burden on the proxy and the wider family.

The legal frameworks are silent on the role of the proxy in considering the person's interests as part of their provision of informed consent as a legal representative, or advice as consultee. This is despite the importance of considering the person's interests (and determining of best interests) being a fundamental principle in all other decisions for adults who lack capacity under the MCA. The CTR refers only to presumed will as the basis for informed consent, and makes no mention of considering the person's interests, save that they would always prevail over those of science and society [Part 5 (15) (22)], or the relative advantages and disadvantages of participation (or not). For professionals acting as proxy,

their caring obligation to the person that can be captured as *primum non nocere* or ‘first do no harm’ may be difficult to reconcile with their role to represent the wishes and feelings or presumed will for someone who is unlikely to have explicitly expressed that wish. This difficulty is evident in the analysis of information sheets provided to proxies reported in Chapter 5, where those given to professionals often lacked information about the legal basis for their decision and instead focussed on eligibility.

The normative account of proxy decision-making for decisions about research participation appears to be different to those about other decisions, including medical treatment, and hence there is a limited account of the role of the research proxy as protector. For decisions about medical treatment it has been suggested that attempting to provide a substituted judgement based on what that person would want is difficult, bordering on the impossible, therefore the only morally acceptable alternative approach is to act in their best interests (26). Thus, making decisions with respect to maximising the person’s welfare, rather than upholding respect for autonomy. As discussed previously, a proxy is not *only* a proxy, and making a decision that is based solely on what the proxy considers the person would have decided, even where they consider it to be to the detriment of the person, is not in accordance with their other obligations as someone who cares for the person. Alternatively, a normative account of proxy decision-making that considers what would provide the best outcome for the person would be in accordance with an account where the proxy considers their interests because *the person themselves* would consider their interests when making a decision.

8.3.6 Seeking authenticity – getting it ‘right’

Many empirical studies in the systematic review focussed on whether proxies can accurately predict what the patient would decide about participating in a hypothetical research study (93,94,99,100,198,199). These studies used the patient’s own prediction as the correct decision or the ‘gold standard’, against which the proxy’s decision or prediction is measured as a form of ‘diagnostic test’ (198). There is increasing attention being paid to ‘an ethics of accuracy’ (352) although such studies have a number of methodological flaws (103). Some studies also explored the degree of freedom or leeway participants would provide to their proxies to go against their currently stated preferences about future research participation. Situations may often arise in which proxies must use their own judgement and make decisions that differ from what the person had previously said, either because the person’s

wishes may have changed, or those wishes cannot be applied to the current situation (353). The emphasis on seeking authenticity may also align with the UN Convention on the Rights of Persons with Disabilities (CRPD) statement that where it is not practicable to determine the will and preferences of an individual, the 'best interpretation' of their will and preferences should be used (General Comment No.1 Article 12) (354).

The majority of participants were willing to give their proxies some or a complete leeway, although it varied by the level of perceived risk and the type (invasiveness) of the study. The main reasons given by participants for granting leeway were that the proxies would have more or better information in the future, that the ratio of the risks/burdens vs. benefits may be different at the time of the study, or that the proxies may be able to better assess the risks at the time. As reported in Chapter 6 and 7, in contrast to aiming for accurate decisions and being granted a margin of leeway, proxies appear to seek 'authenticity' when making decisions, where they aim to make a decision that was in line with what they thought the person would want them to do. This is enabled through the proxy's familiarity with the person's values and the events in their life, which have shaped their individual view of the world and would affect their decisions, and possibly their similarity to this worldview. It has been suggested that rather than substituted judgement being the measure or criterion of whether it constitutes a 'good' decision (whether it is the choice the person would have made, if able), that by proxies basing their decision on 'what the person would have wanted' it may sufficiently fulfil the moral criterion of proxy decision-making as the 'right reason'. This may be achieved through the proxy knowing the biographical history of the person they represent, through sharing their worldview, or that they have common shared values that are relevant to the decision in hand.

Normative questions emerge about whether autonomously determined preferences survive the loss of capacity, given the changes in personhood, preferences, and maybe identity wrought by the events surrounding the loss of capacity. Or whether, given the challenges of psychological continuity and personal identity (355), the extrapolation of previously expressed views, and the requirement for counterfactual reasoning, they are too epistemically opaque to be future binding. This has been the subject of debate about the moral grounds for respecting decisions stated in advance, and whether the moral authority of 'precedent autonomy' extends into a period of incapacity (356). It also raises questions about whether such decisions made in advance can ever be truly informed in terms of the weighing of the specific nature of the study and its potential risks and benefits. Leeway is

said to occur when a person empowers a trusted individual with interpretative discretion to assess novel and perhaps unforeseen circumstances and to make a moral judgement, conceivably even one that might counter the patient's previously expressed wishes (350). However, the relationship between the exercising of (assumed) leeway and the requirement for a substituted judgement, and hence the normative significance of the proxy's decision, has not been well described.

The power to prospectively make legally binding decisions rarely extends to decisions about research participation. In England and Wales, Advance Decisions to Refuse Treatment (ADRT) have statutory force under the Mental Capacity Act 2005 [s24-26](20), and a Lasting Power of Attorney (LPA) for personal welfare may be appointed [s9](20). Advance Statements can record a person's wishes and preferences; however, they are not legally binding. These mechanisms only apply to those with mental capacity and who have the foresight to make prospective arrangements and concern medical treatment and care decisions only. The role of non-binding formally stated advance decisions regarding research decisions in England and Wales is unclear, although in the US and other countries the use of 'Advance Research Decisions' are rare but becoming more common (357), despite a number of concerns being raised (358), including questions about whether antecedent consent can ever be truly informed (359). The legal frameworks offer a tangled approach to respecting antecedent consent. Consent to a clinical trial of a medicine provided when in possession of capacity survives any loss of capacity under the CTR but not for other research governed by the MCA (33). The role of the attorney in providing consent for medical research has also been reported elsewhere to be unclear (237). The MCA Code of Practice merely states that researchers *can consult* attorneys if they are thinking about involving the donor in research [s7.57](235) and that an attorney *is not prevented* from being consulted provided they are not acting in a professional or paid capacity (for example, the person's solicitor) [s11.25](235) (*italics added*).

8.4 Discussion

A number of areas of convergence were seen. The legal requirement for a proxy (either a personal consultee or personal legal representative) to be someone that knows the person lacking capacity well is supported by the empirical data on who patients would and do chose to act as proxy. Given that the vast majority of proxy decision makers are family members,

the prior relationship between the patient and proxy is vital to the decision-making process (360). Their moral authority to act as decision-maker appears to arise through the patient-proxy relationship. The moral responsibilities that result from this relationality underpin the performance of proxy decision-making, both through the 'reason' for allowing proxy decision-making and contributing to the 'decision' itself. The proxy accesses the wishes and feelings of the person through their biographical narrative, which becomes an indispensable mode of access into the phenomenon of personal autonomy (287).

This relationality is supported by the empirical data where, despite the person's explicit wishes often not being known, proxies reported utilising their overall 'knowledge' of the person's values, wishes, past behaviours and decisions, to decide on their behalf. Through this relational approach, those around the person are considered to be co-constituents of the person's identity, interwoven with the person's self over time and expressed through their life narrative. In the event of a loss of capacity, proxies 'uncover' the person from the past and 'co-edit' the future in line with the person's life story (361). This approach attempts to respect the authenticity element of autonomy that is exercised over a lifetime (rather than agency which is exercised with each choice made), creating a 'life that fits' and makes sense within a framework of beliefs and values that the person affirms (136). Attempting to elicit a person's wishes, choices and preferences can help gain insight into their interests, where the person's settled values and beliefs have not been explicitly stated. However, making a decision that fits the person's biographical narrative is distinct from acting upon a person's actual settled values and beliefs (362), and the MCA and CTR provide no guidance for proxies on how 'wishes and feelings' or 'presumed will' can be determined.

Key areas of disjuncture were identified, particularly between the normative and legal claims for substituted judgement, and the experience of decision-making in practice reported through the empirical studies. Proxies and those they care for reported that they preferred other approaches to decision-making, such as best interests or a combination of best interests and substituted judgement, to an approach solely based on a substituted judgement alone. The empirical data reported here captures the complexity and contextual nature of proxy decision-making that does not reflect the reductionist account described in the normative bioethical sequential hierarchy of known wishes, substituted judgement, and best interests (21), and endorsed in legal and ethical codes. Patients did not support a wholly substituted judgement approach but wanted proxies to consider their own interests and those of family members, or following consultation with others (190). This is in accordance

with the reciprocal caring relationship identified in the empirical studies, and previous commentators that suggest that people in real-life are variantists, who use different criteria in different situations, rather than using the principles like a 'skeleton key that can open the doors' of decision-making in all cases (80). The law also assumes that there is a temporal aspect to capacity – that those who lack capacity have previously been capacitous, or at least have formed and perhaps expressed relevant preferences about the issue at hand.

The substantial divergence between the legal instruments primarily arises from their differing legal origins: the MCA codified existing English common law, and the CTR was developed through European law building on ICH GCP (65), which was led by the pharmaceutical industry, rather than the World Medical Association approved Declaration of Helsinki (63). Whilst approaches to the locus of decision-making authority were comparable, and there is a similar basis for their decision-making, the differences in their decision-making role are significant. By extending precedent autonomy to include the ability to provide informed consent by a legal representative, without explicit wishes being necessarily known, the CTR is in stark contrast to the proxy's consultative and advisory role under the MCA. There is no requirement to consult others under the CTR and, unlike the MCA, if the person is capable of forming an opinion and assessing the information to refuse and explicitly wishes not to participate this wish is not binding but must merely be 'considered' by the investigator [Art 5(c)](22). Thus, any dissent has a weaker force in the face of consent by a legal representative, than it does as part of consultation process under the Mental Capacity Act. This raises difficult questions about the moral authority of proxies under the CTR that are not easily answered.

Despite legal provisions for proxy decision-making by a professional consultee or legal representative in the absence of anyone able or willing to act in a personal capacity, there were no empirical data on proxy decision-making by professionals. This is an important area of decision-making, particularly in situations requiring urgent medical care where family members are not available or able to act as a proxy. It may be an increasing issue with an ageing population and accompanying changes in community cohesion and social isolation that may leave older people without personal representation. There were also no data reporting the experiences of proxies for adults who have never possessed decision-making capacity, such as people with profound intellectual or learning disabilities. This is a particular normative challenge to the accepted bioethical hierarchy surrounding the ability to

substitute judgement both for those who have never had decision-making capacity or those whose wishes cannot be adequately determined.

8.4.1 Reflections on the use of triangulation methods

This is the first study that has attempted to examine the tensions between the three ‘poles’ of normative, empirical, and legal requirements concerning proxy decision-making for research. The normative concepts considered in this study are (necessarily) briefly described, which provides little opportunity to capture the widely contested nature of the concepts that have been more fully expounded elsewhere. The legal frameworks that form part of the triangulation are limited to those that govern research in England and Wales. Comparisons with the legal provisions in other jurisdictions are equally valuable, but beyond the scope of this thesis. The empirical studies were largely conducted in North America; countries outside North America may have different attitudes towards proxy decision-making, and experiences may differ in jurisdictions with alternative legal provisions for research involving adults who lack capacity.

Empirical data from the systematic review were largely limited to quantitative surveys or questionnaires that do not sufficiently capture the complexity of proxy decision-making in practice. The use of the terms ‘substituted judgement’ and ‘best interests’ were often undefined by the study authors, and so caution must be used when reporting proxy and patient preferences towards, and their use of, these standards. Data relating to the ‘accuracy’ of a proxy decision, or the ‘leeway’ permitted to the proxy, are only relevant if a reductionist positivist account of substituted judgement is accepted. The empirical studies that examined the accuracy of proxies’ decisions were based on hypothetical scenarios and therefore have important limitations and methodological flaws, not least the assumption that hypothetical and actual decision situations are the same, or that the patient is expressing a prediction not a decision and the proxy is therefore required to ‘match a guess’.

8.4.2 Contributions towards ‘Ideal versus Reality’?

Empirical research is normatively significant, not because it can generate normative conclusions in and of itself, but because it helps examine whether a principle is applicable to a situation and so can play an essential role in generating such conclusions (363). Reflecting on the areas of convergence, disjuncture, and silence between the empirical, normative, and

legal approaches to proxy decision-making has enabled an examination of how the ethical and legal principles apply in real world practice. The findings suggest that existing normative accounts fail to capture the relational nature of proxy decision-making by family members that is evident in the empirical accounts and, to some degree, in the legal provisions. Conversely, the legal requirements that a professional acting as proxy is able to represent the presumed will or wishes and feelings of a person they may have no prior knowledge of, has no empirical data to support or oppose, nor to suggest an alternative account.

The atomistic conception of informed consent based on a person's presumed will and the legal fiction that proxies should be impersonal 'empty conduits' of the person's wishes (364) is in stark contrast to the relationships that proxies as mothers, brothers, etc. have with those that they care for and represent. This suggests that developing a theory of relational proxy decision-making, based on the forming of relationships (rather than the usual focus on individual autonomy), and underpinned by respect for persons (rather than respect for autonomy), may be a more informed and informative approach. This approach would need to be attentive to the inherent relationality of those in society who lack capacity to live fully autonomous lives, as distinguished from an individualistic approach to autonomy, and is alternatively expressed as 'we' and not 'I'. How this might take form, and how this approach might be reasoned to be universal in nature, is beyond the scope of this thesis and is a subject for much future work.

Further development of an account of professionals acting as proxy is also indicated. The relationship and trust between the parties remains a fundamental aspect of their role, but in the absence of knowledge about the persons values and preferences, there may need to be a greater focus on the person's interests rather than solely on attempting to represent their presumed will. It may be that consideration of the 'reasonable person' element of substituted judgement described in Chapter 2 may be helpful here.

8.4.3 Questions for future consideration

A number of key questions remain. Whether the current 'bioethical hierarchy' is sufficiently reflective of the complexity of decision-making in practice? Whether substituted judgement, if accepted as the normative basis for proxy decision-making, is so problematic that it can never be valid, in which case where does that leave the legal frameworks? What, if the choice of proxy is so significant, provides the moral authority for professionals acting as proxy, and

how can the differences between professional and personal proxies, and between providing advice versus consent be reconciled? Building on the empirical data reported in Chapter 6, and the brief discussion here of precedent autonomy, additional areas for further consideration include whether there is value in incorporating research decisions into the appointment under a Lasting Power of Attorney. This is supported by the empirical studies, which found that the choice of proxy is important to patients, participants did not see a distinction between a proxy for research and for treatment decisions, and that decisions are contextually dependent and do not appear to involve the elicitation of clear preferences that are stable over time and through changeable conditions.

Further questions remain about the future development of the legal frameworks, including UK compliance with the UN Convention on the Rights of Persons with Disabilities (CRPD) that requires a change in attitudes and approaches to persons with disabilities with a focus on supported decision-making (156). Consultations about a replacement to the Adults with Incapacity Act are in progress in Scotland (365), and amendments to the MCA in relation to in relation to procedures in accordance with which a person may be deprived of liberty are in progress (366). The imminent introduction of the Clinical Trial Regulation EU No. 536/2014 (367) which replaces the EU Clinical Trial Directive (EC) No. 2001/20/EC (and CTR which transposes it into national legislation (22)) will not significantly alter the current position regarding research involving adults lacking capacity.

8.5 Summary

Although there are some areas of convergence, the epistemological gap between the normative ethical concerns, the legal frameworks, and the lived ethical experience of proxy decision-making for research reveals a number of problematic issues. Whilst many have argued that empirical research merely illuminates current practices and cannot inform normative ethics, this paper has explored the gap between the two which may help open up the space for re-examining ethical norms, and refining policy and practice in this vital area of medical research. It has also been an opportunity to view the law as a 'testing ground for the practice of bioethics' (330). At present, the law fails to adequately address the tensions, instead relying on the legal fiction of the proxy's ability to produce a substituted judgement regardless of the persons' prior expression (or ability to express) of their will. Significant questions arise about the ethical acceptability of proxy decisions made on the basis of what would be in the person's best interests, or another basis, rather than enacting a substituted

judgement process. A response to these concerns may lie in the relational authority of proxies who make decisions about research participation within a caring relationship that has the promotion of the welfare of the person who lacks capacity at its heart.

The disjuncture between the empirical, normative, and legal accounts of proxy decision-making for research and areas of silence highlights the failure of the current legal frameworks' ability to do 'ethics work in the real world' (330). Greater understanding of proxy decision-making and consent for research, which pays attention to the normative accounts of the proxy's role and the wider legal context of supported decision-making, is warranted.

8.6 Learning points

Using triangulation methods, a number of areas of convergence and disjuncture (and silence) between the normative accounts, empirical research, and legal frameworks have been highlighted. Key areas of divergence are between the individualistic accounts of proxy decision-making, which do not reflect the relational nature of proxy decision-making in practice which the empirical data report. Although permitted by the legal frameworks, there is significant silence in both the empirical data and normative accounts relating to how professionals act as proxy, including the appropriate ethical basis for their decision, and how they might reach such a decision based on the person's presumed will. This leads to concerns that a professional's ability to act in the same role and same legal basis as a personal consultee or legal representative is a mere legal fiction.

The origins of the legal frameworks are disparate, and this is reflected in the divergence in approaches to the inclusion of adults who lack capacity in clinical trials of medicines, compared to other types of research. The situating of clinical trials in an individualistic autonomy and informed consent focussed paradigm, and other research in a welfare and interests based paradigm that adopts a consultative approach, muddies the waters when attempting to understand whether the law is indeed doing 'ethics work in the real world'.

The findings suggest that a relational approach to decision-making, which acknowledges that proxy decisions (by family members at least) occur within a dyadic relationship of care, may provide a less problematic account than those that currently exist.

However, a number of key questions remain, particularly around the role of a health or social care practitioner acting as consultee or legal representative and the problematic legal and normative requirements that result. There is currently a lack of empirical data to address this question, which has important legal and practical implications.

Chapter 9 Reflections on the problem of 'autonomy' in research involving adults lacking capacity: a proposal for seeking shelter under respect for persons

9.1 Introduction

The focus of this chapter is to extend the discussion of autonomy from that briefly visited in the literature review (Chapter 2) using the findings from the subsequent chapters. It represents the first steps towards *Changing Ethical Norms* in which studies and other comprehensive analyses are said to use empirical findings to inform ethical principles (368). Usually these are not individual empirical studies in themselves, but rather bioethical analyses of multiple empirical studies. Through reviewing and analysing new empirical findings, there may be an adaption of ethical norms which are founded on underlying principles and build on valid data (368). Similarly, the empirical findings in this project challenge the accepted reductionist individualistic account of proxy decision-making and suggest a need to revisit normative standards and assumptions that underlie prevailing ethical and legal guidelines for proxy decision-making for research. The function of autonomy in proxy decisions about research is explored, including how privileging autonomy fails to take account of a range of other moral concerns. An alternative view of respect for persons is then proposed which may provide an alternative ethical basis for research involving those who lack the capacity to consent to participate in research.

Although the relationship between autonomy and consent is often not developed (369), the prevailing view in research ethics is that the primary function of informed consent is to respect individual autonomy, where consent is considered to be the vehicle by which respect for autonomy is translated into law (21). Autonomy is widely held to be a near universal or fundamental value (370), variously viewed as either a moral principle constituting liberty, self-control, and authenticity, or the capacity of a person to think and reflect, and decide for oneself (369,371). Autonomy can be broadly viewed as having two components or elements (117). Firstly, formal autonomy – or 'agency' – refers to a person's desires and preferences, which lead the person to be self-governing or self-determining; and secondly effective autonomy, or 'authenticity' which refers to the match between a person's autonomous desires, preferences, and decisions and their actual decisions, choices, and behaviours (116).

However, there have been criticisms about the overweighting and problematic overextending of autonomy (372). Persons who lack capacity are neither able to deliberate, nor to act on, their preferences or plans – both of which are considered to be required elements of autonomy – and are therefore considered to have diminished or absent autonomy. Respect for autonomy requires that a competent person's preferences and decisions be respected, but there is less agreement that it requires respect for the prior preferences of a person who has since lost capacity (120).

Where there can be said to be a right to autonomy, the law has positioned mental capacity as the gatekeeper to autonomy (347). Those who have mental capacity are seen as autonomous, and subsequently any attempt to interfere with their decisions (no matter how unwise the decision) is viewed as paternalistic and beyond the role of the state; conversely, those deemed to lack mental capacity can be subject to paternalistic interference with their decisions as they lack autonomy (373). The stark binary divide between capacity and incapacity has resulted in a dichotomisation between those whose autonomy must be respected, and those whose concerns are reduced to concern for their welfare. As described previously, where decision-making capacity is found to be absent, a proxy decision-maker intervenes to provide a substituted judgement. How autonomy, and its function and goals, are conceptualised shapes views about the ethical appropriateness of a proxy decision-maker where a person lacks capacity, and the ethically acceptable range of reasons in their decision-making (374).

9.1.1 Autonomy and adults lacking capacity

Broadly speaking, the law's approach to autonomy is consistent with its endorsement of individual autonomy (347), under both a Kantian conception of 'the good' through linking autonomy and morality as the 'categorical imperative', and Mills' liberal account of autonomy as non-interference. Autonomy is expressed in the first person singular, rather than the first person plural – as 'I' not 'we' (344). However, a focus solely on autonomy and informed consent fails to attend to (or overlooks) a wider range of ethical principles, obligations, and rights that underlie ethically acceptable practices (370). For example, for those who have never had capacity for autonomous action the notion of respect for autonomy can be considered as 'vacuous' (375) and risks those who cannot exercise autonomy being excluded from its protection (376). Informed consent in such situations cannot be viewed as an autonomy-enriching intervention. Where consent cannot be obtained there is no

requirement to seek or obtain consent, but other forms of consultation/permission may be required.

The tripartite bioethical hierarchy previously described - where expressed preferences have priority, followed by substituted judgement, and best interests if no indication of preferences is available – has been referred to as a ‘spectrum of autonomy’ (125). Proxy decision-making by substituted judgement is intended to continue or extend respect for autonomy by ‘leading us to the decision the person would have wanted (28) as part of the ‘liberal hierarchy of authority’ (77), but it is considered a poor means (123) or a weak standard (66) for respecting autonomy, and one that requires a ‘large rhetorical punch’ (124). Respect for a (competent) person’s preferences and decisions requires informed consent to be given in order to respect their autonomy, and a supplementary requirement is that the person is able to apply their own values in the assessment of the benefits and burdens of the research (281), and be accountable for the decision. Neither can take place in circumstances where the person lacks capacity, where it would be unreasonable to make the proxy responsible for a decision the person *would have* made under certain counterfactual conditions (105). Shifting from a decision that has actually been made to what the person would (ideally) consent to means that a proxy decision has less normative weight than a person’s own decision (115), or may override or replace autonomy (375). The proxy’s interposition as an arbiter of how and when the person’s prior preferences should be applied exerts an element of control or limitation that denies the person the ‘meaningful choice’ that is the very essence of autonomy (21) and, therefore, informed consent.

9.2 Discussion

9.2.1 The costs of privileging autonomy

There seems no compelling reason to assume that autonomy has greater value or should be given ‘extra’ priority over other moral considerations - that it should be considered ‘first among equals’ for some reason (377). Whilst holding that autonomy is important value that should be protected and promoted, theories grounded in respect for autonomy appeal only to a single value and neglect other moral considerations that should be taken in account and may even take priority over concerns about autonomy in some cases (29). A number of these other ethical values constitute the framework for research involving human subjects proposed in the Belmont Report (340), which identified three principles: respect for persons, beneficence, and justice. The Report stated that the principle of respect for persons, which

is the cornerstone of the framework, divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy. The origins of the current emphasis on respect for autonomy as a fundamental principle can be traced to Beauchamp and Childress (378), who reduced respect for persons into a sub-category of respect for autonomy, and changed the boundaries to only apply to persons able to act in a 'sufficiently autonomous manner' (378). Lysaght suggests that Beauchamp and Childress' de-coupling of autonomous and non-autonomous persons, where autonomy is defined almost solely by informed consent, means that respect no longer pertains to the non-autonomous, and instead their protection is determined by the principles of non-maleficence and beneficence (376) which lacks the security of respect (379). It is this account of autonomy, and the accompanying requirement for informed consent, that is problematic when attempts are made to extend it to those who lack the ability to make autonomous choices and rely on proxy decision-making.

9.2.2 Seeking shelter under the umbrella of 'respect for persons'

Various accounts of respect for persons have been proposed. Beach et al (380) offer an account of respect as recognising the unconditional value of persons and respecting their autonomy, whilst not accepting that respect for autonomy is a complete or self-sufficient expression of respect for persons. So that respect for autonomy, whilst important in its own right, 'does not exhaust the wider notions of respect for persons' (381). The challenge is to provide a fuller normative account of the ethical concerns that render a person as being worthy of respect, beyond a reliance on autonomy alone.

Brannmark draws on a human rights based account and takes a taxonomical pluralistic approach to consider five distinct ethical concerns as making up 'respect for persons' (379). These consist of: autonomy, dignity, integrity, privacy and vulnerability, which overlap with many of the principles outlined in ethical governance frameworks, including the Declaration of Helsinki (63). Other concerns may be relevant and so this is not considered to be an exhaustive account.

These core elements are interconnected and irreducible to one another, and the relative weight given to each will vary between persons and contexts (379), where respect-orientated values such as dignity and integrity are greater considerations where autonomy is diminished or absent. The principle of respect for persons goes further than merely seeking

consent from those with capacity, and beyond maintaining confidentiality and privacy for all participants, to providing protection for those with diminished autonomy (340). Respect for persons, recognising each person has intrinsic value, is a fundamental value, which must form the basis for all interactions, and is therefore central to ethical considerations. It includes taking care to ensure the person's understanding and comfort in their participation through active engagement in promoting their interests and empowering them in decisions that concern them so that supported decision-making (rather than substitute decision-making) (156) can maximise their ability to make decisions wherever possible. An approach based on the person's 'will and preferences', or the best interpretation of what their will and preferences are, can be enacted through exploring echoes or reflections of their views held by those who knew them well.

Vulnerability can be understood as a universal ontological condition (382) arising from our socially reliant existence (383), however the exact ways in which we might be especially vulnerable will always be socially constructed (379). Therefore the particular experience of vulnerability must be understood at an individual level, where the experience of 'embodied' vulnerability varies according to the quality and quantity of resources available to us (382). Caution must be exercised to avoid conceptions of the 'vulnerable adult' on the basis of a set of fixed, intrinsic, human characteristics which focuses on protection from risk and results in disempowering the 'vulnerable adult' (384). Rather, universal vulnerability can be seen as having a positive value - one that encourages, and in many ways necessitates, the forming of relationships of care and support (373). A holistic account of human vulnerability requires meaningful engagement with the person's experience of vulnerability (384). Decisions about participation of those who lack capacity in research requires sensitivity to vulnerability; it clearly goes beyond matters of consent but should still be respectful of them as persons (379).

In addition to the relationship between autonomy and dependency, there is also a relationship between vulnerability and trust which invokes an ethical obligation of trust (370). The relationship between vulnerability and trust has been described as inseparable (342). The relational authority of the proxy is based on a relationship formed out of love and care and trust, recognising that the person requires support in all other areas, and where decisions about research are seen as part of the wider context of care. It is this account of respect for persons that features in triadic relationships between the person and their proxy

and the researcher, where vulnerability and trust is the thread that runs through the deliberation about the ethical suitability of a research project (385).

The concept of respect for dignity is particularly problematic to 'pin down', as Weinrib states: 'human dignity is everywhere invoked and everywhere contested' (386). McCrudden's view is that the concept of human dignity arises as an ontological claim about 'what the intrinsic worth of the individual human being consists in' (387). This echoes the Kantian view of inherent dignity (*menschenwürde*) as the 'intrinsic worth' of persons which makes them valuable 'above all price', or at least equal to that of every other person (388). Dignity can also be understood as a self-directed value, and respect for dignity as an other-regarding value (389). Feldman expands on this to present two conceptions of dignity: the first concerns a subjective sense of self-worth and a readiness to accept responsibilities for consequences of our actions and decisions, and the second is more objective where it concerns the attitudes of others towards an individual or group (390). Thus people who lack the capacity for dignity in the subjective sense may still benefit from dignity in the objective sense, such as actions that may violate the dignity of an unconscious person even if they remain unaware of the violation, thereby denying them the respect that is due to them as persons (347). Decision-making capacity is not a requirement for experiencing a subjective sense of self-worth, nor is dignity in an objective sense derived from capacity, as persons share a common moral universe regardless of capacity status (390). Respect for dignity may simply prohibit 'bad things' such as inhuman or degrading treatment, or in the case of medical research dignitary harm resulting from being enrolled in research one may not have wanted to participate in (391), rather than as serving a more foundational role that is of primary interest (379). However, as Brannmark states, dignity can trump autonomy at times, therefore it cannot simply be reduced to matters of autonomy (379).

The meaning of privacy, and the basis for distinguishing privacy rights from other kinds rights, has been the subject of much debate (392). Although privacy underpins human dignity and other key values, it can be understood as consisting of two forms: privacy of the person and information privacy (392). Privacy represents a sense of identity and the occupying of a personal space: creating a boundary between self and others (393). Others' unwanted intrusion into those spaces can be experienced as violating the boundaries of self, where the harm arises not just from the exposure of formerly private behaviours to public view, but in the dissolution of boundaries that insulate different spheres of behaviour from another (394). Informational privacy concerns confidentiality, where strangers should not obtain

knowledge of personal data without the person's permission (395) and where confidential treatment of information is an important way of honouring the person's right to privacy. While there may be a temptation to understand the right to privacy in terms of autonomy (understood as a negative liberty), through appeals to metaphors of space or 'elbow room'(344) privacy is protected beyond that for which consent to access either data or personal space has been provided (379). Respect for privacy has similarities to respect for dignity in that it has a fundamental role in defining relations between persons, but is unique amongst the values that come under the umbrella of respect for persons in that it largely regulates behaviour that happens without direct interactions with the persons in question (379). Capacity is not a requirement for privacy as breaches of privacy can occur when someone has cognitive access to one's person or information about one's person, even if they do not make use of this access (393).

Integrity is strongly connected to a sense of self and identity, where integrity and identity can be considered integrated accounts of the good life (396). Integrity is generally conceptualised as respect for physical and mental integrity, although Fjellstrom proposes that there are five directions of interpretation including elements of health, identity, rights and the integrated self (397). Integrity also refers to the person's 'soundness' or uncorrupted character, uprightness, honesty and good character (397), or having an untouchable core with boundaries with acceptable and unacceptable contact which should not to be crossed (379). Although there are overlapping areas with other moral concerns such as dignity, some violations of boundaries can only be attributed to a violation of the right to integrity (379). The integration of integrity and identity suggests that integrity is not wholly capacity dependent. Consider a person who no longer has capacity, but who has lived a life based on the values and convictions, which they considered essential to create a good life. Decisions made on their behalf which would conflict with the values and convictions they held, such as investing their savings in tobacco company shares which they would find abhorrent, could violate their integrity although they would have no awareness of that violation. Thus, actions carried out in accordance with a person's wishes are not solely linked to any attempt to extend their autonomy but can also be viewed as respecting their integrity.

9.3 Summary

An individualised conception of autonomy, arising from the notion that people are independent, self-determining and rational decision-makers, which pervades informed consent to medical research, fails to fulfil the function or goal of respecting the autonomy of those who lack capacity for autonomous decision-making for research. As we have seen in earlier chapters, decision-making in practice for adults lacking capacity occurs in what Herring describes as the ‘muddled give and take of everyday caring lives’, which has greater resonance than the image of independent rights and interests (398). The failure of ethical and legal instruments concerning research to engage with the broader ethical concerns beyond autonomy for those who lack capacity, such as dignity and integrity, may be due to the ‘inherently vague’ nature of the concerns in comparison with the ‘straightforward’ autonomy-based frameworks (347). However, this isolates decisions about their research participation in a sea of artificial individualism as a consequence.

The de-coupling of respect for autonomy from respect for persons has resulted in the dichotomy seen in the ethics and regulation of research, particularly for those who lack capacity to consent. Autonomy is held to be of greatest importance, and in its absence, there is a requirement to protect those who are unable to consent. In part, this autonomy-welfare dichotomy arises from the claim that all research participants are vulnerable and in need of protection, which can be remedied by the provision of informed consent. The more specific claim that some participants are more vulnerable than others, particularly those unable to provide consent, requires additional obligations to protect these groups from harm (383). However, the relationship between this universal and special vulnerability has been little examined, and the designation of some individuals as especially vulnerable is problematic (383).

Rather than defining persons in terms of cognition alone, they can be considered as a complex entity with emotional and relational aspects that have moral significance, and where a misplaced emphasis on rationality results in diminished concern for a range of other moral concerns (399). The overlap between moral concerns such as integrity, dignity, and autonomy should not be seen as a weakness of this account; but as evidence of the complementary nature of these fundamental values and their importance for our self-understanding (400). Understanding respect for persons, and all that it entails, as the appropriate principle to underpin ethical research alongside ethical concerns of beneficence

and justice, allows for broader ethical considerations beyond merely those of autonomy. Legal considerations of autonomy, and the requirements for proxy consultation and consent, should be attentive to the inherent relationality of persons, and seek to develop a more appropriate approach than that offered by a framework focused solely on autonomy conceived as non-interference. This opens a way of describing a principle of respect for persons that accommodates a principle of respect for autonomy, in addition to other ethical concerns. Lysaught calls to mind the lyrics of Aretha Franklin's hit where she sings 'R.E.S.P.E.C.T, Find out what it means to me', and argues that the challenge is that in order to uphold our respect for a person we have to first find out what is of relevance to them as an individual (376).

The approach outlined here does not undermine the idea that respect for autonomy is often well-expressed through informed consent but challenges the acceptance that is a complete or self-sufficient expression of respect for persons. Instead, it broadens the applicability of respect for persons, recognising that there are degrees of autonomy, and cautions against the focus being on finding a substitute that can sign a consent form for individuals who lack capacity and therefore autonomy (379) in an attempt to mimic processes for those who are autonomous. The position sketched here, that the locus of the ethical basis for the inclusion of adults who lack capacity to consent to research lies within a conception of respect for persons, requires considerable development. However, this view opens up the respect for autonomy-welfare dichotomy and provides space for a broader account of the ethical considerations involved in research with persons lacking autonomy. Attempting to frame legal decisions about the inclusion of those who lack capacity through this account might be a more realistic goal than continuing to pursue the 'irrationality on stilts' (104) that a substituted judgement based on individualistic notions of autonomy invokes.

9.4 Learning points

The individualistic and rationalistic conception of autonomy, which requires that a competent person's preferences and decisions be respected, pervades the informed consent paradigm. Privileging autonomy fails to sufficiently acknowledge the other ethical concerns that are engaged when respect for autonomy is extended to those who lack capacity for

autonomous decision-making for research. As a result, this account fails to sufficiently address the full range of ethical concerns and therefore protect adults who lack capacity.

An alternative human rights-based account, which considers five distinct ethical concerns as coming under the umbrella of respect for persons, consisting of autonomy, dignity, integrity, privacy and vulnerability, is explored.

This enables a conception of autonomy that is situated within, and is attentive to, the broader ethical concerns to be outlined. Alongside the ethical concerns of beneficence and justice, this account may provide a more appropriate principle to underpin ethical research, allowing for broader ethical considerations beyond merely those of autonomy.

Chapter 10 Implications and recommendations for the legal frameworks governing research involving adults who lack capacity to consent in England and Wales

10.1 Introduction

This chapter draws together the findings relating to the law from the previous chapters and reflects on the implications for the legal frameworks. This includes building on the triangulation work in Chapter 8 that explored the legal '*Ideal versus Reality*' and which described the law as the 'testing ground for the practice of bioethics' (330), and the preceding proposal in Chapter 9 to reframe research under the umbrella of respect for persons, as well as identifying areas that require clarification and amendment following the findings identified in earlier chapters.

10.2 Discussion

10.2.1 Current legal conceptions of autonomy in research involving adults lacking capacity

Broadly speaking there are two legal mechanisms for protecting the autonomy of persons who lose decision-making capacity (347). Firstly, precedent autonomy can be preserved through either formal advance directives or by taking account of past views and preferences through more informal processes. Secondly, supported decision-making can enable the person to participate in the decision-making process to the fullest extent possible. The legislation governing the involvement of persons who lack capacity in research in England and Wales currently focuses on the former.

The legislation governing clinical trials of medicinal products in the UK, the Medicines for Human Use (clinical trials) Regulations 2004 (CTR) (22), lays out the principles and conditions which apply in relation to incapacitated adults' participation in clinical trials (Schedule 1, Part 5). All other forms of research come under the auspices of the Mental Capacity Act 2005 (sections 30-34) (MCA) (20) which also governs decision-making regarding healthcare,

welfare, and financial matters for adults lacking capacity in England and Wales. The MCA arose out of common law, through consolidating and codifying the existing law (401) which had developed through various cases concerning the health and welfare, as well as property disposal, of adults who lack capacity. In contrast, the origins of the CTR lie in the European Convention on Human Rights (402), and the evolution of ICH GCP (65) which requires that 'informed consent was freely given by the subject or the subject's legally acceptable representative' (4.8.9). The disparate origins of the legislation appear to have given rise to two contrasting approaches to autonomy, as conceived for those under their protection. There is a requirement for informed consent to be provided by a surrogate or proxy for research governed by CTR, however research under MCA proceeds without consent as a consultation process replaces consent. This duality of consent/no consent introduces an additional binary into the 'patchwork of binaries' (403) as seen in the autonomy/paternalism, capacity/incapacity, empowerment/protection, and invulnerability/vulnerability divisions.

10.2.1.1 Clinical trials legislation

The CTR implemented the EU Clinical Trials Directive 2001/20/EC (404) into UK law. They permit the inclusion of adults lacking capacity in clinical trials, subject to conditions such as sufficient justification for their inclusion, and the level of risk permitted (22). They also permit a legal representative, who has been informed about the risks and inconveniences of the trial, to provide informed consent on behalf of the person taking part in the trial. The legal representative is someone who 'by virtue of their relationship' with the person who lacks capacity is 'suitable to act as their legal representative' for the purposes of that trial (Schedule 1, Part 1, 2(a)(i)(aa)), and their consent represents the person's 'presumed will' (Part 5 (12))(22). There is no requirement for the legal representative to consult others who may be involved in caring for the person. The 'presumed will' basis is required for all those who lack capacity to consent, regardless of whether their 'will' can be determined or not, or whether they had prior capacity or not. If a capacitous person provides consent to participate in a trial and subsequently loses capacity, that consent remains legally valid, providing the trial is not significantly altered.

The omnipresence of the requirement for informed consent in the CTR, even for those who lack capacity where consent is achieved vicariously through a substituted judgement, signals an individualistic approach to autonomy. This is reflected in the basis for the legal representative's role – that of the person's presumed will – which adopts a positivist

approach to substituted decision- making that assumes a fully autonomous decision can be 'unearthed' by the representative and presented to the researchers, regardless of whether the person had prior capacity or not. The legal representative is empowered to act on the person's behalf as they, by virtue of their relationship, are expected to be able to access or unlock this fully reasoned decision, thereby enacting the person's autonomous choice as they are no longer capable of such agency. It assumes that a dichotomous yes/no response could be replicated by the legal representative, without reference to the complex contextual issues that are relevant to the decisional situation, particularly given the circumstances that have led to the loss of capacity for the person.

The CTR itself has its roots in EU enterprise and (pharmaceutical) industry groups, and as such is driven by concern for the risks associated with patient and public safety, but also with economic and commercial concerns (405). The conception of individualised autonomy reflected in the CTR must be understood as part of the risk assessment paradigm that is fundamental to the CTR, but which is engaged with the economics and politics of developing novel health technologies as much as it is with ethics and human rights concerns (405). It appears in stark contrast to the level of dependency and vulnerability associated with the reality of living with incapacity (287), rather than the wholly atomistic independent life that individual autonomy requires, and fails to recognise the inherently social nature of persons, particularly those incapable of autonomous choice who are inevitably situated within relationships of care.

10.2.1.2 Mental capacity legislation

The MCA has been criticised for the pervasiveness of a Millian conception of autonomy as non-interference, where those with capacity to make decisions for themselves are seen as autonomous and consequently the state is prohibited from interfering in their decisions, and those lacking capacity who can be subject to paternalistic interference in the name of best interests as they lack autonomy (373). This stark binary divide is highlighted by the Code of Practice which states that '... the Act also aims to balance an individual's right to make decisions for themselves with their right to be protected from harm if they lack capacity to make decisions to protect themselves' (235). The suggestion that 'autonomy' and 'protection' are in need of being balanced reinforces their separateness and tension (403). Although the general provisions of the MCA include the requirements to 'permit and encourage the person to participate' in decisions (s4(4)) and consider their 'past and present

wishes and feelings' as well as their 'beliefs and values,' (s4(6)); it also requires that carers and others with interests in the person's welfare are consulted as to their views (s4(7))(20). There is no emphasis on supported decision-making under the general provisions of the Act.

The position becomes more complex regarding decisions about research participation. Unlike the general provisions of the MCA, which is orientated towards making decisions in the best interests of the person, decisions about research are explicitly excluded from a best interests determination[64]. An individual 'engaged in caring' for the person lacking capacity, or 'interested in their welfare' is consulted by the researcher under s30-34 of the Act. The consultee provides advice as to whether the person should take part in the research or not, and what the person's wishes and feelings would be about taking part if they had capacity in relation to the matter (s32(2)) (20). Herring (398) suggests that rather than this being seen as a radical departure from the fundamental principle requiring any interference to be in the person's best interests, that this is seen as an example of best interests being construed as the interests of 'one' being ultimately continuous with those of others. Under this view, the MCA could be considered to take a relational approach to decision-making.

The process of consulting those who are engaged in caring for the person, situates the decision-making process within a relationship characterised by care and attentiveness to the needs of the person, as well as attending to their wishes and feelings. Although there is no temporal framing of these wishes and feelings, as the MCA uses the future conditional tense, the consultee may take account of their previously expressed wishes as well as any current preferences. It also adds a probability element through the use of 'likely to be' (s32 (4)(b))(20), which encourages the consultee to construct a scenario in which the views of the person can be interpreted to form advice to the researcher, accessed through knowing the person. This 'knowing' is aligned to the concept of relationality, which conceives of persons as socially embedded, with social identities formed and expressed through relationships.

The law's emphasis on individualised autonomy reflects a particular understanding of personhood and the self, which ignores and devalues the care that is central to human flourishing (398). Medical law is based on a fundamental distinction between those that have capacity, where the law is dominated by the right of autonomy conceived as non-interference, and those who do not who are governed by protections afforded by best interests and human rights approaches (398). Critics of the extant individualised conception

of legal personhood emphasise its inability to contend with connectivity, by conceptualising people as essentially 'discrete, bounded units, beings who come in ones, not twos' (406).

10.2.2 Implications for the legal frameworks of a move towards respect for persons

In comparison to the CTR, the MCA appears to demonstrate a more attentive approach to respect for persons, not least because it is situated within the broader context of care, and not treated as an isolated issue devoid of contextual understandings. However, the MCA is not without its critics, not least because there has been substantial doubt cast over its compliance with the 2006 United Nations Convention on the Rights of Persons with Disabilities (407). Examination of the theoretical underpinnings which inform and guide the MCA have led to criticisms that the Act's individualistic approach to the concept of mental capacity does not adequately reflect the reality and lived experiences of those deemed to lack capacity or their informal carers (408). Although others suggest that the MCA, by giving parity to the determinative strength of a person's own values, whether they have capacity or not, requires that decision-makers take a respect for persons approach (159). An example is the requirement that attention be paid to the person's will and preferences which can be said to respect the person's dignity (347) which the preceding chapter proposed was one of the elements of a broader respect for persons. Similarly, the legal weight given in both the MCA and CTR to any refusal or indication that the person who lacks capacity does not wish to participate in intrusive research (20,22) protects them from any unwanted intrusion and thereby demonstrates respect for privacy.

There have been calls for a legal system that starts by acknowledging vulnerability as the human condition and is more representative of the lived experience (382). This approach challenges the unsatisfactory dichotomy between 'autonomy' and 'protection' by acknowledging the importance of other moral concerns that make up a fuller account of 'persons' than merely appealing to the primacy of respect for autonomy. There have been appeals to provide more distinct legal understandings of autonomy – particularly at the 'margins' of capacity – which would be more in keeping with the ethos of the MCA itself (409). This thesis proposes that developing a theory of relational proxy decision-making, based on the forming of relationships and underpinned by respect for persons (rather than respect for autonomy), may be a more informed and informative approach. The question is whether the regulatory frameworks surrounding research that involves adults lacking

capacity can also engage with this alternative approach. Thus the longer term challenge is to identify a fuller, more realistic account of the legal realities of those affected, to allow appreciation of 'the rich thicket of reality' (406).

10.2.3 Recommendations for the development of the legal frameworks in England and Wales

In the interim, there are five main areas relating the law governing research involving adults who lack capacity that require clarification or amendment: 1) the application of the statutory principle of 'best interests' to research involving a person who lacks capacity, 2) the relationship between Lasting Power of Attorney (LPA) arrangements and consultee involvement, 3) guidance on the role of nominated consultee/professional legal representative and the basis for their decision, and 4) the application of Advance Decisions to Refuse Treatment (ADRT) and research.

10.2.3.1 Highlighting the exception of 'best interests' in proxy decision-making for research

The fifth statutory principle of the MCA is that 'An act done, or decision made, under this Act for or on behalf of a person who lacks capacity must be done, or made, in his best interests' (Part 1(1)) (20), although the MCA Code of Practice also refers to *any* act done or *any* decision (p.20) (235). The only exception to this principle relates to decisions regarding participation in research (and advance decisions to refuse treatment) where other safeguards apply (2.12)(235). However, this is not stated in Chapter 11 of the MCA Code of Practice, which covers research projects involving a person who lacks capacity and, as identified in this research, appears to be widely unknown amongst the researcher and practitioner communities.

The survey reported in Chapter 4 of this thesis provided evidence that health care professionals, social care practitioners and the wider research community are not aware of this exception (216), and this has been encountered anecdotally when conducting research in a range of settings. The content analysis of Participant Information Sheets (PIS) for consultees and legal representatives reported in Chapter 5 found that some information sheets incorrectly stated that best interests was the legal basis for the consultee's decision, and included references to best interests such as they are required to 'assess whether study enrolment is in the patient's best interest' [ID 19] (240). This may impact on decisions made

regarding research participation, where the consultee is required to advise what they think the person's feelings and wishes would be, if they had capacity to decide whether to take part rather than determining what would be in the person's best interests as a basis for the decision. This misunderstanding may in part be linked to the template information sheets developed by the Health Research Authority (HRA) for studies involving adults who lack capacity, which states in the introduction 'We'd ask you to consider what you know of their wishes and feelings, and *to consider their interests.*' (241). The National Institute for Health Research (NIHR) also refer to decisions about research involving adults who lack capacity needing to be taken in accordance with the person's best interests, such as in the 'Frequently Asked Questions' section of the NIHR Join Dementia Research registry website (410).

Information about this exception should be more widely understood and disseminated to those involved in research and/or the care of adults with impaired capacity, including greater clarity in the guidance from the HRA and the NIHR. A consultation process is currently underway by the Ministry of Justice to update the MCA Code of Practice. It is recommended that a clear statement regarding the exception to the 'best interests' principle for decisions about research are added to Chapter 11 of the Code of Conduct and highlighted in every list of principles about best interests in order to address this misconception.

10.2.3.2 Clarifying the role of Lasting Power of Attorney and decisions about research participation

There is a lack of clarity around whether a person acting as personal consultee for research involving a person who lacks capacity is required to have Lasting Power of Attorney in order to act as a consultee. Whilst other commentators have suggested that the role of an LPA or Deputy in decisions about research remains unclear (237), an LPA for Health and Welfare is generally limited to health and care decisions, rather than medical research. The MCA does not require the individual acting as a personal consultee or legal representative to be a legally appointed attorney or deputy, only that they are someone who cares for the person or is interested in their welfare (s32(2)) or someone nominated who has no connection with the project (s32(3)) and that 'The fact that a person is the donee of a lasting power of attorney given by P, or is P's deputy, *does not prevent* him from being the person consulted under this section.' s32(7)(20) (italics added). The position regarding attorneys and involvement in decisions about research is only implied in the MCA Code of Practice which states in in Chapter 7 about LPA 'It is *good practice* for decision-makers to consult attorneys about any

decision or action, whether or not it is covered by the LPA' and 'Researchers *can also consult* attorneys if they are thinking about involving the donor in research' (7.57, p130)(235) (italics added). The CTR make no reference to Power of Attorney arrangements.

The role of being a donee of an LPA for health and welfare matters and decisions about research participation are not clearly understood by researcher and practitioner communities. As reported in the survey reported in Chapter 4 of this thesis, health and social care professionals who care for those who lack capacity to consent commonly assumed that an LPA was needed in order to act as a consultee or legal representative (216). The content analysis of PIS for consultees and legal representatives reported in Chapter 5 found that some information sheets mentioned the involvement of the role of an LPA when acting as consultee or legal representative. In the DECISION Study qualitative interviews reported in Chapter 6, those acting as a proxy also believed that the role of a Welfare Attorney includes decisions about research participation. The NIHR refer to an LPA being required for decisions about research involving adults who lack capacity, such as in the 'Frequently Asked Questions' section of the NIHR Join Dementia Research registry website which has a section titled 'If I hold Lasting Power of Attorney can I consent someone into a study?' (410). Currently, despite an emphasis on advance care planning, there is no legal mechanism for prospectively appointing an individual to make decisions about research in the event of a loss of capacity. Consultees and legal representatives are appointed retrospectively by researchers and/or care providers. Extending the role of LPA to include decisions about research promotes the autonomous choices of those who may lose capacity, and may help address the current uncertainty and concern of health and social care professionals about where the locus of authority lies in decisions about research (216). Participants in the DECISION Study reported in Chapter 6 supported the extension of a Health and Welfare LPA to optionally include decisions about research. Additional interview data further exploring this topic is not included in this thesis but has been submitted as a peer-reviewed journal article (manuscript under review).

Recommendations regarding the need for additional guidance on this issue were made by the Nuffield Council of Bioethics in their 2009 report on the ethical issues in dementia (288). They recommended that consideration be given to the role of the welfare attorney being explicitly extended to include decisions about research, both within the MCA and the CTR, and that in the meantime the MCA Code of Practice should provide guidance on the role of the welfare attorney in decisions about participation in research governed by the MCA CTR

(Recommendation 19)(288). The research presented in this thesis supports the recommendations from the Nuffield Council on Bioethics that a clear statement regarding the role of LPA in decisions about research in the MCA and/or the MCA Code of Practice would bring greater legal clarity. There is a need to clarify the role of an LPA in research, and to re-examine the extension of the role to explicitly include decisions about research participation. Further questions remain about and the legal basis for decisions for those whose lifelong disabilities would limit any ability to represent their wishes and feelings about research participation.

10.2.3.3 Developing guidance regarding the role of nominated consultees and professional legal representatives

Both the MCA and CTR have provisions for circumstances where there is nobody able or willing to act as a personal consultee or legal representative. In these situations, the researcher must nominate a person to be the consulted (s32(3))(20). Unless it is a clinical trial in which case this should be the doctor primarily responsible for their medical treatment or a person nominated by the relevant health care provider (Schedule 1, Part 1(2(a(ii))). In both cases this must be someone who is not connected with the conduct of the clinical trial or study. Findings from a supplementary study of trials involving adults lacking capacity not included in this thesis (in press) found the use of nominated consultees is widespread. As an example, in practice, many care home residents will only have care home staff to act as a consultee.

There is a lack of understanding about who can act as a nominated consultee in both research and practitioner communities. The content analysis of information sheets reported in Chapter 5 showed considerable discrepancy around information given to nominated consultees or professional legal representatives about their role when compared to those acting in a personal capacity. The MCA Code of Conduct provides no information about who might act as a nominated consultee, only stating that the researcher must follow guidance from the Secretary of State for Health in England or the National Assembly for Wales (11.26)(235). However, the 'Guidance on nominating a consultee for research involving adults who lack capacity to consent' produced in 2008 (411) was archived in 2013 and it is not clear if this is considered current guidance or if there is any further guidance planned. The CTR offers no guidance about the circumstances under which a doctor or other person might act. This is particularly relevant as non-medical prescribers (nurses, midwives, and

Allied health Professionals) are increasingly common. There appears to be no current guidance from statutory bodies for health and social care professionals who may be approached to act as a consultee or legal representative.

It is recommended that the current revision of the MCA Code of Conduct should more clearly reflect s32(2) and s32(3) of the MCA. Additionally, the HRA or other bodies should consider developing specific guidance for health and social care professionals acting as nominated consultee. In addition, the exploration of '*Ideal versus Reality*' reported in Chapter 8 identified the problematic nature of the legal basis for their decisions being the same as for those acting in a personal capacity, that of their presumed will or wishes and feelings. Further exploration of this area is required.

10.2.3.4 Clarifying the application of Advance Decisions to Refuse Treatment and decisions about research participation

There is a lack of clarity around the role of ADRT and decisions about research participation. The MCA Code of Practice states '[Researchers] must not do anything to go against any advance decision to refuse treatment or other statement the person has previously made expressing preferences about their care or treatment.' (11.30 p.211)(235). This has been interpreted by the HRA as applying to decisions *about research* in their guidance for studies involving adults who lack capacity. Their template information sheet states 'Please let us know of any advance decisions they may have made about participating in research. These should take precedence.' (241). The analysis of information sheets in Chapter 5 of this thesis showed that this statement has been used by some researchers, such as 'any advance decisions about participating in research the patient may have made (ID 15)'(240).

It is recommended that a clear statement regarding the role of ADRT in decisions about research would bring greater clarity. In addition, there is currently no legal mechanism for formally stating preferences regarding research participation in the event of a loss of capacity. The Nuffield Council on Bioethics in their dementia report recommended that the UK Departments of Health should commission research on the feasibility of developing some form of (non-binding) advance statement on research participation which could influence decisions on research participation after loss of capacity (Recommendation 18)(288).

10.3 Summary

This chapter has drawn together the empirical findings from the previous studies and legal requirements for proxy decisions about research participation to discuss the implications for the legal frameworks. A number of areas of the law that require development have been identified, and recommendations made. The findings have formed the basis of submissions to the public consultation on the MCA Code of Practice that was (fortuitously) open during the writing of this thesis.

10.4 Learning points

The autonomy and informed consent paradigm that underpins the legal frameworks governing research involving adults who lack capacity, particularly the CTR, does not reflect the relational nature of proxy decision-making. The frameworks create a dichotomy between those considered to have capacity, whose freedom to make decisions is to be respected, and those considered lacking capacity whose vulnerability requires their protection. The requirement for the person's wishes and preferences to form the basis for nominated consultees and professional legal representatives, and for all other cases when those preferences can never be known, is especially problematic.

A number of specific interim recommendations are made including: the need for clarification of the role of LPA in decisions about research; correcting the widespread application of the 'best interests' principle to research decisions; the application of ADRT to research participation; and the need for further guidance regarding the role of professionals acting as consultee or legal representative.

Chapter 11 Development of an intervention to support informed decision-making by family members acting as research proxy for an adult who lacks capacity to consent

11.1 Introduction

Chapter 6 explored the experiences of proxy decision-making for research and identified the impact experienced by family members acting as research proxies. The findings showed that there can be a decisional and emotional burden for family members, who may therefore benefit from decision support. The final part of the doctoral project was to develop a decision support intervention for those family members making a decision about research on behalf of a person who lacks capacity to provide their own consent. When making a decision, the decision-maker must choose between alternative courses of action, or between action and inaction (412). Decision-making processes have four basic properties: that there is a choice between a finite number of alternatives or 'prospects'; that each alternative carries risks and benefits which cannot be anticipated with certainty; it takes time to gather information and to deliberate about the relative merits of each alternative; and each stage of decision-making integrates the achievements of earlier stages (413).

There is ongoing debate around whether the presumption that a proxy is actually making a 'decision', as opposed to having the authority to accept or refuse what a healthcare provider recommends, is correct (certainly regarding medical treatment decisions) (24). For research governed by the Mental Capacity Act 2005 (MCA) (20) the proxy's role is that of a consultee who provides advice to the researcher, who remains the legal decision-maker. However, throughout the significant body of empirical research included in the systematic review (Chapter 3) and the interviews conducted with proxies that are reported in Chapters 6 and 7, proxies themselves describe a process of making decisions that goes beyond accepting or rejecting an option, particularly where the research opportunity is sought out by the proxy or where the approach comes through other sources such as a research registry or via a care home. In addition, under the Medicines for Human Use (Clinical Trials) Regulations 2004 (CTR) (22) the proxy provides informed consent on behalf of the person who lacks capacity, and so would particularly be viewed as the decision-maker in this context.

Complex interventions are widely used to bring about change in the health service, public health practice, and in areas of social policy that have important health consequences (414). Complex interventions may alter a discrete aspect of practice (e.g how doctors interact with patients) or something more far-reaching (e.g smoke-free legislation) (415). Decision aids are interventions that support patients by making their decisions explicit, providing information about options and associated benefits and harms, and helping to clarify congruence between decisions and personal values (416). A recent Cochrane review established that decision aids can: (1) improve knowledge; (2) reduce decisional conflict; (3) clarify expectations of possible benefits and harms; (4) lead to choices consistent with informed values; and (5) result in greater participation in decision-making (416). However, it is less clear what effects these interventions have on interactions between patients (or their families) and clinicians, and which components are the essential ingredients for improving decision processes and outcomes (416). Insight from research in decision and communication sciences should be integrated with bioethics to assist and understand processes of informed decision-making (417). This chapter reports the development of a *de novo* decision support intervention for family members acting in the role of research proxy on behalf of someone who lacks capacity to consent.

11.1.1 Preference sensitive decisions

In health care, patients' decisions about treatment and screening are often described as 'preference sensitive', where they may involve important trade-offs between length and quality of life or between comfort and efficacy of procedures (418). Preference sensitive decisions require the patient to make a choice when there is no clear evidence to support one option over another, therefore the patient's values are important in optimising the decision (419). For decisions regarded as preference-sensitive, the relative importance a patient attaches to various outcomes and processes has a large, if not determining, influence on what is decided (420). Quality decision-making is therefore said to be the extent to which the chosen option matches the informed decision-maker's values for benefits, harms, and uncertainties (421). The decision to participate in a research study such as a randomised controlled trial is considered just such a preference sensitive decision (43). Proxy decisions about research participation would require the proxy to pay attention to the relative importance the person who lacks capacity would attach to various outcomes, and therefore could also be considered to be preference sensitive although it is the other person's preferences that are of relevance.

Prior to deciding whether to participate in a research study, potential participants, or their proxies, are provided with information in the form of a Participant Information Sheet (PIS). Existing Participant Information Sheets (PIS) provided to potential participants do not function well as decision-making tools, primarily because they do not contain information to support decision-making about trial participation (243) or, as reported in Chapter 5, about the proxy's role in deciding on behalf of another. Whilst enabling sufficient knowledge and understanding are important elements for quality decision-making, they are not the only important factors. Therefore, interventions which aim to support the process of decision-making, as well as improving knowledge, may hold additional benefit for participants considering clinical trial participation (43). This is likely to hold true for proxy decision-makers who are required to make a decision about research participation on behalf of another, although it is that person's, and not the proxy's, values and preferences that should at the very least be considered precatory if not determinative.

11.1.2 Decision support interventions

Decision support interventions, also known as decision aids (DAs), are intended to facilitate patient involvement in decisions about their healthcare leading to decisions which are informed and consistent with one's values (243,422). DAs differ from traditional information materials in many ways, including that they are not intended to encourage a particular choice or action (423). DAs can take many formats, for example a paper-based booklet, video, or website (424). DAs combine several important goals, such as informing patients about options, helping clarify their values, supporting the preference construction process, and enabling patients to more actively engage in shared decision-making with their health care providers (418). A focus on improving decision-making has also raised questions about 'decision quality', specifically, the means by which we assess whether someone has made a 'good' decision (425).

Many DAs encourage patients to approach a decision using conscious, deliberative and analytical processes, and so include decision strategies such as making lists of pros and cons, as well as explicitly rating and weighting these pros and cons (418). DAs often incorporate values clarification methods (VCMs) as deliberative processes to help elicit patients' treatment values to help them to make decisions (418). However, interventions focussing solely on reasoning and deliberation can be problematic and may even be harmful (418). Decision-making can also involve intuitive processes, which are derived from the apparently

effortless integration of available information and give rise to decisions based on affective responses, gut feelings, or 'fast and frugal' decision-making strategies (heuristics) (418). The complexity and duration of the decision process varies with the nature of the choice to be made – simple heuristics are usually sufficient for routine choices but more significant decisions involve more deliberation and consultation because the risks and the uncertainty are higher (111). Extensive research in the values and preferences literature suggests that although preferences are always context sensitive, they are not always calculated to the same extent. Some preferences are retrieved based on an existing attitude or instinct, whereas others are based on the integration of multiple inputs (426).

Evidence suggests that in decision contexts characterized by uncertainty and time constraints (e.g. health-care decisions), fast and frugal heuristics may perform better than complex rules of reasoning (427). Intuitive processes may allow people to integrate larger amounts of information and to better use accurate affective cues, however strong emotional reactions can cause bias and error in decision-making (428). It has been suggested that both intuition and deliberation are critical components in decision-making, and that whilst they serve different goals in the decision support context, they might work best when working together (418). This can be achieved through explicitly encouraging decision-makers to become informed before making a decision, ensuring that information is presented in such a way that heuristics and biases are minimized, and encouraging decision-makers to articulate preferences and the reasons through an exercise placed late in the decision process (418).

11.1.3 Decision-making and informed consent

Studies into medical decision-making show that patients do not always base their choices on rational grounds, and rely on trust, intuitions, emotions and (irrational) beliefs (316). Decision-making that is lacking in rationality and is subject to bias and limitations has been described as particularly problematic when the decision is regarding the provision of informed consent (429). For example, in heuristic decision-making incomplete and/or incorrect information may play a disproportionate role in decision-making, which may therefore fail to fulfil the condition of 'with understanding' that is necessary for an autonomous authorisation to be given (316). The requirement for consent to be 'with understanding', including the conditions of it being an informed and well-considered choice, may not always be possible nor conducive to 'good' decision-making (316). Attempts to seek

improvements in informed consent processes that address the issue of the ‘limitedly rational’ decision-maker include strategies to enhance well-considered, informed choice, like decision aids (316). However, intuitive and emotional reactions, feelings, beliefs and previous experiences are also a source of information that are needed to make an autonomous choice (316). Most choices, especially difficult choices, involve integrating both cognitive and emotional contributions (430). DAs can bridge the gap between the informed consent doctrine and real-world choice behaviour, by sustaining and promoting authentic, autonomous decision-making by the ‘limitedly rational’ decision-maker (316).

11.1.4 Decision aids for research participation

Decision aids have been developed for a range of medical treatment and healthcare decisions, and have been shown to positively influence several aspects of decision-making, including improving knowledge; reducing decisional conflict, which can lead to choices consistent with informed values and result in greater participation in decision-making (416). Subsequently, several interventions have been developed to promote informed decision-making about participating in clinical trials (431–433). However, many of these interventions focus on the content and structural components by aiming to improve presentation of information, or mode of delivery, rather than the process of decision-making itself (43).

A recent systematic review of decision aids for trials identified only one study that evaluated the effectiveness of decision aids compared to standard information in the informed consent process for clinical trials (43). Although the search strategy specifically sought to include studies that included guardians of, or proxy decision makers for, potential trial participants, no decision aids for use by proxies were identified (43). The reviewers concluded that more high quality RCTs of decision aids to support the informed consent process for clinical trials are needed (43). A qualitative exploration of stakeholders’ perceptions of decision aids designed to support the decision-making process for randomised controlled trials suggested that decision aids have the potential to better engage potential participants in the decision-making process and allow them to make more personally relevant decisions about their participation (434).

11.1.5 Decision aids for proxy decision-makers

No previous decision support tools have been developed for use by research proxies. However, a number of tools have been developed for proxies who are making other decisions on behalf of a person who lacks capacity, such as around the use of antipsychotic medication, place of care, retiring from driving due to dementia, and receiving mechanical ventilation (424,435–437). The DAs intended for use by proxies invariably make the assumption that the evidence that decision tools are effective in increasing knowledge and reducing decisional conflict is transferable to proxy decision-making, and there is some limited evidence of this. A small study examining the impact of a DA on proxy decision-makers' perceptions of feeding options for people with dementia found it improved knowledge scores and reduced conflict (438). A feasibility study of an intervention to support family carers make decisions about place of care for a person living with dementia also found that it reduced decisional conflict, although it did not remove all barriers to decision-making and some unresolved conflict remained (435).

11.1.6 Complex interventions and complex systems

The term 'complex interventions' are primarily used to refer to interventions as system changes that are focused on health promotion, social interventions, and public health more broadly. What makes an intervention 'complex' has historically concerned the active ingredients of an intervention and the synergies between intervention components, but complexity is increasingly being conceived in terms of how interventions interact with their contexts; where contexts are broadly defined as any feature of the circumstances in which an intervention is conceived, developed, implemented and evaluated (439). An alternative view places interventions as 'events' within complex systems, which foregrounds the system as the primary source of complexity (440). There is a call for intervention researchers to move away from viewing interventions as discrete bundles of components which can be described in isolation from their contexts, and better understand the systems into which change is being introduced (441). Thus there is a focus on interventions viewed as disruptions to complex systems, rather than on the intrinsic properties of interventions (442). Although not widely viewed as complex interventions, DAs, particularly one to be used by proxies, can be considered to have properties of complexity on both accounts. It is a complex intervention with several interacting components (443), entailing complex behaviours and a range of

effects (444), and also as an event occurring within inevitably complex systems such as within a family, legal and ethical frameworks, and a healthcare system.

11.1.7 A socio-ecological approach to proxy decision-making

For the development of this complex intervention, a socio-ecological model (SEM) of proxy decision-making was created which was adapted from the model most commonly used for health promotion and behaviour change interventions (440). An ecological perspective recognises that individuals are located within a broader social context (445,446). In this model, behaviour is conceived as being determined by five levels of analysis: intrapersonal factors, interpersonal processes, community factors, institutional/organisational factors, and public policy or socio-cultural factors (447). Current dynamic ecological-systems thinking goes beyond seeing these as just multiple levels, but stresses the importance of linkages, relationships, feedback loops and interactions between the various system's parts (440). Using ecological theories about behaviours within relationships, an intervention can be seen as a critical event leading to the evolution of new structures of interaction and new shared meanings (440). Interventions are therefore often complicated (multicomponent) or complex programmes that are designed to affect change at several levels of the socioecological model (448).

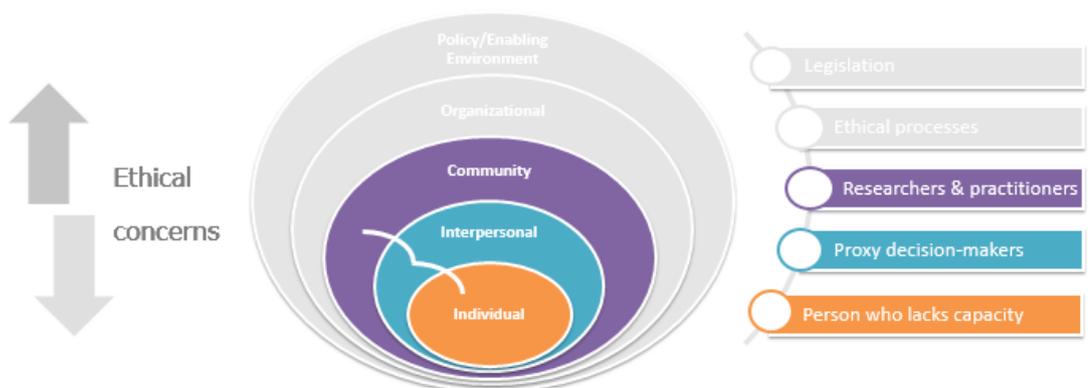
Proxy decision-making for research, whilst not traditionally thought of as a behaviour, is similarly situated within complex systems, which can be perceived as having a number of levels that have contextually dependent dynamic interactions between them. In addition to this socio-ecological systems approach, other commentators have described an 'ecological turn' in ethics (364). This is supported by the complex and relational nature of proxy decision-making reported in the findings from the DECISION Study and is reflected in the multidimensional approach taken throughout this thesis. The SEM can be seen as a useful organising construct for proxy decision-making (**Figure 11-1 Socio-ecological model of proxy decision-making for research**). This doctoral project as a whole has explored many different factors or levels, including the legal frameworks at both a policy and socio-legal level, the ethical organisational processes involved, the knowledge and attitudes of the researcher and practitioner community, the interpersonal relationship between the proxy and the person they represent, which ultimately centre around the person who lacks capacity to consent. The levels are all set within a range of normative ethical concerns.

Figure 11-1 Socio-ecological model of proxy decision-making for research



The main influences on the issue being examined can also be classified according to the socio-ecological model distinguishing between the different levels of the model (448). Thus, the intervention described in this chapter spans the individual-interpersonal-community spheres. Where the aim of the intervention is to improve informed decision-making by proxies that reflects the wishes and preferences of the person they represent, whilst ensuring it pays attention to the ethical principles and corresponds to the relevant legal frameworks. (**Figure 11-2 Location of intervention to support proxy decision-making for research in socio-ecological model**). As identified in Chapter 4, the intervention will also need to be attentive to the informational needs of the healthcare professional, social care practitioner, or researcher who will be delivering the intervention to ensure that they are knowledgeable and confident in the inclusion of adults lacking capacity in research.

Figure 11-2 Location of intervention to support proxy decision-making for research in socio-ecological model



11.1.8 Theoretical framework

Prospectively identifying all of the important contextual factors is likely to be difficult for novel interventions, therefore the development of a programme theory that identifies the key dependencies between intervention and context may be helpful (439). All interventions have an implicit or explicit theoretical framework underpinning how they are intended to bring about the desired outcomes (448), and many of the intervention development frameworks support a theory-driven approach (439,448,449). However, there have been warnings that an uncritical assumption that an intervention explicitly based on theory is inherently superior can carry significant risks (441). Alternatively, researchers should develop a clear understanding of how the problem under consideration is created and sustained in context through exploring the ecological fit of interventions with the systems whose functioning they attempt to change (441).

Theories of decision-making and choice generally fall into two categories: normative theories of cognition such as probability theory and decision theory, and descriptive theories of cognition which describe how people actually think when making decisions (277). It is these descriptive theories that are relevant to this project exploring the processes through which proxies make choices. A review of the descriptive theories of behaviour and decision-making is beyond the scope of this thesis. However, a brief high-level summary of selected relevant theories is required to provide some theoretical context to the intervention development described. These are broadly grouped into theories based on modelling choice between risky options (which focus on rationality and predictions), models of heuristics (which are also concerned with capturing the underlying cognitive process), process theories, factors affecting decision-making, and 'self-other' differences in decision-making.

11.1.8.1 Probabilistic and heuristic approaches to decision-making

Rational choice theories, such as the expected utility theory, suggest that individuals choose options with the highest overall benefit or utility mathematically by multiplying an outcome's probability with its worth or utility (450). As most decisions involve risk, where the probabilities of the various possible outcomes are known, there is a substantial body of work on 'risky' decision-making (277). However, many important decisions involve uncertainty, where the probabilities are unknown and have to be estimated or inferred, rather than risk, which is less well understood (277). Importantly, decision-making, including that regarding medical decisions, constantly deviates from rational choice theories (417). Alternative

approaches have been developed to reflect that people often do not make judgements that are consistent with these theories of 'rational' decision-making.

In the dual process view of decision-making, it has been argued that two modes of thinking are involved: system 1 thinking (intuitive) and system 2 thinking (analytical) (451). Although it is thought they probably represent the ends of a continuum, rather than being two distinct modes (452), and that any kind of serious, complex thinking employs both analytical and intuitive thought (453). There is an assumption that encouraging decision-makers to follow deliberative, analytical processes in comparing available choice options is the preferable strategy for improving decisions (454). However, this assumption lacks a solid theoretical or empirical basis, and is in conflict with the understanding that decisions are not purely analytical and also depend strongly on intuition (418).

A considerable body of research has identified a number of biases and heuristics (or mental shortcuts or 'rules of thumb') (455) that are present in decision-making. These include: affect heuristic, anchoring bias, availability bias, information framing effects and outcome bias, and have a significant effect on decision-making through their impact on understanding, intentionality of the decision-maker, and effective autonomy (113). Applied decision-making seeks to describe and improve decision-making in real-life situations through prioritising areas of practical relevance, with one such approach being the use of fast and frugal heuristics (FFH) (456). FFH recognises that it is often impossible to optimize decision-making in the real world, and so is geared toward obtaining solutions that suffice to satisfy the decision maker's goals (457). Given that people are not rational and perform different tasks in different environments, the FFH approach assumes that people do not rely on a single cognitive strategy but rather select an adequate heuristic from what has been dubbed an 'adaptive toolbox' (457). This approach exploits features of the decision environment and the individual capabilities of the decision maker to improve decision-making, whilst retaining speed, transparency, and efficiency which are all characteristics of FFH (457). Using the conceptual lens of FFH, an emphasis is placed on specifying how people make decisions, instead of focusing on predicting outcomes of people's decisions. This allows researchers who are seeking to improve or aid decision-making to develop strategies that help people follow that process, and alter the decision environment to enable people to follow this process more easily (457).

Prospect theory asserts that people make decisions based on the gains or losses associated with possible outcomes, and that losing something causes more mental distress than gaining something of the same value (458). Importantly, for the topic of this thesis, the tendency toward taking such risks may differ from one person to another due to level of expertise with uncertainty information, or indeed may differ from one domain (e.g. health or finance) to another (459). Therefore, Prospect Theory argues, when making a decision on behalf of another person, the same decision-problem might be framed differently by the people involved, either because they hold different values/attitudes or because the outcome will have different impacts on the individuals involved (277).

11.1.8.2 Role of emotion in decision-making

Choice making has both cognitive and emotional components (277). It has been argued that emotions reduce information processing, and are particularly likely to play a role in decisions characterised by uncertainty and incomplete knowledge (460). There is also evidence that decisions are influenced by anticipation of regret, which is a negative, cognitively-based emotion experienced when realizing or imagining that the present situation would have been better had we decided differently (461). In general people are regret-averse and in many cases this results in risk-averse choices (277). However, a number of studies suggest that people's ability to predict future emotional states, including regret, is often poor (277). The 'risk-as-feelings' hypothesis proposes that rather than a purely cognitive assessment, risk preferences are the result of emotional attitudes (such as fear) towards risk (291). This emotional response is affected by factors such as the vividness with which the outcome is described or imagined by the decision-maker and the time interval to the realisation of that outcome, which in turn impacts on the probability weighting given by the decision-maker to the various outcomes (291). Thus an individuals' emotional reactions to risk will differ from their cognitive evaluations of those risks, and be affected by factors such as vividness, mood, and time to outcome (291), and so will differ between individuals and over time.

11.1.8.3 Self-other differences in decision-making

Recent research has examined proxy decision-making to explore why decisions made for other people are different to those we make for ourselves, in particular the self-other differences in risk preference (290). This is said to support the risk-as-feelings hypothesis, as decisions we make for strangers are less affected by our perception of risk than those we make for ourselves or our friends (290). However, this and other theoretical models of

decision-making do not yet properly explain or take account of decision-making in close relationships (277), such as between the proxies included in the DECISION Study and those they represented.

Researchers argue that dyadic decision-making, which occurs in the context of a pre-existing, close relationship, is distinctly different to other 'configurations' of decision-making (277), and decision-making may of course involve more than two people. The relationship quality determines the kind of decision-making process used, where the relationship between the decision-makers is not only something that has to be taken account of within the decision-making processes, but also impacts on the way decisions are achieved (462). Dyadic decision-making involves implicit understandings, limited discussion, abbreviated comments, mental shortcuts in thinking, and brief conversations to reach a quick decision rather than a long deliberation (463). This may be due to the reduced psychological distance between the two parties which means that the recipient's experience of the outcome is more likely to be taken into account by the proxy (129), or that the relative empathy gap between them is small, meaning that there is greater emotional involvement in the decision process compared to those who are not in close relationships (131).

11.2 Methods

A *de novo* decision support intervention was developed for family members acting in the role of proxy, which would supplement the study-specific information contained in the Participant Information Sheet (PIS). An iterative approach to development of the decision support intervention was used. The purpose, structure, and content of this decision aid was informed by a wide range of resources, drawing on the findings from the previous theoretical and empirical work reported in previous chapters which underpinned this intervention development. The development process followed a number of established development frameworks described below, including a framework for the development and evaluation of decision aids for people considering taking part in a clinical trial (464). This framework proposed five steps, comprised of selecting an underpinning theoretical approach to the development process, developing the decision aid, assessing and testing feasibility, evaluating the decision aid, and implementing the decision aid in practice (464). The first of these steps relating to the development of the intervention are described here. The

development process also adopted methods found to be effective regarding the development of the format of other DAs (437).

11.2.1 Decision support theoretical framework

The Ottawa Decisional Support Framework (ODSF) is an evidence-based, practical, mid-range theory for guiding patients making health or social decisions and to address the uncertainty or decisional conflict that may be encountered when making choices (421). This theoretical framework consists of three components: (1) decisional needs; (2) decisional support; and (3) decisional quality. The ODSF has been used to develop decision aids for a variety of dementia-related decisions, such as respite service choices by carers of people with dementia (465), and feeding options in end-stage dementia (466). The ODSF asserts that decisional needs affect decisional quality, such as making informed and values-based choices, which in turn affect action, behaviour, and emotions such as regret (421). The development of this intervention was based on the DECISION Study findings (reported in Chapter 6), which explored proxies' decisional needs.

11.2.2 Decision support quality criteria framework

The International Patient Decision Aids Standards (IPDAS) Collaboration was established to develop an international consensus-based framework of quality criteria for patient decision aids to be used by developers and users (467). This evidence-informed framework provides a set of criteria which aims to improve decision aid content, development, implementation, and evaluation (467). Alongside ongoing development and refining of the IPDAS checklist, a 44-item minimum standards version has been developed that is designed to rate the quality of the development process and decision-making design elements (425). Relevant dimensions and items from IPDAS and IPDASi 3.0 (**Appendix 11. International Patient Decision Aid Standards instrument**) were used to inform the development of this decision support intervention. Checklist items considered not relevant, and hence excluded from the development process, included: information relating to the condition or problem and associated probabilities as this would be included in the study specific PIS, and information related to screening or tests as this was not applicable.

11.2.3 Values clarification methods

IPDAS guidelines for the development of patient DAs recommend that they include a process for helping people clarify their values (467). The recommendations are based on the belief that, by clarifying individuals' values, the medical treatment they receive will be more reflective of their personal preferences and goals, although this has been widely debated (468). These processes, usually termed values clarification methods (VCM), are defined as strategies intended to help individuals to evaluate the desirability of options or attributes of options within a specific decision context in order to identify which option they prefer (468). VCMs can be implicit and non-interactive (e.g., the individual thinks about what is important to their decision), or explicit and interactive (e.g., using a rating scale for each attribute to reflect the importance of each to their decision) which is much more widely studied (468). VCMs are theoretically informed, and should aim to facilitate, either explicitly or implicitly, at least one or more decision-making processes: 1) identifying options, 2) identifying attributes of the situation and/or the options which affect the individual's preference in a specific decision context, 3) reasoning about options or attributes of options, 4) integrating attributes of options, 5) making holistic comparisons, 6) helping decision makers retrieve relevant values from long-term memory (468).

Whilst DAs have been found to be effective in reducing decisional conflict and increasing knowledge, the effect of specific strategies such as VCMs is less clear (469). As outlined earlier in the discussion of selected decision-making theories, deliberation may not always be beneficial for decision-making as it may overshadow important intuitive feelings that are more difficult to formulate but may be just as important in decision-making (418). However, the use of VCMs in decision aids is now widespread, with 57.1% of DAs in a recent systematic review including explicit methods to clarify values (416).

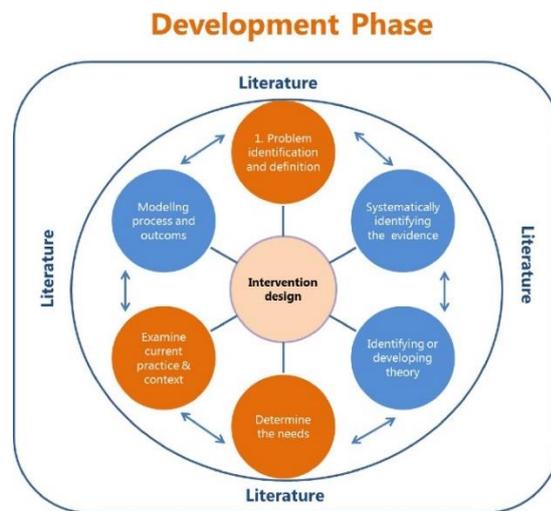
A number of process theory-based design recommendations have been made, which include that that VCMs should: help optimize mental representations; encourage consideration of all potentially appropriate options and their attributes; delay selection of an initially favoured option; encourage the consideration of relevant values; facilitate the comparison of options and their attributes; and offer time to decide (470). A systematic review of the design features of explicit VCMs, such as the use of visual metaphors, found a diverse array of VCMs are in use, and it is not known whether a given VCM might be equally effective for different decisions (471). The authors did not recommend the use of any particular design features,

but suggested that developers of VCMs should carefully consider each of the design features in their taxonomy and publish adequate descriptions of their designs (471).

11.2.4 Complex intervention development frameworks

To successfully develop a complex intervention, it needs to have a strong evidence and theoretical base and be developed using a comprehensive iterative intervention development approach (472). A number of frameworks and guidance are available for the development of interventions, including the MRC Developing and evaluating complex interventions (414), Intervention Mapping (473), and the PRECEDE–PROCEED model (446). However, these tend to be orientated towards behaviour change in individuals, and either provide little specific detail on intervention development or require great technical skills, time and resources (448) or not specify how to select and apply theory or a model of behaviour (474). The MRC framework describes an iterative process of development, feasibility/piloting, evaluation, and implementation of interventions (414) but has limited guidance for the development phase itself. Recently, a model (6Squid) has been developed which describes how the process of designing an intervention can be broken down into six crucial steps: (1) defining and understanding the problem and its causes; (2) identifying which causal or contextual factors are modifiable: which have the greatest scope for change and who would benefit most; (3) deciding on the mechanisms of change; (4) clarifying how these will be delivered; (5) testing and adapting the intervention; and (6) collecting sufficient evidence of effectiveness to proceed to a rigorous evaluation (448). Whilst the process is described in six steps, in practice it is non-linear and collaborative. This, the authors suggest, is a more resource-light systematic approach to intervention development as well as rigorous evaluation (448). Researchers have also proposed adopting a comprehensive approach to intervention development through combining the elements of the development phase of the MRC Framework (414) with elements of existing development models such as 6Squid to enhance the intervention design (**Figure 11-3 Adapted MRC Framework development phase** (from Bleijenberg et al 2018))(472).

Figure 11-3 Adapted MRC Framework development phase



*Blue elements are from the original MRC Framework (414)

This ‘enriching’ approach to the development phase (472) has been adopted for developing this decision support intervention. This has been through conducting empirical research described in previous chapters to identify the problem, determine needs, and examine current practice and context, and supported by revisiting to the literature throughout the iterative development processes. The steps of the 6Squid approach conducted as part of this doctoral project, and therefore reported in this chapter, are steps 1 – 5. Although considered an iterative process, the methods used in the five steps are shown in **Table 11-1 Six steps in development of the decision aid intervention** and are described in more detail below.

Table 11-1 Six steps in development of the decision aid intervention

Step in intervention development	Method used
1) Define and understand the problem and its causes	Systematic review, content analysis, qualitative data, survey data
2) Clarify which causal or contextual factors are malleable	Logic model
3) Identify the change mechanism	Qualitative data
4) Identify how to deliver the change mechanism	Qualitative data, review of current DAs
5) Test and refine on small scale	Review by PPI and stakeholder groups
6) Collect sufficient evidence of effectiveness to justify rigorous evaluation/implementation	*Does not form part of this thesis*

11.2.5 Defining and understanding the problem and its causes

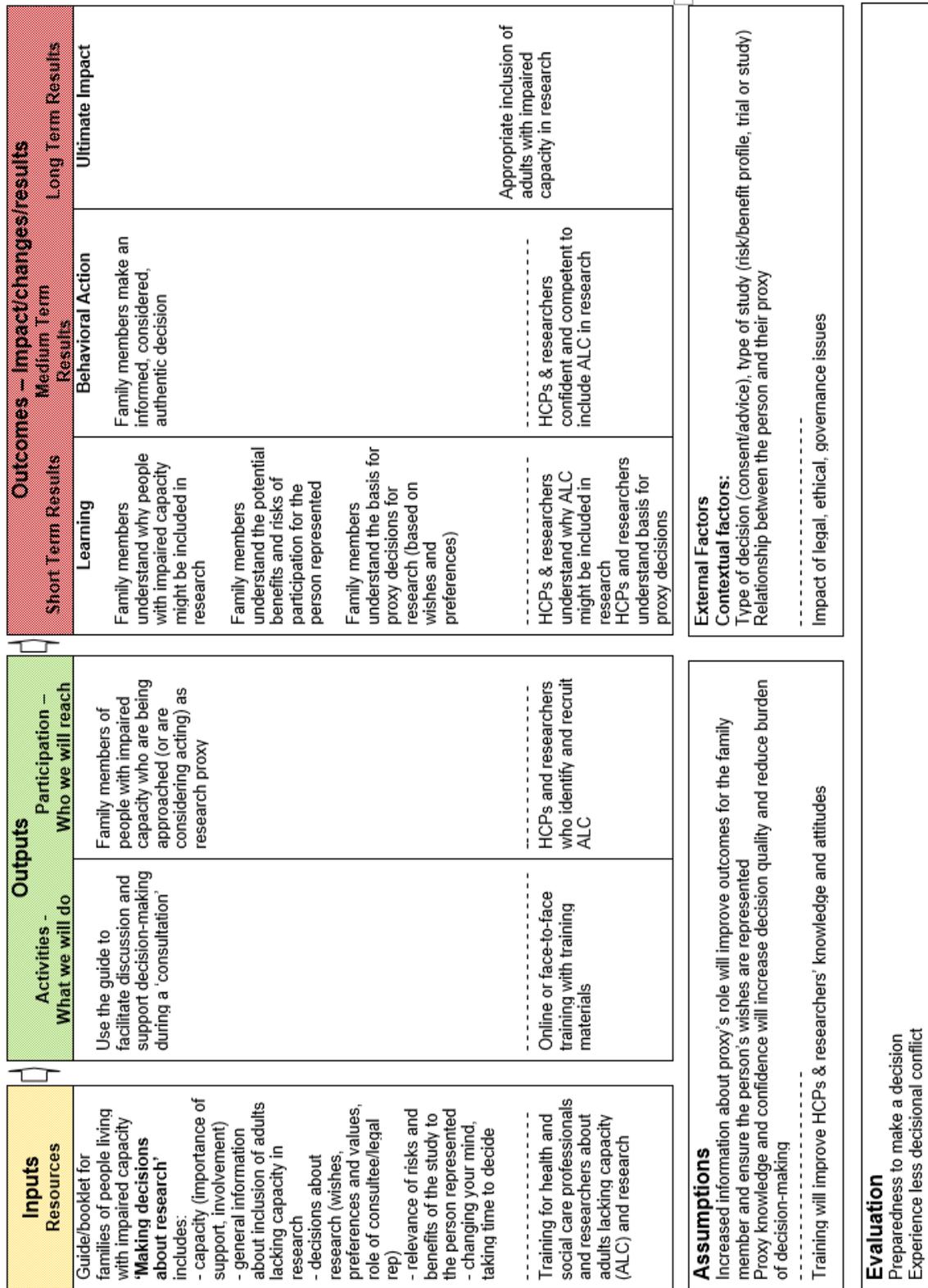
Clarifying the problem using the existing research evidence and in consultation with stakeholders is the first step in intervention development (448). As described in Chapter 3, a systematic review was conducted to synthesise the existing empirical evidence. This, together with the content analysis of information already provided to proxies reported in Chapter 5, indicated that proxies are generally well provided with information about the study itself, but are not well informed about their role as proxy decision-maker. The qualitative interviews reported in Chapters 6 and 7 described the complexity of proxy decisions, and the burden that can be experienced as a result. The survey data reported in Chapter 4 suggested that healthcare professionals, social care practitioners, and researchers also have a lack of understanding about proxies' roles, which may impact on how they approach and support proxies acting as consultees and legal representatives. The 'problem' can therefore be defined as proxies having insufficient knowledge and understanding about their role and experiencing decisional and emotional burden when making decisions about research. As the majority of the participants were proxies of someone living with dementia, the intervention was developed with this population as its focus, although there is no reason

to suggest it would not be appropriate for proxies of people with other conditions associated with cognitive impairment.

11.2.6 Logic model development

In order to clarify which causal or contextual factors might have the greatest scope for change, a logic model was developed (448). As described above, theory-based approaches can provide additional insights in intervention development, and logic models are an important tool for implementing a theory-based approach (475). A logic model has been described as a graphic description of a system designed to identify important elements and relationships within that system, and includes a graphical summary of the pathways from the intervention (or individual intervention components) to anticipated outcomes (475). Logic models can help in areas of complexity by depicting intervention components and the relationships between them, making underlying theories of change and assumptions explicit, and displaying interactions between the intervention and the system within which it is to be implemented (476). Different types of model and approaches to logic modelling have been identified (475). For this intervention an iterative logic model approach was used, in which an initial logic model is created which is not expected to map all elements and possible causal links, but instead is viewed as organic and subject to adaptation and modification as new insights emerge and as needs and demands change (476). The logic model developed (**Figure 11-4 Logic model for proxy decision support intervention**), although not considered to be comprehensive, forms the starting point for developing this *de novo* intervention.

Figure 11-4 Logic model for proxy decision support intervention



11.2.7 Incorporating findings from the qualitative data

Qualitative research which explores the lived experiences of decision-makers can be used to inform the development of effective decision support interventions (2). The qualitative findings presented in Chapter 6 showed that proxy decisions about research participation are complex and highly contextually dependent. The further Grounded Theory analysis reported in Chapter 7 showed that proxies attempt to integrate the person's own preferences and values when making a decision that they hope will best for them. The advantages and disadvantages of participating in the study (or not) were considered in the light of the person's previous biographical life, and within their current circumstances. Proxies sought to make a decision that was authentic to the person they represented. Proxies also reported the emotional burden of both caring for someone and 'running their lives' on their behalf. Decisions, including those about research, were problematic for some who experienced decisional burden as a result. Proxies identified that support when making decisions about research may be helpful for some, and that this could include information about their role, which orientated the proxy towards considering what the person themselves would want. Some expressed the view that this could take the form of an additional information sheet.

The importance of including additional information about involving the person themselves in the decision as much as possible, the relevance of any Lasting Power of Attorney arrangements, and clarifying their role as either consultee providing advice or a legal representative providing informed consent arose from a combination of the empirical research and literature reviews conducted as part of the project.

11.2.8 Review of existing decision support aids in dementia and consent

As this intervention is the first of its kind, existing interventions in two areas were reviewed: informed consent for people (with capacity) considering clinical trials, and interventions for various areas of decision-making by proxies of people living with dementia. This decision support intervention can be seen as occupying the crossover area between these two.

11.2.8.1 Decision aids for proxies of people living with dementia

Decision aids for proxy decision-makers are relatively uncommon, with a systematic review published in 2015 finding only three studies, which described interventions that sought to improve decision-making [81]. One DA that was particularly aimed at carers of people with decreased decisional capacity was developed to assist carers to make evaluative judgements about community services, particularly respite care (465). It recognised that carers need access to realistic, contextually relevant information in order to make decisions and may need support to weigh up available options, and so concluded that carers of people with dementia are a suitable group for targeted DAs (465). A workbook (the GOLD Book) format was selected as it was anticipated that paper-based approaches were more accessible for the target group of older community dwelling carers (465). A pilot study found that the intervention group had less increase in burden, a decrease in decisional conflict and increased knowledge compared to control group participants (465). Another trial piloted a palliative care assessment and Advanced Care Planning (ACP) discussion intervention with carers of people with severe dementia in hospital (477). This was a two-component intervention: 1) assessment of the palliative care needs of patients; and 2) a framework for the discussion of advance care planning with carers which was recorded in a standardised format (477). There were challenges around recruitment to the pilot trial, and the intervention proved problematic to implement (477). A third study evaluated the use of an audio booklet decision aid (Making Choices: long-term tube feeding placement in elderly patients) for decisions about long-term feeding for hospitalised people with dementia (478). The small scale before-and-after study found that the DA decreased decisional conflict and promoted decisions that were informed and consistent with personal values (478).

Additionally, a small number of DAs for use to support decisions concerning people living with dementia have been developed. A decision aid for drivers with dementia has been developed to aid decisions about retiring from driving. It was developed using the ODSF and IPDAS frameworks and aims to meet the decisional needs of drivers with dementia by providing them with adequate support so as to enhance the quality of their decision-making process (437). They presented the DA in booklet format which consisted of four key steps: 1) clarification of decision and values; 2) decisional needs and support; 3) considering the options; and 4) advising others of one's decision (437). Pilot testing showed that the DA improved knowledge, and was an acceptable and useful tool (437). One decision aid to reduce levels of carers' decisional conflict when deciding whether their relative with

dementia can continue to be cared for in their own home has been developed, although it is intended as a shared decision-making intervention (435). Similarly, to the development of this DA, it was based on qualitative interviews, although this was with people living with dementia in addition to their carers (435). A recent feasibility study of the intervention showed that it was acceptable, useful, and family carers who received the intervention reported less decisional conflict, compared with the control group (435). This DA is in the format of a manual that participants read and complete with the support of a 'decision coach' (435). Other DAs are in the very early stages of development, such as a decision aid to help care home residents with dementia and their family caregivers regarding decisions about the initiation of antipsychotic medications (424). However, it has been suggested that providing proxies with information to make decisions which have not previously been considered may increase feelings of conflict, suggesting decision aids should be carefully targeted (479).

11.2.8.2 Decision aids for informed consent for clinical trials

A 2015 Cochrane review of decision aids for people considering taking part in clinical trials found only one study that investigated the effectiveness of decision aids, compared to standard information, in the informed consent process (43). The study reported on two separate DA randomised controlled trials (RCTs) nested within two breast cancer trials and found that the paper-based DAs led to lower levels of decisional regret to a small degree, although it was considered low quality evidence (43). The review authors concluded that there was insufficient evidence to determine whether decision aids that support the informed consent process for clinical trials are more effective than standard information (43). Although DAs for proxy decision-makers for adults who were unable to consent for themselves were included in the searches, no DAs for proxies were identified.

Since the Cochrane review, a further randomised trial of a web-based DA (CHOICES) versus usual care (the cancer centre's website) examined whether the DA improved decision-making about cancer clinical trial participation (480). The trial found improvements in decision outcomes including knowledge, self-efficacy, certainty about choice, and values clarity among, and concluded that web-based DAs can support informed decisions about trial participation among cancer patients facing this preference-sensitive choice (480). A subsequent RCT which modified the same web-based DA for rural populations (R-CHOICES) had mixed results, and most (13/31; 41.9%) participants chose to alternatively complete the

study procedures via a paper-based modality (481). A DA concerning participation in a prostate cancer trial (RAVES) has been developed in accordance with IPDAS with content based on a literature review and consultation with experts (432). The RCT which evaluated this paper-based booklet DA found reduced decisional conflict and improved trial knowledge in the intervention arm (432).

The number of trials evaluating DAs for informed consent are small and a number of methodological issues limit the usefulness of the evidence generated. In particular, the populations, DA modality and content, intervention delivery methods, and outcome measures are too heterogeneous to draw any meaningful conclusions. However, it is encouraging that some measurable effects have been observed, and that methods of intervention development and implementation have been shown to be feasible. DAs, particularly in paper-format, have been generally found to be acceptable to people making decisions about clinical trial participation. Important limitations for this project are that these were all decisions about clinical trials and did not include other types of research study, and that of course these are potential participants making decisions for themselves – decisions made on behalf of someone else are materially different.

11.2.8.3 Summary of review of relevant decision aids

In summary, the number of DAs for proxies making decisions on behalf of a person with reduced capacity are small, and the number of DAs for people considering participation in a clinical trial are also small. No DAs have been identified which include both areas of decision-making (i.e. proxy decisions about research participation). DAs for research proxies are an uncharted territory that is being explored for the first time in this doctoral project.

However, there are important messages from the review of the DAs that have already been developed and evaluated to some extent. Understanding and taking account of the context it is to be developed within is key (439). Embedding the DA within much broader communication strategies and ensuring that both the mode and content is acceptable and feasible for the populations concerned are essential elements of intervention development.

11.2.9 Collaborative development with stakeholders

Consultation with relevant stakeholders is an important step in the intervention development process (448). This doctoral project has benefitted enormously from having the

support of a lay advisory panel from the first drafting of the research questions, through to the development of the intervention itself. Their lived expertise as carers, family members, and advocates of people with a range of cognitive impairments has made a significant contribution to the project as a whole, and particularly during the development of the decision intervention. The lay advisory group, also known as a Public and Patient Involvement (PPI) group attended a discussion meeting to review the first draft of the decision aid, broadly following a cognitive debriefing approach to instrument development which can identify difficult or confusing areas of the item being reviewed and propose a better version (482). The aim is also to identify whether the interpretation of an item differed between those reviewing it (482).

Additionally, a larger group of stakeholders was consulted to gain a broader perspective from a range of those who have experience as either researchers who involve people who lack capacity in their research, family members who may be approached to act as a proxy, and those familiar with supporting family members of people with dementia. The importance of the involvement of practitioners and other stakeholders in developing and prototyping interventions, to ensure that they can be adopted, implemented and maintained in the contexts for which they are intended, is emphasised in many of the frameworks guiding intervention development (439,448). Their role is important throughout the process, but particularly when determining the content, format, and delivery of the intervention (448). The stakeholders were consulted through a discussion and feedback half-day event at which they were provided with the prototype DA. This followed on from the lay advisory review, after which the DA had undergone some amendments and had been professionally illustrated by a graphic design company. A short acceptability questionnaire adapted from a previously developed acceptability tool (483) was completed by participants (**Appendix 12. Acceptability tool for stakeholder feedback on the decision aid**) and facilitated small discussion groups enabled participants' views to be explored in greater detail (**Appendix 13. Prompts for stakeholder discussions on acceptability of the decision aid**).

11.3 Results

A DA was developed to support family members acting as research proxy to supplement the study-specific information and support informed decision-making (**Appendix 14. Decision aid for family members acting as research proxy**). The content was largely informed by

existing DAs for clinical trial participation and the format largely influenced by existing DAs for both clinical trials and decision-making around issues relating to dementia. Both content and format were developed in conjunction with decision support frameworks and complex intervention frameworks as previously described.

11.3.1 Content of decision aid

The content was developed in accordance with IPDASi (v4.0) (425). This requires the DA to contain information about: the choices available and probabilities associated with each option (contained in the accompanying Participant Information Sheet in this case); relevant values and which positive and negative features of the options matter most to them (or the person they represent in this case) either implicitly or explicitly; step by step guidance to make a decision; and tools like worksheets or lists of questions (425).

The content was informed by the qualitative interviews reported in Chapter 6, during which participants suggested that the DA should include items that they considered would support proxies when making decisions about research (**Table 11-2 Items for inclusion in decision aid from the qualitative interview findings**).

Table 11-2 Items for inclusion in decision aid from the qualitative interview findings

1. Why people with cognitive impairment are included in research
2. That the proxy's decision or advice should be based on what the person's wishes and feelings about taking part would be if they had capacity to decide
3. That the proxy should consider if there is any reason why the person would not have wanted to participate
4. The relevant advantages and disadvantages and how they relate to the person themselves
5. That the person should be involved in the decision as much as possible
6. That the proxy can take time to decide and they can always change their mind

The content was presented in the order used in other examples of DAs for decisions about clinical trials (431,434). This presented information about the positive and negative features of taking part in the trial, followed by structured guidance in deliberation or 'making a

decision’ that was adapted from existing clinical trial DAs (431,434). The suggested decision-making process was through the six steps detailed in **Table 11-3 Six stage decision-making process** (adapted from Juraskova et al 2008)(484).

Table 11-3 Six stage decision-making process

1. Understand the purpose of the study and what is involved as fully as you can
2. Understand how the study relates to any other options for their treatment or care
3. Review the advantages and disadvantages of taking part (and not taking part)
4. Assess how important the advantages and disadvantages are to the person you represent
5. Prioritise the advantages and disadvantages of the study for the person you represent
6. Get more information or clarification about any uncertain areas

This was then followed by an exercise as part of utilising values clarification methods (VCM) which enabled proxies to trade-off positive and negative features of the decision to facilitate decision-making that was personal and meaningful for the person being represented.

11.3.2 Impact of the ‘new’ understandings of proxy decision-making

Developments in the conception of proxy decision-making that have been outlined throughout this thesis have informed the DA. In terms of their role, the DA does not suggest that the proxy should (or can) accurately report what the person they represent would have decided, and that there is no ‘right’ or ‘wrong’ answer. Alternatively, the DA encourages the proxy to reflect on what they know about the person and their wishes and preferences within the context of the particular study in question, thus seeking a decision that is authentic to the person’s values as described in earlier chapters. The values clarification exercise enables the proxy to consider the potential advantages and disadvantages of the study to be considered, thus facilitating the process of integrating the persons’ preferences and interests identified in the ethical framework of proxy decision-making in Chapter 7. The DA is compliant with both the Mental Capacity Act (20) and Clinical Trial Regulations (22). The empirical evidence presented in this thesis has enabled a fuller and more nuanced

understanding of proxy decision-making, whilst remaining within the requirements of the relevant legal frameworks regarding who is eligible to act as a personal consultee or legal representative, their role in consultation or consent provision, and the legal basis for their decision.

References are made to the relevance of any LPA, and that the basis for their decision will be different depending on the type of research study. The emotional and decisional burdens that may be experienced by proxies are addressed through providing reassurance; including that there may be remaining uncertainty even when using the DA. The proxy is reminded that they are not making a decision for themselves but to think about what the person they represent would want. Whilst this perhaps over-simplifies the complexity of the understanding of proxy decision-making as laid out in this thesis, it is a pragmatic approach based on empirically derived knowledge about the problems encountered by proxies when attempting to conceptualise proxy decision-making during the qualitative interviews.

11.3.3 Format of the decision aid

The DA was presented as a 12-page A5 paper booklet, which could be printed or read as a PDF document. The prototype DA was enhanced by a graphic designer to improve the accessibility and visual impact of the tool. A range of strategies was used to enhance reader understanding of the DA. Information was presented clearly and concisely using colour-coded sections to navigate the booklet. A Flesch Reading Ease score of 69.9 (fairly easy to read) was achieved and a Flesch-Kincaid Grade Level suggested that most 8th grade students would be capable of reading the booklet. Space, with prompts, was provided for notes and questions at various points in the booklet, and a space for additional questions was provided at the end of the booklet.

The original choice of visual metaphor for the VCM was a weighing scale, in line with existing DAs for clinical trials (431,434). However, the VCM graphic was the area of the DA that most divided the opinions of the lay advisory group, where some members found the visual metaphor as the most valuable part of the DA and others strongly disliked the format. As there is a diverse array of VCMs in use, and the effectiveness of any given VCM is unknown (471), the metaphor was changed to an image that represented both direction and strength of response. There was also a difference of opinion around the use of example narratives to illustrate the range of possible scenarios, however it was felt that these may be unduly

persuasive or, as the intervention may be used in a wide range of decision contexts, proxies may not identify with the scenarios.

11.3.4 Additional components of the intervention

In addition to the need for decision support for proxies arising from the qualitative interviews, the data from the survey and content analysis in Chapters 4 and 5 indicated that there were additional researcher/clinician informational needs that needed to be addressed. For the purposes of this intervention, it suggested that an additional component was required to provide information about the legal frameworks to those who would be delivering the intervention (see **Figure 11-4 Logic model for proxy decision support intervention**). This is in the form of the summary of the legislation governing proxy consent for research participation by adults lacking capacity in the UK, which was provided to participants in the survey described in Chapter 4 following their participation (**Appendix 8. Legal summary of research involving adults who lack capacity**). A short one-page guide to the key messages of the decision support booklet was also developed as part of the intervention (**Appendix 15. Key messages for using decision support intervention**).

11.3.5 Establishing acceptability of the decision aid

Acceptability of an intervention has been defined as ‘a multi-faceted construct that reflects the extent to which people delivering or receiving a healthcare intervention consider it to be appropriate, based on anticipated or experienced cognitive and emotional responses to the intervention’ (p.4)(485), and can be considered to have both cognitive and affective components (486). In order to establish the acceptability of the decision support tool, a stakeholder group was convened. This stage forms the ‘alpha’ testing of the intervention which is described as an iterative process of testing by people directly involved in the development process, and considered to be a necessary part of the development of decision aids (487). The stakeholder group provided an opportunity to consult both those who represent the population who would receive the intervention and those who would be implementers. A discussion and feedback event was also organised which was led together with a co-facilitator and involved nine participants. Six participants were researchers or research nurses in a range of fields including dementia, stroke, and Multiple Sclerosis; two had experience of caring for a family member living with dementia; and one considered themselves to have prior experience as both a researcher and family carer.

The acceptability questionnaire showed that almost all participants felt that the decision support tool was the right length (89%, 8/9) and contained the right amount of information (78%, 7/9), and all participants thought that it would be useful. Open-text responses showed that participants liked the simplicity of the language used and the presentation and 'flow' of the information. The colour-coding of sections was thought to be particularly helpful, although different colour combinations were suggested that participants thought would increase the contrast and therefore the readability of the text. The 'people' illustrations were generally well received although the lack of diversity in the ethnicity and age of the characters was widely commented on.

The discussion groups revealed that participants viewed the format of the decision support tool as good, and participants were universally in favour of it being used within the context of a 'consultation' between the researcher and the family member(s) and as a supplement to the Participant Information Sheet. It was thought to be both applicable and useful in a wide range of contexts beyond families of people living with dementia, including in emergency or critical care settings requiring deferred consent or a waiver where family members are approached once the emergency has passed to decide about the continued participation of a patient who lacks capacity. Participants felt that the information contained in the tool was well balanced about participation or non-participation and the potential advantages and disadvantages. They felt that rather than persuading families, it would empower them to make an informed decision. Participants recognised that the extra time burden or information burden for family members could act as a barrier but felt that this was offset with the importance of making informed decisions about the inclusion of those who lack capacity. Suggestions for ways of overcoming these barriers or increasing the usefulness of the tool included having an additional online version of the tool, embedding it in dementia 'pathway' information provided to people living with dementia and their families, and increasing awareness of the topic and the decision support tool through including them in existing training for researchers and healthcare professionals such as during Good Clinical Practice training.

11.4 Discussion

Decision-making incorporates both deliberative and intuitive components; it is influenced by perceptions of risk and risk avoidance, and subject to a number of biases and heuristics.

Decision-making on behalf of another is even more complex and is affected by the psychological and emotional distance between the parties involved. Preference sensitive decisions are those based on matching the option to the person's values and views about the benefits, harms, and uncertainties. Decision support interventions are intended to lead to decisions, which are informed and consistent with the person's values. This chapter has described the uses of decision support tools in healthcare decisions, explored the theoretical insights into how decisions are made on behalf of another person, and what factors might influence dyadic decision-making. Relevant decision support tools have been reviewed, and the theoretically informed process of developing a new decision support tool for research proxies.

A taxonomy of approaches to developing interventions, programmes or innovations to improve health has been published (488). The approach used for developing this intervention was that described as a combination approach, which is developed through a systematic approach using evidence and theory whilst paying attention to its use in real world settings (488). The prototype decision support booklet was also developed in conjunction with stakeholder groups representing both those who would receive the intervention and those who would be implementers. Work to explore the acceptability of the intervention has indicated that both the content and the format is acceptable. However, considerable further work is needed to establish whether the intervention is feasible in practice, before a trial to determine whether it is effective could be planned and conducted. This may include qualitative work, potentially embedded within a small feasibility study, and an exploration of appropriate outcome measures. As the DECISION Study mainly involved family members of someone living with dementia, further work to establish the transferability of the intervention to other populations experiencing impaired capacity may be required.

11.4.1 Outcome measures

The appropriate outcomes (and for whom) that should be assessed in any future trials of interventions to improve decision-making in this context requires further work (489). As this is a novel intervention there are no existing outcome sets on which to draw, and so alternative methods of identifying appropriate outcomes and generating an outcome set is needed. This may include considering validated measures used in other relevant decision support tools, such as: knowledge, decisional conflict, satisfaction with the decision-making process, values congruence, anxiety, decision regret, and trial specific measures such as

recruitment and retention (43). A review of patient-reported measures for informed consent for clinical trials found considerable heterogeneity across outcome measures, with 179 individual items found across 14 instruments, the majority of which assessed understanding (490). The authors note that, whilst understanding of information is an important component of informed consent for clinical trials, other important aspects of decision-making such as preference construction and integration of information with personal values and goals is often not measured (490). They recommend that interventions take a more holistic approach to informed consent by going beyond merely seeking to improve understanding, to consider other important aspects of the decision-making process (490).

It is important to note that measuring and evaluating the effectiveness of interventions to improve decisions is inevitably linked with the concept of what makes decisions 'good'. There are concerns that using outcomes to measure the quality of decision-making fails to make a clear distinction between the process of deliberation and the step of determining a decision, or between the decision-making process and the decision itself (430). Alternatively, attempting to define and evaluate what is considered a good decision-making *process* will help inform the development of interventions which typically address factors that influence the decision determination phase (430). This is particularly relevant with decisions made in the context being examined here, where measures such as values congruence have the additional challenge that it is the proxy's representation of the person's values against which congruence is being measured, which cannot be independently verified. Unlike decisions about trial participation made for oneself, additional considerations (see Chapter 2) include that what is valued about proxy decisions is not just the outcome that is chosen but how it was chosen and by whom.

11.5 Summary

Decision support has received considerable attention over the previous decade for preference sensitive decisions, and a number of tools have been developed to support a wide range of areas of decision-making. Recent years have seen an interest in the use of decision support tools for informed consent for clinical trials. There has also been a growing recognition that decisions made on behalf of others, such as people living with dementia, can be problematic, which has led to the development of decision-specific support tools. However, no previous interventions have been developed for decisions about research

participation made on behalf of someone who has impaired decision-making capacity. The development of the first such intervention, which is both theoretically and empirically informed and collaboratively developed, has been described here. The supplemental decision support intervention is designed to sit within the context of a socio-ecological model of proxy decision-making and is attentive to the dyadic relationship within which family members make proxy decisions. Considerable further work is needed to establish the feasibility of this intervention, and to identify appropriate outcome measures. However, it is a first step towards supporting family members who are approached to act as consultee or legal representative and who may find proxy decision-making challenging and burdensome.

11.6 Learning points

Existing decision aids have been developed for decisions about participating in clinical trials, and for specific decisions relating to the care of people living with dementia. However, currently there is no support available for family members making decisions about research on behalf of a family member who lacks capacity to provide consent.

A socio-ecological model of decision-making for research participation was developed which provides an understanding about the context within which proxy decisions are made. Empirical evidence and theoretical frameworks were used to develop a *de novo* decision support aid for family members acting as proxies.

The decision support booklet was designed to be accessible and included values clarification methods to support the proxy through the decision-making process. A collaborative approach was used to develop the intervention, and to explore the acceptability with a broad range of stakeholders.

Further work is needed to establish the feasibility of the intervention, and to determine appropriate outcome measures, prior to evaluating the effectiveness of the intervention.

Chapter 12 Discussion

12.1 Summary and interpretation of findings

The aim of this thesis was to explore the normative, empirical and legal accounts of proxy decision-making for research involving adults who lack capacity to consent, present the beginnings of an account that is grounded both empirically and theoretically, and describe the development of a novel decision support intervention. Returning to the overarching organising framework of the thesis, this interdisciplinary project has involved: an exploration of the *Lay of the land* of the core issues of proxy decision-making through a range of perspectives and the contexts within which proxy decisions occur (Chapters 2 to 7); investigation into how real world proxy decisions are made in comparison to the ethical and legal 'ideals' through examining *Ideal versus reality* (Chapter 8); identifying potential areas that may prove amenable in terms of *Changing Ethical Norms* (Chapter 9) and *Recommendations for Amending the Legal Frameworks* (Chapter 10); and it concluded with the development of a complex intervention to support *Improving Decision-making* (Chapter 11). The findings, and their interpretation in terms of a theoretical understanding of proxy decision-making and decision-making in practice, are summarised below.

The literature review in **Chapter 2** identified a number of theoretical and practical problems arising from the tripartite bioethical hierarchy of known wishes, substituted judgement and best interests with respect to proxy decisions about research. The most problematic area was the standard interpretation of substituted judgement, which has been described as dangerous legal fiction (87), where the proxy is required to undertake a near impossible task. These, and other problems around the stability of preferences and representation of others, have led to calls for an alternative interpretation or even an different standard (60). Proposed alternative interpretations of substituted judgement or alternative models of proxy decision-making were reviewed, and the 'ingredients' of a new approach presented. The chapter concluded by identifying the need to focus on a person-centred approach that takes account of the context of the decision; with the proxy-patient relationship being both the key that allows proxies to make decisions on behalf of another, and the tool to provide an answer.

The empirical data included in the systematic review reported in **Chapter 3** captured the complexity and contextual nature of proxy decision-making, where the findings did not reflect the reductionist account described in the normative bioethical sequential hierarchy of known wishes, substituted judgement, and best interests (21), and endorsed in legal and ethical codes. Patients and members of the public did not support a wholly substituted judgement approach but wanted proxies to consider their own interests and those of family members, or perhaps to make a decision following consultation with others. The studies suggested that the relationship between the patient and the proxy has a fundamental role, where their relationship is the reason the proxy is chosen, and also enables the decision-making process through their knowledge of the person. An empirically informed framework for proxy decision-making for research was presented which takes account of the contextual use of substituted judgement and best interests approaches, and the balancing of the active elements in the decision-making identified in this systematic review.

Chapter 4 reported a survey of a range of health professionals and social care practitioners, which explored their levels of understanding and knowledge about the relevant legal frameworks. The vast majority of participants did not recognise that the basis for enrolling an adult who lacks capacity in research is what the person themselves would have wanted if they had capacity to decide, but believed that it was based on whether participating was in the person's 'best interests'. Participants failed to understand that the locus of authority lies not with the multi-disciplinary team, but with those best placed to advise what the person's wishes would have been, usually a family member. The low levels of knowledge and understanding described in this study are concerning as it may impact on professionals' confidence and competence to include those in their care in research and lead to legally and ethically legitimate enrolment processes not being adhered to. The findings suggest that there is a need for interventions, including enhanced education and training, focussing on the legal frameworks governing research involving adults who lack capacity to consent. Greater clarity is also needed regarding the role of a Lasting Power of Attorney (LPA) and decisions about research as many participants reported the view that holding an LPA was needed in order for a family member to act as proxy.

Chapter 5 reported an analysis of the content of written information provided to both family members and professionals acting as consultees or legal representatives. The results found that some information sheets failed to include sufficient information to allow the proxy to understand why they were being approached and the basis on which they should make a

decision. Many information sheets contained inaccuracies both in terms of terminology and legal interpretations. Of note, was the disparity in information sheets provided to professionals compared to family members, both in terms of content and format. Information about the proxy's role should be provided to those acting as consultees and legal representative in order for them to be fully informed prior to providing advice or consent. Further guidance may be needed for researchers who draft study documents, particularly for clinical trials of medicinal products, and studies conducted in acute and critical care settings where professionals are involved as consultees or legal representatives.

In the first of the chapters presenting data from the DECISION Study, **Chapter 6** reported a thematic analysis of proxies' experiences when making decisions about research. The findings suggest that proxy decisions are complex, contextualised, and guided by proxies' hope for benefit for the person they represent whilst seeking to protect them from any further harm. The close relationship between the person and their proxy means that the potential benefits and harms of participating are seen as relational, where the concept of relationality is founded upon persons being conceived as socially embedded, and where social identities are formed and expressed through relationships. Proxies 'co-edit' the person's future in line with their life story (361) to construct an authentic decision within the context of their temporal, dyadic, trusting relationship. This approach attempts to respect the authenticity element of autonomy to create a 'life that fits' and makes sense within a framework of beliefs and values that the person affirms. Decisions are also influenced by proxies' prior experiences, their emotional attitude to risk, and perceptions about the value of the research. However, decision-making can have emotional and decisional burdens for some proxies, who may benefit from support when making decisions about research. This may be through acknowledging that decisions can be difficult, and to orientate them towards considering the person's views and preferences about participation. Although there are legal provisions for nominating an attorney to make decisions about issues relating to health and welfare, there are no provisions for prospectively nominating someone to make research decisions despite previous recommendations. Participants viewed participation in research as being intrinsically linked to the person's health and wellbeing, and so decisions about research weren't made in isolation from other areas of decision-making that a welfare attorney would be responsible for. Rather than seeing a legal divide, proxies saw decisions about research as being part of their 'holistic' role as carer for the person they represented. Proxies recognised that nominating a research proxy may provide legal clarity around who can act as decision-maker and may help facilitate discussions about someone's wishes and

preferences about future research participation in the event that they lose capacity. The results lend some support to previous recommendations that LPA provisions be extended to cover decisions about research.

As the second chapter reporting the DECISION Study data, **Chapter 7** presented an analysis using modified Grounded Theory to explore the ethical practice of proxy decision-making through 'interrogating' the conceptual framework developed in Chapter 3. The findings demonstrate the way in which proxies' attitudes and beliefs about the value of research, together with their trust relationship with the person they represent, play a fundamental role in their decision-making. Proxies make decisions that pay attention to the person's preferences and interests, whilst seeking to achieve a decision that is authentic to the person. Thus, they seek to make a decision that they consider is 'best' for the person through bringing them the most good (29), whilst making the 'right' decision that is in line with what the person would have wanted. The findings contrast with the normative accounts of proxy decision-making and the hierarchy of ethical principles identified in Chapter 2. This exploration of the ethical practice of proxy decision-making enabled the framework to be further refined to present an account that is both empirically and theoretically grounded.

Chapter 8 attempted to draw together and analyse both existing and new empirical findings and underlying principles and build on these data to inform a revised ethical conception of proxy decision-making for research participation. Triangulation methods were used to compare the three 'poles' of normative, empirical, and ethical accounts to look for areas of convergence, disjuncture, and silence as a form of analysing the 'Ideal versus Reality'. A number of key areas of divergence lie between the individualistic normative accounts of proxy decision-making and the relational nature of proxy decision-making in practice reported in the empirical data. There is significant silence in both the empirical data and normative accounts of how professionals act as proxy, which is permitted by the legal frameworks, including the appropriate ethical basis for their decision, and how they might reach such a decision based on the person's presumed will. The disparate origins of the legal frameworks are reflected in the divergent approaches to the inclusion of adults who lack capacity in clinical trials of medicines, compared to other types of research. The findings suggest that a relational approach to decision-making, which acknowledges that proxy decisions by family members occur within a dyadic relationship of care, may provide a less problematic account than those that currently exist. The development of a theory of

relational proxy decision-making, based on the forming of relationships, and which is attentive to the inherent relationality of persons, may be a promising future path.

The last three chapters presented the development of new ways forward in normative, legal, and practical accounts of proxy decision-making, which built on the previous chapters. In **Chapter 9** the role of autonomy is explored, where the primary function of informed consent is considered to be the vehicle by which respect for individual autonomy is translated into law [4], and the problematic extension of the autonomy-based consent paradigm to those with reduced or absent autonomy. The accepted view that autonomy is a complete or self-sufficient expression of respect for persons is challenged. The chapter concludes that, rather than defining persons in binary terms of capacity/incapacity and autonomous/non-autonomous, they can be considered as complex beings with emotional and relational aspects that have moral significance, where a misplaced emphasis on autonomy results in a diminished concern for a range of other moral concerns. The alternative account outlined broadens respect for persons as an 'umbrella' for other concepts such as integrity and dignity, such that the locus of the ethical basis for the inclusion of adults who lack capacity to consent to research lies within a broader conception of respect for persons.

Chapter 10 brought together the findings from the preceding chapters that relate to the current legal frameworks governing research involving adults who lack capacity in England and Wales (and the rest of the UK for clinical trials). The current legal conceptions of autonomy in research involving adults lacking capacity were explored, and the implications for the legal frameworks of a move towards respect for persons proposed in the preceding chapter were discussed. A number of recommendations for the development of the legal frameworks in England and Wales, including areas requiring clarification and guidance, were made. These included the need for clarification of the role of LPA in decisions about research; addressing the widespread misapplication of the 'best interests' principle to research decisions; the need for clarification regarding the application of ADRT to research participation; and the need for further guidance regarding the role of professionals acting as proxy.

Having examined the ethical and legal basis for proxy decisions, and explored how proxies actually make decisions, it is important to then address how to enable and support proxies to make 'good' decisions (364). **Chapter 11** sought to address the burden of proxy decision-making identified in Chapter 6 through the development of a decision support tool.

Theoretical frameworks of decision-making were explored, together with complex intervention development methods and decision aid development frameworks. A socio-ecological model of proxy decision-making was presented which helps situate the decision support tool within the wider context and systems within which it would operate. Interventions can be considered to operate at an individual, interpersonal, community, organisational, and policy or legislation level. The *de novo* decision support tool presented here spans the individual-interpersonal-community spheres. The aim of the intervention is to improve informed decision-making by proxies that reflects the wishes and preferences of the person they represent, whilst ensuring it pays attention to the ethical principles and corresponds to the relevant legal frameworks. The iterative development process included a review of existing decision tools in similar areas, the involvement of a lay advisory panel, input from a professional illustrator, and finally consultation with a stakeholder group which included both those who would receive the intervention and those who would be implementers to establish acceptability.

12.2 Novel aspects of this work

The body of work presented in this thesis was produced through adopting an innovative methodological approach to address the ethically complex issue of proxy decision-making for research. This enabled both empirical and normative questions to be attended to in order to achieve the aim of presenting an account that is both empirically and theoretically grounded, and the development of a *de novo* decision support intervention set within the ethical and legal frameworks. As such, it can be considered both methodologically novel, and novel in terms of improving our understanding of proxy decision-making and the contexts within which it occurs. For simplicity, the novel aspects are summarised in **Table 12-1 Summary of novel aspects of this work** below.

Table 12-1 Summary of novel aspects of this work

Chapter no.	Summary of novel use of methodology and/or findings
Chapter 2	<ul style="list-style-type: none"> • This chapter reports a comprehensive critical review of literature relating to proxy decision-making for research, including the novel exposition of a number of theoretical and practical problems, and a review of existing alternative accounts. • A number of ‘ingredients’ of a further alternative account are proposed for the first time.
Chapter 3	<ul style="list-style-type: none"> • Previous uses of systematic review methodology in empirical ethics have been extended to the use of a framework synthesis for the first time. • A novel empirically grounded conceptual model was developed which identified a number of framing criteria and active elements involved in proxy decision-making and described the relationship between these concepts. • A number of methodological issues and research gaps in existing empirical studies were identified, including the need for further research to explore real-world decision-making rather than hypothetical scenarios. • The systematic review was published in American Journal of Bioethics: Empirical Bioethics (167).
Chapter 4	<ul style="list-style-type: none"> • Chapter 4 reports the first exploration of health and social care professionals’ knowledge and understanding of the legal frameworks governing research involving adults who lack capacity to consent in the UK. • Novel findings included worryingly low levels of knowledge across a range of professions and areas of practice involving adults who may have impaired capacity, despite high levels of involvement in research. • It identified for the first time a need for educational interventions to improve levels of legal literacy in this area, and a need to further explore attitudes towards the inclusion of adults lacking capacity in research. • The results were published in Journal of Medical Ethics (216).
Chapter 5	<ul style="list-style-type: none"> • Previous uses of content analysis to examine documents such as participant information sheets have been extended to the first examination of written information provided to proxies. • Novel findings included: the lack of information provided about the proxy’s role and the basis for their decision, the disparity between documents provided to those acting in a professional role as opposed

	<p>to a personal capacity, and that despite undergoing review by a Research Ethics Committee, many documents contained inaccuracies in terminology and some incorrectly interpreted the legal requirements.</p> <ul style="list-style-type: none"> • It identified for the first time a need for greater accuracy in information sheets provided to proxies, and a need for further guidance for those drafting study documents, which may include additional templates from authorities such as the Health Research Authority. • This study was published in Trials journal (240) and an additional paper presenting further data was also published in Trials (491)
Chapter 6	<ul style="list-style-type: none"> • This is one of the few studies to have explored real-world experiences of proxy decision-making for research, and the first to have explored such experiences in the UK. This is important as the legal frameworks differ between jurisdictions, and so findings from other studies may not be generalizable to the UK. • The study was also unique in including proxies who had both agreed to, and declined, a broad range of studies. • Novel findings included that: proxy decisions are relational, constructed, and highly contextually dependent, and decision-making occurs within the context of a caring dyadic relationship, where the advantages and disadvantages of participating (or not) are viewed as relational. • The findings also included the emotional and decisional burden experienced, and the need for decision support. • Novel findings included the assumption by proxies that their role as welfare attorney automatically included decisions about research. • The findings acknowledge for the first time that decisions about research are not taken in isolation from all other decisions made about a person's health and wellbeing. • The findings also suggest that extending Power of Attorney to include research may have some advantages, including facilitating discussion about future preferences. • A manuscript reporting the main findings is in press in Age and Ageing.
Chapter 7	<ul style="list-style-type: none"> • This chapter reported the use of interviews to interrogate the novel conceptual framework developed in Chapter 3. • Multi-grounded theory methods were used, which appears to be the first time this method has been used to explore proxy decision-making. • The findings enabled a richer understanding of proxy decision-making from the previous studies that were included in the systematic review, including: the importance and value of research, the

	<p>fundamental role of the relationship between the proxy and the person they represent, and the following principles that enable proxies to reach their desired outcome (making the decision that is best, but also authentic to the person).</p> <ul style="list-style-type: none"> • The findings enabled the ethical framework to be further refined so that it is both theoretically and empirically grounded.
Chapter 8	<ul style="list-style-type: none"> • This chapter reports the novel use of triangulation methods to explore the differences between the normative, empirical, and legal accounts of proxy decision-making for research. • A number of important areas of convergence and disjuncture are articulated for the first time, and key questions that remain are highlighted. • The divergence between the normative individualistic approach to proxy decisions grounded in autonomy, and the relational approach identified in the empirical data is seen as the basis for developing a new relational theory of proxy decision-making that is based on the forming of relationships and underpinned by respect for persons may be a more informed and informative approach.
Chapter 9	<ul style="list-style-type: none"> • This chapter identifies the problematic extension of respect for autonomy to those considered to be lacking autonomy, and the resulting ethical concerns around a lack of protection where informed consent cannot be obtained. • An existing alternative account of respect for persons is applied to the case of research involving adults lacking capacity to consent for the first time, and this is further extended to present an account of respect for persons that may provide a better basis for attending to the range of ethical concerns rather than attempting to find an alternative consent provider.
Chapter 10	<ul style="list-style-type: none"> • This chapter draws together the findings from previous chapters and presents the first socio-legal analysis of the legal frameworks governing research involving adults who lack capacity. • A number of recommendations for the development of the legal frameworks and areas that require greater clarification are made. • This is the first attempt to empirically support the recommendations made by the Nuffield Council on Bioethics in 2009 (288). • A manuscript reporting the role of LPA to research decisions is under journal review.
Chapter 11	<ul style="list-style-type: none"> • This chapter presents the first depiction of a socio-ecological model of proxy decision-making for research. This enables a novel understanding of the levels and systems that provide the context within which decisions are made.

	<ul style="list-style-type: none"> • The literature in relation to making decisions about research participation on behalf of another is summarised for the first time. • This chapter also reports the development of a <i>de novo</i> complex intervention, a decision support tool for family members acting as a consultee or legal representative, and the work to date to establish acceptability.
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As stated, the findings reported in Chapters 3, 4, and 5 have been published in peer-reviewed journals and other work from this thesis is currently under journal review, as well as associated work not central to the thesis. In addition, work from this PhD has been presented at various national and international conferences and has received a number of conference awards; as well as being presented at a number of practitioner workshops (see **Appendix 16. List of conference presentations and workshops given as part of PhD**). This adds further strength to the value of this body of work, demonstrating that the contributions made are both novel and are of importance and value to both the academic and practitioner communities.

12.3 Reflections on the methodological approach

Methodological limitations relating to each individual study are acknowledged within the relevant chapter; however, other elements relating the broader methodological approach of this work need to be recognised. The concept that proxies are engaged in ‘decision-making’ is contested by those who consider instead that proxies either accept or reject an invitation to participate made by a clinician or researcher, and by those who approach the topic from a purely mental capacity law perspective and see proxy (or rather consultee) involvement as purely consultative rather than determinative. As a counter to these claims, firstly the wider international literature uses the term ‘proxy (or surrogate) decision-making’ and so it seems logical to adopt the same phraseology. Additionally, some proxies actively seek opportunities for the person they represent to participate in research, particularly where it relates to aspects of care or social activities, and so the medical model does not apply universally to research involving those who lack capacity. Thirdly, mental capacity law is only one part of the legal framework, and so proxies may be providing consent for a clinical trial as a legal representative, which does not fit the consultative approach. Lastly, as the DECISION Study has found, family members acting as proxies do not distinguish between their advisory and

consenting roles, and very much consider themselves decision-makers even when acting as consultees. It is also important to recognise that whilst the doctoral project set out to include all populations of adults with impaired capacity, the practical challenges of recruiting proxies who had represented people with learning disabilities, and the lack of existing empirical data and literature relating to this group, limits the overall findings.

A more fundamental point about the overarching methodological approach needs to be recognised. There are a number of epistemological and ontological challenges when conducting empirical research both within the fields of social science and bioethics. This project spans both disciplines and so may be the subject of challenges from both quarters. It might engage criticism for the (perhaps controversial) use of pluralistic qualitative analysis methods, the use of systematic review methods in bioethics and, perhaps more profoundly, the use of empirical 'is' research to shed light on the 'ought' of normative ethics. However, this topic is one of great complexity – normatively, empirically, and legally – and therefore an interdisciplinary approach, which necessarily involves a plurality of methodologies, seems the best approach to fully explore and address these complexities. It is acknowledged, however, that the challenges of combining these methods and findings into one thesis means that there is little scope or space for fully addressing the limitations and criticism that it may invoke.

12.4 Theoretical, practical and methodological applications

There are a number of aspects of this work that have relevance to a theoretical understanding of proxy decision-making and the practical application for those involved. These can be summarised as relating to the '*who, why, and how*' aspects of proxy decision-making. The dyadic, trusting relationship between the family member acting as proxy and the person they represent has been shown to play a fundamental role in proxy decision-making, and therefore *who* acts as proxy must be chosen on the basis of their relationship. Rather than focusing on accurately predicting the preferences of the person they represent; proxies seek to make a decision that respects their wishes and feelings and pays attention to their welfare. The proxies' dual obligation towards the person, which incorporates aspects of both preference-promoting and interest-protecting elements, is the reason *why* proxies are considered to have decision-making authority in some spheres. When considering *how* proxies make decisions, the proxy uses their relationship and familiarity with the person's

biographical history, together with their knowledge of the person's values, to construct a decision that is authentic to that person.

12.4.1 Implications for practice

The findings will be of practical use to those designing, conducting, and regulating research involving adults who lack capacity, as well as those engaged in caring for populations, which may include those with impaired decision-making capacity. This work addresses a number of research questions identified as priorities for improving the process of recruiting people to trials, such as to how to include under-represented or vulnerable groups in randomised trials, and how to improve informed consent processes (492). Practical implications include the need for researchers or clinicians seeking to include a person who lacks capacity in research to identify those family members best able to represent the person by virtue of their relationship, which may not necessarily be the closest 'next of kin' in its traditional sense. The principle of informed consent requires that consent given by the 'subject or the subject's legally acceptable representative' be fully informed (65). Explicit information about their role, the legal basis for their decision, and how they might undertake the decision-making process should be clearly provided to those acting as proxies.

The qualitative findings showed that proxy decisions are highly contextually dependent and multi-factorial where the advantages and disadvantages of participating (or not) are viewed as relational. The findings also highlighted the emotional and decisional burden experienced by some family members, and the need for decision support. These findings will be useful to those involved in approaching or supporting family members who are involved in decisions about research participation. The ethical practice of proxy decision-making described, and the focus on making authentic decisions, may help to address the anxieties of those concerned about the lack of 'accuracy' reported in many (hypothetical) studies. The findings about the role of Lasting Power of Attorney in research decisions may also be useful and bring some clarity for those involved in seeking the involvement of consultees and legal representatives.

Understanding that proxy decision-making sits within a broader context, and that there are many levels with the wider socio-ecological model, may help those seeking to improve decision-making and informed consent processes for adults who lack capacity to consent. The decision support tool developed may be useful for researchers, professionals, and

practitioners who seek to involve adults who lack capacity in research and therefore approach family members to act as consultee or legal representative. However, considerable further work to establish the feasibility and effectiveness of the decision support tool is needed before its use could be recommended.

12.4.2 Implications for developing the legal frameworks

This work highlights the complexity of the current legal frameworks in practice. The subsequent lack of knowledge and understanding found in health and social care professionals, researchers, and to some degree those involved in providing ethical review, indicates a need for further education and training resources for those involved. Those responsible for drafting study documents should pay particular attention to the use of accurate terminology and correct interpretation of the legal frameworks, which may be assisted through engagement with those knowledgeable about mental capacity law and clinical trials regulations in relation to adults lacking capacity.

The findings have practical implications for the legal frameworks and research governance processes. The findings suggest that focussing on risk-avoidance, and individualistic autonomy and consent-based approaches to ethical governance for research involving adults who lack capacity fails to address the ethical concerns surrounding the exclusion of those who would wish to participate, and the injustice and (ethical) harms that may result. The legal frameworks also fail to address these issues, and the disparity between the requirements for consent for clinical trials whilst requiring consultee advice for other types of research, has no normative basis and adds unnecessary complexity. There is similarly no coherent normative justification for requiring those acting as proxy in a professional capacity to provide advice or consent based on the person's presumed will or wishes and feelings. There may be scope for amending the legal frameworks and research governance processes in the future in order to better reflect the normative and empirical accounts. In the meantime, further guidance is needed on the role of professionals acting as proxy, the role of LPA, and more generally on proxy involvement in research involving adults who lack capacity.

12.4.3 Theoretical implications

There are a number of theoretical implications arising from this work. The account of proxy decision-making proposed, which is built on a broad conception of respect for persons encompassing a range of ethical concerns such as autonomy and dignity, may have implications for those exploring this and other topics in bioethics. The conceptual framework developed may prove a useful starting point for developing a fuller account, which may help address the key areas of divergence and silence between the normative, empirical, and legal accounts of proxy decision-making for research. The complexity of decisions described, where there are a number of following principles and standards, and where relationality is a fundamental concept, may have implications for those who are developing alternative accounts. Further development of an account of professionals acting as proxy, where the relationship and trust between the parties remains a fundamental aspect of their role, but where a greater focus is on the person's interests rather than solely on their presumed will, may build on the work presented here.

12.4.4 Methodological applications

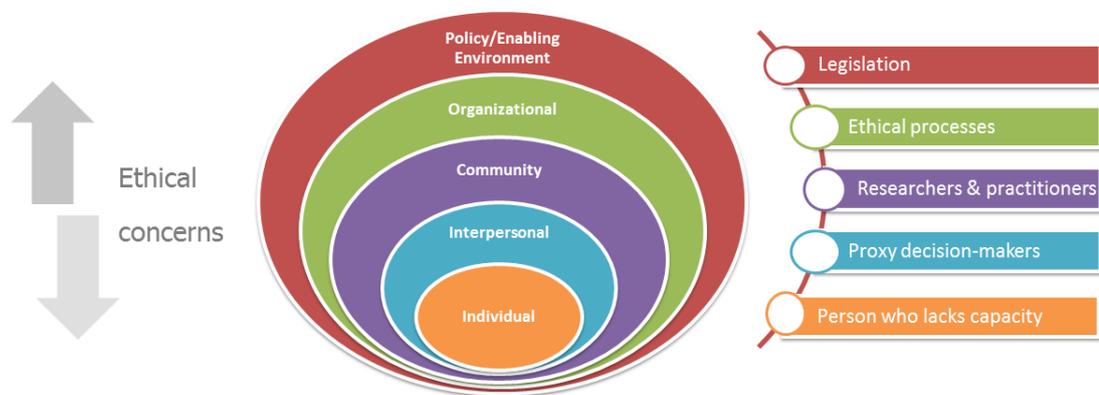
In terms of methodological implications, the overall methodology adopted for this project has enabled a nuanced account of proxy decision-making to be provided, that is attentive to the ethical and legal requirements and the broader context and systems within which it is located. The hierarchy of individual studies, which built on initial work to describe the lay of the land, then compared the reality with the 'ideal', identified methods of improvement, before generating new accounts, may have implications for other empirical ethicists seeking to explore an ethically complex area. In terms of specific methods, using a framework synthesis of empirical studies provided a comprehensive account of the existing data, allowing the methodological limitations to be acknowledged and gaps in existing literature to be identified. It also enabled the development of a conceptual framework, which could then be used to inform the qualitative interviews. The pluralistic qualitative analyses of the qualitative data allowed a multi-dimensional and rich exploration of the data beyond that which would have been provided through the use of a single method. This approach may be useful to those exploring phenomena requiring analysis of the ethical dimensions as well as others such as experiences and attitudes. The methodological approach to the development of a complex intervention to support proxy decision-making, which has a strong theoretical

and practical basis, used in this project may have applications when developing complex interventions in other similar contexts.

12.5 Further areas for research

There are a number of strands of work that could be taken forward from this thesis. These are summarised below using the socio-ecological model presented in Chapter 10 to describe the level or system within which that further research is located (**Figure 11-1. Socio-ecological model of proxy decision-making for research**).

Figure 11-1 Socio-ecological model of proxy decision-making for research



1. Individual Further research is needed to explore whether the process of setting up an LPA provides an opportunity for a discussion about future research preferences, and whether this has an impact on proxy decisions or proxies themselves in terms of the burden they may experience.

2. Interpersonal (a) Empirical data is needed to investigate the role of a health or social care practitioner acting as a consultee or legal representative, to explore how such proxy decisions are made in practice, and to the legal and normative requirements and practical implications. This may also include any informational and decision support needs.

3. Interpersonal (b) The DECISION Study primarily included family members of someone living with dementia. Further research is needed to explore the experiences of proxies

representing family members who have experienced a sudden or acute loss of capacity, and family members of people with life-long disabilities.

4. Interpersonal (c) Research is needed to establish the feasibility of the decision support aid that has been developed. Additional work should focus on establishing outcomes that are considered relevant and can be measured and the feasibility of using a decision support tool in this context, prior to a trial to investigate the effectiveness of the intervention in supporting decision-making by family members.

5. Community Further exploration is needed of health and social care professionals' application of the legal frameworks in practice, and their attitudes towards the inclusion of those with incapacity in research. This may further inform the development of education and training interventions to improve levels of knowledge and understanding about the legal frameworks.

6. Legislation Further exploration is needed of the views of the public and stakeholders about extending the role of welfare attorneys to research, the subsequent impact on the ability to conduct research involving adults who lack capacity, and the feasibility and value of developing a non-binding advance research statement.

12.6 Concluding remarks

This thesis has investigated the ethical, legal, and practical challenges that are encountered when proxy decisions are made about research participation, by presenting theory and empirical research as being mutually informing throughout the doctoral project, with relationality being the unifying concept. The new evidence generated has been outlined, and areas in which further developments are warranted have been indicated.

It is hoped that this work and recommendations will be useful for those involved in caring for people experiencing impaired decision-making capacity, those seeking to involve them in research, and those responsible for the regulation and oversight of such research. Above all, the hope is that it makes a contribution towards a more inclusive approach to research, where the benefits of research can be distributed amongst all members of society, regardless of their cognitive abilities.

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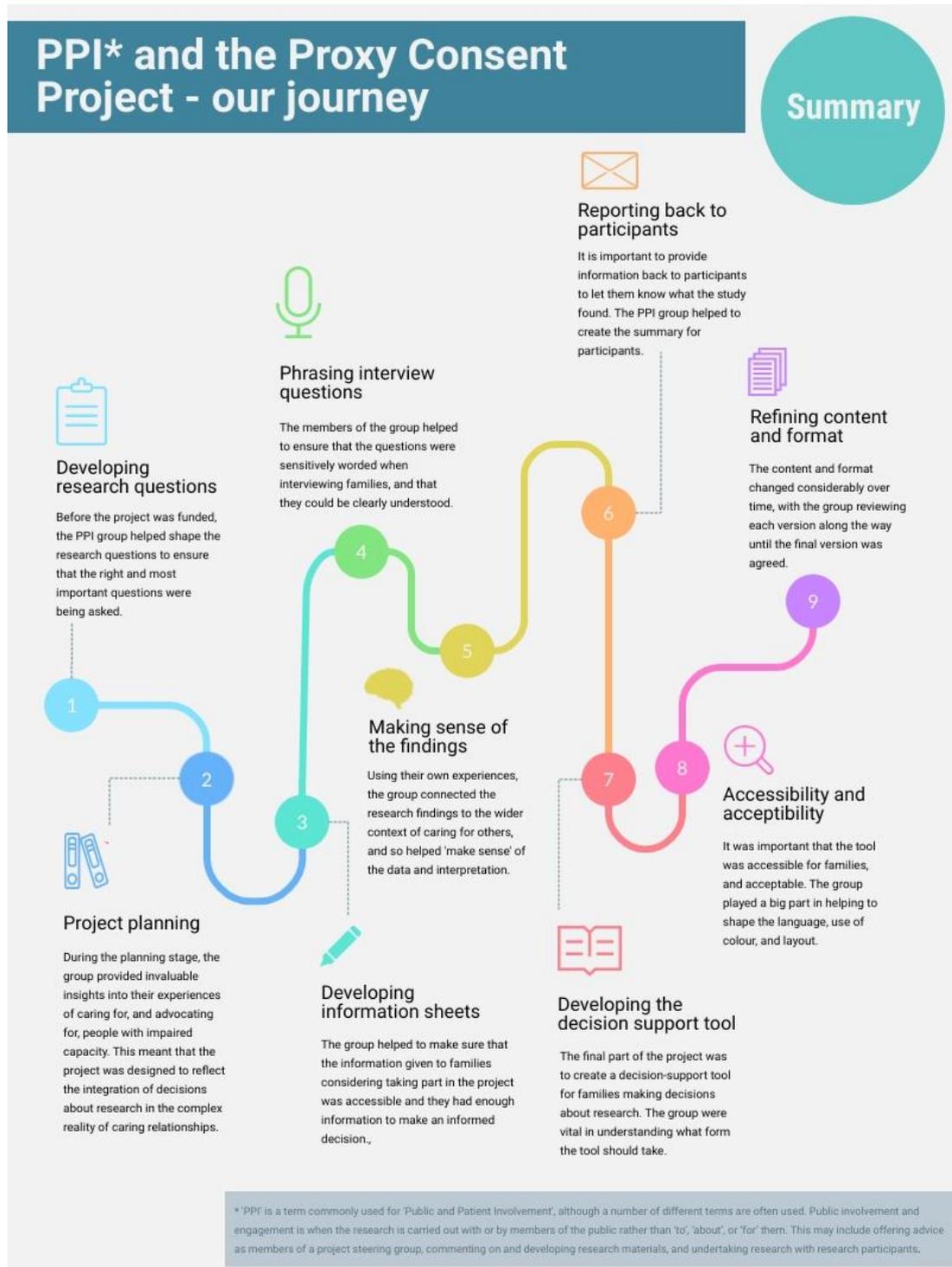
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Appendices

Appendix 1. Public and Patient Involvement in doctoral project



PPI and the Proxy Consent Project - our journey

1

Before the project was funded, the PPI group was formed with Sian and Jonathan. Meeting at this early stage helped to shape the research questions being developed to ensure that the right and most important questions were being asked. It also meant that the focus of the project, decisions made about research participation on behalf of someone else, wasn't viewed in isolation from the other aspects of care and decision-making. This enabled the research questions to take account of the wider context of caring relationships.



2

Once the project was funded, the PPI group grew as we welcomed Ian to the group. During the project planning stage, the group provided invaluable insights from their wide variety of experiences of caring for, and advocating for, people with impaired capacity. This was from both a personal and professional perspective. The wealth of their experience meant that the project was planned to be inclusive of people who care for people living with a range of conditions such as dementia and people with learning disabilities.



3

One of the main parts of the project was an interview study to explore family members' experiences of making decisions about research on behalf of a family member. The group helped to make sure that the Participant Information Sheet given to families considering taking part in the project was accessible and contained enough information for them to make an informed decision about taking part. Some of the interviewees spoke positively about the information they had received and commented on the sheet's clarity.



4

The interviews were 'semi-structured' which meant that they were based on particular questions, but the family member was also encouraged to talk more widely about their experiences and views. The members of the PPI group reviewed the questions when they were being developed. This helped to ensure that the questions were sensitively worded, which is important when interviewing families about what can be difficult issues, and that they could be clearly understood.



5

The interviews went very well, and very valuable information was collected about how family members make decisions about research, set in the context of their wider caring relationships. Once the first stage of the data analysis had been completed, the early findings were discussed with the PPI group. Using their own experiences, the group helped to connect the research findings to the wider context of caring for others, and so helped 'make sense' of the data and its interpretation.



6

It is important to provide information back to participants who have taken part in research to let them know the results of the study. For this project, that meant informing family members who had taken part in interviews about what we had learnt about families' experiences of making decisions. The PPI group helped to create the summary for participants and ensured it contained the right information and accessible language. This was then sent out to all those who had taken part.



7

Further along the project journey, the PPI group expanded again to welcome Lily who joined at the point of creating the main output of the project. This was to use all the information that had been learnt through the interviews and other pieces of work to create a decision-support tool for families making decisions about research. Through lots of discussion the group was vital in understanding what format the tool should take, who might it be most suitable for, and how it might be used in real life.



8

In order for the decision-support tool to be effective, it is important that it is accessible for family members, and acceptable to those using it. The group played a big part in helping to shape the language, use of colour, and layout. There were also lots of discussions about the visual images used, particularly for the exercise that helped explore which of the options (to participate or not) most closely matched the values and preferences of the person being represented. An alternative image was chosen based on these discussions.

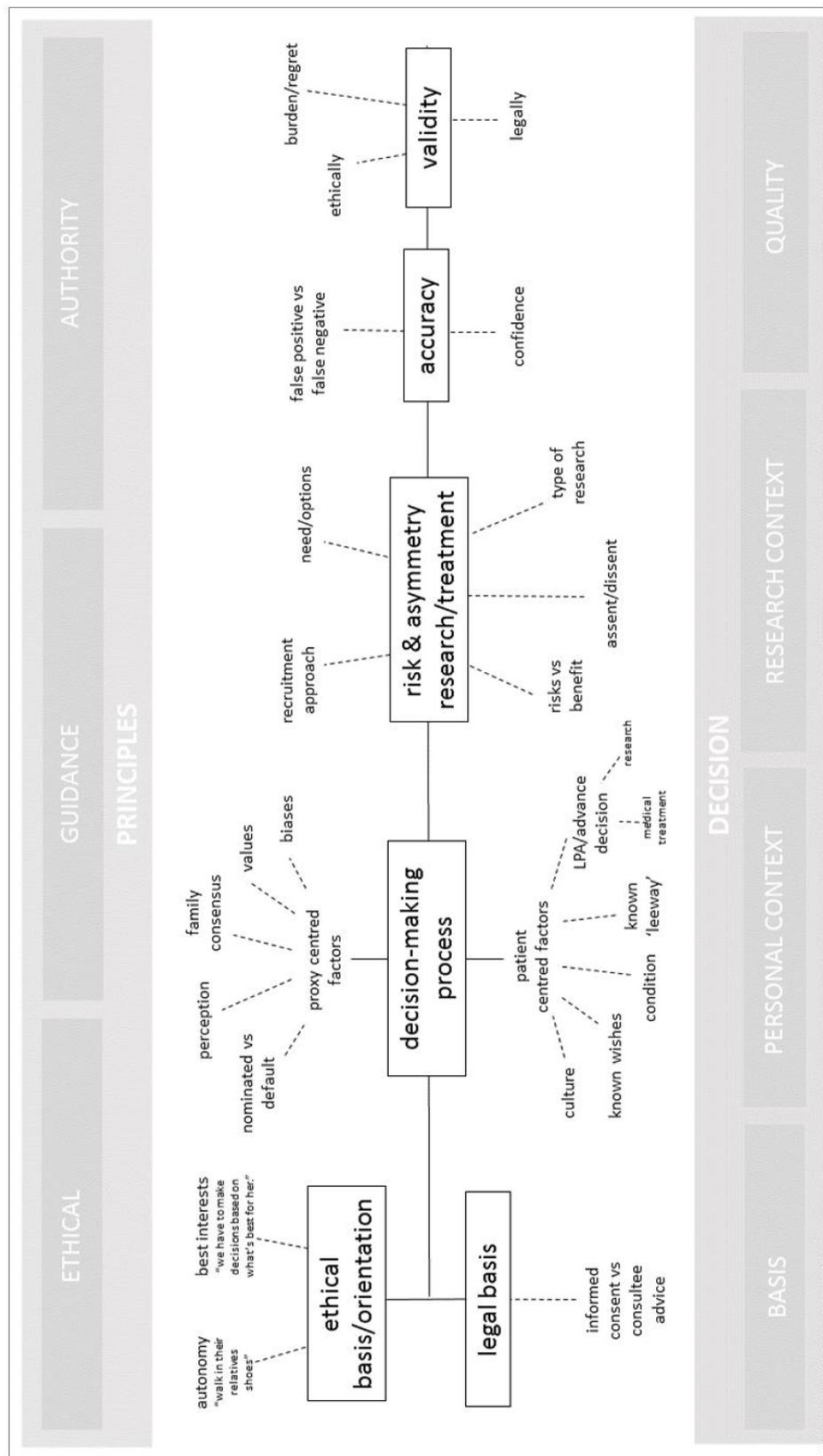


9

The content and format of the decision-support booklet changed considerably over time. A graphic designer helped illustrate the booklet, which was then taken to a wider group of external stakeholders, including members of the public, who provided feedback which helped to refine the booklet. The PPI group reviewed each version and agreed the final version. After this project, the next steps will be to explore how effective the booklet is at supporting family members - hopefully with the continued support of the group!



Appendix 2. Initial conceptual framework of proxy decision-making for research



Appendix 3. Search strategy for systematic review of empirical studies

Initial searches were developed in December 2016 using MEDLINE. A literature review of the analytical/philosophical literature helped to develop the initial conceptual framework and inform the initial search strategy. Subsequent searches were developed with attention to the conceptual framework and terms used in the literature. Final searches were conducted in January and February 2017.

Electronic resources

- Ovid MEDLINE <1946 to January Week 3 2017>
- EMBASE <1996- 2017 January 03>
- PsychINFO <1806 – present>
- CINAHL plus with full text <1986-present>
- BNI <1985-present>
- SCOPUS <1966-present>
- Web of Science <1900-present>
- EUROETHICS

Studies were limited to those in the English language, the search was not limited by date. Supplementary searches were conducted including citation tracking, reference lists of included papers, and electronic table of contents (eTOC) of key journals for the last two years.

Example search strategy

Ovid MEDLINE <1946 to January Week 3 2017>

1. exp Proxy/
2. proxies.tw.
3. exp Informed Consent/
4. exp Third-Party Consent/
5. (consent adj3 (informed or proxy or proxies or surrogate*)).tw.
6. (proxy* adj3 (consent or choice* or decision* or decide or choose or prefer or permission or view*)).tw.
7. (proxies adj3 (consent or choice* or decision* or decide or choose or prefer or permission or view*)).tw.
8. (surrogate* adj3 (consent or choice* or decision* or decide or choose or prefer or permission or view* or preference*)).tw.
9. (informed consent adj3 (proxy or proxies or surrogate*)).tw.
10. (substitute* adj3 (consent or choice* or decision* or decide or choose or prefer or permission or view*)).tw.
11. (principle* adj2 ethic*).tw.
12. (accuracy adj4 (proxy or proxies or surrogate* or decision*)).tw.

13. substituted judgement*.tw.
14. best interest*.tw.
15. comfort.tw.
16. (trial* or study or studies or research).tw.
17. (empirical* adj3 (study or studies)).tw.
18. (philosoph* adj3 (study or studies)).tw.
19. exp "Surveys and Questionnaires"/
20. (("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire*)).ti,ab.
21. or/11-15
22. or/16-20
23. or/1-10
24. 21 and 22 and 23

Appendix 4. Summary of key characteristics of studies included in systematic review

Reference	Country	Clinical context	Study design	Study aim	Scenario: real or hypothetical	Study sample	Direct experience of context/condition?
Ayalon 2009	US	Dementia	Survey	Public attitudes to proxy consent	Hypothetical	1469 members of public	N
Barrett 2012	Canada	Critical care	Interview	Examine attitudes to involvement in consent	Hypothetical	137 proxies	Y
Berger 2005	US	Dementia	Interview	Preferences for proxy consent	Hypothetical	10 patients	Not stated
Black 2012	US	Dementia	Interview	Decision-making for dementia research	Real & hypothetical	39 patients, 46 proxies	Y
Bolcic-Jankovic 2014	US	Critical care	Interview	Confidence in proxy's ability	Hypothetical	214 patients, 445 proxies	Y
Bryant 2013	US	Stroke	Survey	Level of patient-proxy agreement	Hypothetical	200 patients, 200 proxies	N
Burns 2017	Canada	Critical care	Interview	Experiences of proxies	Real	28 proxies	Y
Cioldi 2007	France	Critical care	Questionnaire	Proxies' accuracy	Hypothetical	100 patients, 100 proxies, physicians	Y
Clarridge 2015	US	Critical care	Survey	Biasing effects in substituted judgement	Hypothetical	445 proxies	Y
Coppolino 2001	US	Critical care	Interview	Proxies' accuracy	Hypothetical	100 patients and 100 proxies	N
De Vries 2010	US	Dementia	Survey and discussion group	Intervention to support proxies' decision-making	Hypothetical	212 proxies	Y
Del Guidice 2009	US	Subarachnoid haemorrhage	Questionnaire	Willingness to participate	Hypothetical	907	N
Dubois 2011	Canada	Dementia	Survey	Comfort with proxy consent	Hypothetical	679 members of public, 384 informal caregivers, 495 physicians, 177 researchers, 325 REB members	Mixed
Dunn 2012	US	Dementia	Interview	Understanding proxies' decision-making	Hypothetical	40 patients, 40 proxies	Y
Dunn 2011	US	Dementia	Interview	Attitudes towards research	Hypothetical	82 patients, 82 proxies	Y

Karlawish 2001	US	Dementia	Interview	Proxy-patient decision-making	Real	22 proxies	Y
Karlawish 2008	US	Dementia	Interview	Proxy-patient decision-making	Real	59 patients, 60 proxies	Y
Karlawish 2009	US	Dementia	Survey	Attitudes towards research	Hypothetical	538 members of public	N
Kim 2009	US	Dementia	Survey	Attitudes towards proxy consent	Hypothetical	1515 members of public	N
Kim 2005	US	Dementia	Survey	Attitudes towards research	Hypothetical	229 patients	N
Kim 2010	US	Dementia	Survey	Intervention to support proxies' decision-making	Hypothetical	212 patients	Y
Kim 2013	US	Dementia	Questionnaire	Attitudes towards proxy consent	Hypothetical	212 members of public	N
Lim 2013	Singapore	Critical care	Questionnaire	Attitudes towards proxy consent	Hypothetical	305 members of public	N
Mehta 2012	Canada	Critical care	Questionnaire	Proxy decision-making	Real	95 proxies	Y
Muncie 1997	US	Nursing home	Interview	Proxy decision-making	Hypothetical	315 residents, 315 proxies	Y
Newman 2012	US	Critical care	Survey	Proxies' accuracy	Hypothetical	69 patients, 60 proxies	Y
Overton 2013	US	Dementia	Survey and interview	Proxies' decision-making	Hypothetical	25 patients, 25 proxies	Y
Sachs 1994	US	Dementia	Interview	Proxy-patient decision-making	Hypothetical	42 patients, 64 proxies, 60 members of public	Y
Scales 2009	Canada	critical care	Interview	Patient preferences for proxy consent	Hypothetical	240 patients	Y
Shelton 2015	US	Critical care	Questionnaire	Intervention to support proxies' decision-making	Hypothetical	134 visitors	Y
Stocking 2006	US	Dementia	Interview	Proxy-patient decision-making	Hypothetical	149 patients, 149 proxies	Y
Sugarman 2001	US	Dementia	Interview	Proxies' decision-making	Real	49 patients, 49 proxies	Y
Warren 1986	US	Nursing home	Questionnaire	Proxies' decision-making	Hypothetical	168 residents, 151 proxies	Y
Wendler 2002	US	Dementia research	Interview	Attitudes towards proxy consent	Hypothetical	246 people	N

Appendix 5. Coding index for studies included in systematic review

CODE	DESCRIPTION
Framing criteria of decision-making	
Substituted judgement	<i>Making the decision that the person themselves would have made, if they had capacity</i>
Best interests approach	<i>Deciding what is best for the person in order to maximise or maintain their health and welfare</i>
Combination of substituted judgement and best interests	<i>Using a combination of what the person would have wanted, and what is best for them, to decide for the person</i>
'Something else'	<i>An alternative basis for the decision, possibly using a combination of other factors</i>
Knowing the person	
Choice of proxy	<i>The person the patient would/did chose to act as their proxy, including the reasons for that choice</i>
Knowing their values	<i>The proxy's intimate knowledge of the person they are acting on behalf of and their values</i>
Knowing their wishes	<i>The proxy's intimate knowledge of the person they are acting on behalf of and their wishes that are relevant to the decision or situation</i>
Altruistic tendencies	<i>The principle or practice of concern for the welfare of others, selflessness, or willingness to help others</i>
Advanced directives	<i>Alternatively known as advance decisions or a 'living will'. In the UK they are generally drafted to refuse specific treatments, although individuals may also make some requests about future treatment or state whether they are willing to participate in (specific types of) research after they have lost capacity</i>
Current preferences	<i>Contemporaneous expressions of willingness or discomfort or refusal to participate in the research study – may be verbal or non-verbal and may relate to the study as a whole or a particular study element or procedure (e.g blood sample)</i>

Relationship between the patient and the proxy	
Responsibility towards each other	<i>Family ties</i>
Love and caring	<i>Relationship built on love and/or care</i>
Mutual trust	<i>Two-way trusting relationship between family members</i>
Consulting others	<i>Consulting the wider family group for consensus or validation</i>
Accuracy of the decision	
Level of agreement	<i>Agreement between the patient's hypothetical choice and the proxy's prediction of the patient's hypothetical choice</i>
False positive	<i>Agreeing for the patient to take part in a study that they would not have agreed to, if they had capacity</i>
False negative	<i>Declining for the patient to take part in a study that they would have agreed to, if they had capacity</i>
Contradiction to preferences	<i>Knowingly contradicting what the proxy knows the patient's preference would be (may be false positive, false negative, or another outcome)</i>
Confidence	<i>Patient's confidence in the proxy's ability to choose 'correctly' on their behalf, the proxy's confidence that they have decided 'correctly', or confidence in the decision</i>
Patient's own prediction	<i>The patient's response to a question about whether they would participate in a (hypothetical) research study should they lose capacity at some future point and be considered eligible for the study</i>
Leeway given to proxy	<i>The margin or flexibility the patient would give their proxy when deciding on their behalf. It may include decisions where the proxy does not know what the patient would have wanted or entitle the proxy to override a decision they believe the patient would have made – even if contrary to their known wishes.</i>
Balancing risks, benefits and burdens, and attitudes towards proxy decision-making	

Risks vs benefits	<i>Assessment of any risks or burdens of study participation, balanced against any (current or future) benefits, for those involved. May relate to the principles of beneficence and non-maleficence.</i>
Comfort with proxy decision-making	<i>Acceptability of a proxy making decisions on behalf of oneself or another person, or acceptability to make decisions as a proxy on behalf of another</i>
Burden of decision-making	<i>The strain or weight of the decision process, or decision outcome, on those involved. May include feelings of uncertainty or regret</i>
Acceptability of proxy decision-making	<i>Acceptance that others are able to make a decision on our behalf, if we are unable to do so</i>
Willingness to take part	<i>Willingness to take part in a proposed hypothetical research study (assuming eligible to do so)</i>

Appendix 6. Tabulated findings from studies included in systematic review

Theme	Studies
Framing criteria of decision-making	
Substituted judgement	Black et al 2012, Dunn et al 2012, Karlawish et al 2008, Overton et al 2013, De Vries et al 2010, Shelton et al 2015
Best interests	Black et al 2012, Dunn et al 2012, Karlawish et al 2008, Overton et al 2013, De Vries et al 2010, Shelton et al 2015
Another criterion	Black et al 2012, Dunn et al 2012, Karlawish et al 2001,
Relationship between the patient and the proxy	
Responsibility, trust, love and care towards each other	Del Guidice et al 2009, Sachs et al 1994, Berger et al 2005, Black et al 2012, Warren et al 1986
Accuracy of the decision	
Level of agreement or contradiction to preferences	Bryant et al 2013, Bolcic Jankovic et al 2014, Ciroidi et al 2007, Coppolino et al 2001, Newman et al 2012, Stocking et al 2006, Muncie et al 1997, Warren et al 1986,
Leeway given to proxy	Ayaalon et al 2009, Kim et al 2013, Karlawish et al 2009, Kim et al 2010, Berger et al 2005, Stocking et al 2006,
Knowing the person	
Knowing their wishes, values, and preferences	De Vries et al 2010, Overton et al 2013, Dunn et al 2012, Burns et al 2017, Berger et al 2005, Del Guidice et al 2009, Sachs et al 1994, Sugarman 2001, Wendler et al 2002, Kim et al 2005, Dubois et al 2011 Mehta 2012, Dunn 2011, Karlawish et al 2001

Appendix 7. Vignettes used in cross-sectional survey

Vignette 1

Mrs Jones has advanced dementia, and because of her condition she is unable to understand when something is explained to her. Since her husband died, she has lived with her daughter. There is no Lasting Power of Attorney or court order in place. A researcher from the University is doing a study to look at whether classical music has a beneficial effect on people with dementia. The study does not involve any serious risk for the participants. The researcher would like Mrs Jones to take part.

Vignette 2

Mrs Jones (from Vignette 1) is admitted to the local hospital with a fractured femur. An anaesthetist is carrying out a clinical trial into a new medication to relieve postoperative pain that may result in less side effects, such as confusion, in patients with dementia. The known side effects of the medication include nausea and headache and, rarely, kidney or liver failure. Mrs Jones is assessed by her consultant as eligible for the trial.

Vignette 3

Mr Smith is living in a nursing home following a severe stroke that has left him unable to understand information given to him or communicate in any way. A company has developed a device that monitors facial expressions to help staff understand how a person may be feeling (pain etc) and are carrying out a research study which Mr Smith's care home is taking part in. The study does not involve any serious risk for the participants. His son now lives a long way away but visits every two months and speaks to the care home staff weekly on the phone.

Vignette 4

Mr Smith (from Vignette 3) is admitted from the care home to the Intensive Care Unit of the local hospital with pneumonia. The University is conducting a study looking at all pneumonia admissions to hospital from care homes in the area. The study involves accessing patients' medical notes and results of investigations. The study does not involve any serious risk for the participants. His son is staying nearby while his father is in hospital and visits daily.

Vignette 5

Miss Lewis is 21 years old and has profound and multiple learning disabilities and lives in a small residential care home close to her mother who visits most days. There is no Court of Protection order in place. She is on long-term medication intended to control muscle contractures. This medication may not be effective for this type of problem and can result in side effects. Her General Practitioner is taking part in a study to look at whether such medication can be reduced or withdrawn safely without any worsening of symptoms. There may be some risks for the participant.

Appendix 8. Legal summary of research involving adults who lack capacity

Background

Research is an important way for us to understand illness and disabilities, and to improve the treatment, care and support people receive. Sometimes this research can only be carried out if it involves people who lack the mental capacity to provide informed consent to take part. Capacity can only be assessed in relation to a particular decision and a particular time – a person may have the capacity to make some decisions but not others, or their capacity to make a decision may vary over time. Adults are presumed to have capacity to make decisions about themselves unless proven otherwise through a formal assessment.

For those who are unable to provide informed consent for themselves, there are alternative legal provisions for their participation in research. The law allows such research to take place but sets out strict rules to protect people who lack capacity to decide to take part in the research and to make sure their current or previous wishes are taken into account.

The legal framework

There are two separate laws governing research involving adults who lack capacity to consent in England and Wales. The Mental Capacity Act 2005 (MCA) governs how adults lacking capacity can be involved in research, although it excludes clinical trials of investigational medicinal products (CTIMPs) which are regulated separately by the Medicines for Human Use (Clinical Trials) Regulations 2004 (CTR).

Although there are many similarities between the two regulations, there are important differences. Clinical trials of medicines require **consent** from a Legal Representative, whereas all other types of research require **consultation** with a Consultee. A summary of the main differences is shown in **Table 1** below. The situation will be largely unchanged by the new incoming Clinical Trials Regulations (No 536/2014) expected to come into force in 2019.

Who is involved in decisions about adults who lack capacity to consent?

The researcher must consult a person who, by virtue of their relationship with the person who lacks capacity, is suitable to act as an advisor on their behalf and is available and willing to act. They are either termed a Personal Consultee under the MCA, or Personal Legal Representative under the CTR. A number of people may be able to act as a Personal Consultee or Personal Legal Representative, but they should be someone whom the person who lacks capacity would trust with important decisions about their welfare (MCA (s32(2)) and CTR Part 5). Usually it will be someone with a close personal relationship with the person, for example his or her spouse/partner, adult child or parent, but it can be a close friend. They do not have to hold Power of Attorney. If a potential consultee does not feel able to take on the role, they may suggest that someone else takes on the role or ask that a Nominated Consultee or Professional Legal Representative be appointed.

A Nominated Consultee (MCA) or Professional Legal Representative (CTR) is required when no one who knows the person in a personal capacity is either available or willing to act. This is usually a healthcare professional or another nominated individual involved in their care, but they cannot be connected with the research study.

The person lacking capacity should be informed about the research and involved in the decision as much as possible, even if they are unable to provide informed consent. If they have fluctuating capacity or are likely to regain capacity, the decision should be delayed until they regain capacity where possible. The researcher must take into account the wishes of

the person who lacks capacity about whom to consult (e.g. their partner, or a particular friend or carer) and to act in accordance with any relevant previous statement or wishes.

How should the decision be made?

Careful thought is needed before including in research projects any adults who lack the capacity to make their own decisions. Unlike other decisions covered by the Mental Capacity Act, such as those about medical treatment and care, 'best interests' procedures do not apply to decisions about taking part in research (Code of Practice). Instead, each individual decision is based on what the person would have decided if they had capacity to do so.

The Consultee must be given information about the project and gives advice as to whether the person should take part in the project, and what the person's wishes and feelings about taking part in the project would be if they had capacity to decide (MCA s32(4)). The Consultee gives advice on what they think the participant would want to do, rather than give consent themselves. If the Consultee so advises, the participant must not take part and, if already taking part, must be withdrawn. The responsibility whether to include the participant lies with the researcher. If the person who lacks capacity indicates (in any way) that they wish to be withdrawn from the project, they must be withdrawn without delay.

For clinical trials of medicines, the Legal Representative is provided with information about the trial that includes the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted. They are then asked to provide informed consent that represents the person's presumed will. The person who lacks capacity should also have received information (according to their capacity of understanding) about the trial, its risks and its benefits. If the person is capable of assessing the information and forming an opinion, any refusal to participate should be considered by the researcher.

The basis for a decision by a Nominated or Professional Legal Representative is the same as for someone acting in a personal capacity (i.e. advice under MCA, informed consent under CTR) based on what the person themselves would have decided.

What if it is in an emergency situation?

Research carried out in emergency situations pose unique challenges in terms of obtaining consent. Emergency research is when treatment needs to be given urgently, and it is necessary to take urgent action for the purposes of the study. In some emergency situations people may lack capacity to give consent themselves and obtaining consent from a legal representative/consulting others is not reasonably practicable. In England and Wales, the law allows adults who lack capacity to take part in emergency research without prior consent from a legal representative or consulting others, if certain conditions are met (Medicines for Human Use (Clinical Trials) Amendment (No 2) Regulations SI 2006 2984, MCA s32(8)).

Following enrolment in the study, a consultee should be consulted as soon as possible to seek advice on the person's likely views and feelings, and for a CTIMP consent should be sought from a Legal Representative as soon as possible. Informed consent should also be sought from the person themselves as soon as possible following any regaining of capacity. Consent may be required for the person to continue in the study, or for the continued use of data or samples obtained.

Table 1. Summary of the provisions for adults lacking capacity under Mental Capacity Act 2005 (MCA) and Medicines for Human Use (Clinical Trials) Regulations 2004 (CTR)

	MCA	CTR
Who acts as decision maker	<p>The researcher must consult a Consultee.</p> <p><i>Personal Consultee</i> - a person who is engaged in caring for the person or is interested in their welfare, except as a professional or for remuneration – friend, relative, unpaid carer, attorney acting under LPA, or court appointed deputy.</p> <p><i>Nominated Consultee</i> - a person who has no connection with the project – such as a healthcare professional, or nominated individual</p> <p>The responsibility whether to include the participant lies with the researcher.</p>	<p>A Legal Representative - a person who, by virtue of their relationship, is suitable to act as their legal representative and is available and willing to act.</p> <p><i>Personal Legal Representative</i> – such as a friend or relative.</p> <p>If there is no-one suitable/available to act in a personal capacity, this may be a <i>Professional Legal Representative</i> – such as the doctor primarily responsible for their medical treatment, or a person nominated by their health care provider. They must not be connected with the trial.</p>
Basis for the decision	<p>The Consultee is asked for <i>advice</i> about whether the participant should take part, and what, in their opinion, the person’s wishes and feelings about taking part in the project would be if they had capacity.</p>	<p>The Legal Representative is required to decide whether the participant would have wanted to participate had they capacity to do so. <i>Informed consent</i> is therefore given by the Legal Representative which represents their presumed will.</p>
Provision of information	<p>The MCA does not specify any provisions that the person has to be informed about the research once they have been assessed as lacking capacity. Good practice requires the person to be provided with information according to their capacity.</p>	<p>The person lacking capacity must have received information about the trial, its risks and benefits, according to his or her capacity before they can be involved.</p>
Dissent/objection	<p>Weight is given to any refusal or dissent from the individual lacking capacity, even when the person has little or no ability to understand the situation. If the person indicates (in any way) that he wishes to be withdrawn from the project he <i>must be withdrawn</i> without delay.</p>	<p>The explicit wish of a subject who is capable of forming an opinion and assessing the information to refuse participation in, or to be withdrawn from, the clinical trial at any time <i>must be considered</i> by the investigator</p>
Level of risk permitted	<p>Research must be connected with an impairing condition in the functioning of the mind or brain affecting the person, or its treatment. There must be reasonable grounds for believing that the risk to the person is <i>negligible</i> and that anything done in relation to the person will not interfere with their freedom of action or privacy in a significant way or be unduly invasive or restrictive.</p>	<p>The clinical trial must relate directly to a life-threatening or debilitating condition clinical condition from which the person suffers. There must be grounds for expecting that administering the product will <i>produce a benefit to the person outweighing the risks or produce no risk at all</i></p>

Where can I find more information?

Health Research Authority (HRA)

<https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/mental-capacity-act/> and <http://www.hra-decisiontools.org.uk/consent/principles-ALC.html>

Health and Care Research Wales

https://www.healthandcareresearch.gov.wales/uploads/News/research_and_impaired_mental_capacity_in_adults-guidance_for_researchers.pdf

Medical Research Council (MRC)

Guidance issued by the Medical Research Council on medical research involving adults who cannot consent

Guidance on nominating a consultee for research involving adults who lack capacity to consent

http://webarchive.nationalarchives.gov.uk/20130123193236/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_083131

NIHR CRN Informed Consent with Adults Lacking Capacity

<https://www.nihr.ac.uk/our-faculty/clinical-research-staff/learning-and-development/national-directory/good-clinical-practice/our-courses/introduction.htm> This course is designed to provide an introduction to informed consent with adults lacking capacity. It explores the requirements of the Mental Capacity Act and Medicines for Human Use (Clinical Trials) regulations when involving adults who lack capacity in non-CTIMP and CTIMP research.

References

The Medicines for Human Use (Clinical Trials) Regulations 2004

Mental Capacity Act 2005

Mental Capacity Act 2005 (Loss of Capacity during Research Project) (England) Regulations 2007

Mental Capacity Act 2005 (Loss of Capacity during Research Project) (Wales) Regulations 2007

DH Mental Capacity Act 2005 guidance page

Mental Capacity Act 2005 Questions and Answers

Mental Capacity Act Code of Practice

Ethics Guidebook – a resource for Social Scientists

NIHR Clinical Trials Toolkit

About this summary

This summary forms part of a project to explore how decisions are made about research involving adults who lack capacity. It is being carried out as part of an NIHR Doctoral Research Fellowship at Cardiff University. For more information, please contact Victoria Shepherd ShepherdVL1@cardiff.ac.uk

Appendix 9. Characteristics of studies included in content analysis

Study ID	Classification		Recruiting countries			Funder			Sponsor			Population
	CTIMP	non-CTIMP	UK	EU	Other	NIHR	Charity	Other	HEI	NHS	Other	
01	X		X			X			X			learning disability
02		X	X			X			X			learning disability
03		X	X			X				X		learning disability
04		X	X			X			X			learning disability
05		X	X			X			X			care home residents
06		X	X			X			X			care home residents with dementia
07		X	X	X	X						X	progressive CNS disorder
08		X	X			X			X			care home residents
09	X		X			X				X		ventilated in ICU
10		X	X			X				X		people with dementia
11		X	X			X			X			care home residents with dementia
12		X	X			X				X		care home residents
13		X	X				X			X		care home residents
14		X	X			X			X			care home residents
15		X	X			X				X		care home residents
16		X	X			X			X			care home residents
17		X	X			X			X			ventilated in ICU
18		X	X	X	X	X			X	X		traumatic brain injury
19	X		X				X		X			massive haemorrhage
20	X		X	X		X			X			intracerebral haemorrhage
21	X		X	X	X		X		X			intracerebral haemorrhage or stroke
22		X	X				X			X		ventilated in ICU
23	X		X			X				X		ventilated in ICU
24	X		X				X	X	X			traumatic brain injury
25	X		X			X			X			acute CNS disorder
26		X	X				X			X		acute cardiac event
27	X		X	X		X	X		X			stroke
28		X	X					X	X			stroke
29		X	X			X			X			surgery
30		X	X			X				X		ventilated in ICU

Key:

CTIMP	Clinical trial of an investigational medicinal product - governed by CTR
Non-CTIMP	Research other than a clinical trial of an investigational medicinal product - governed by MCA
EU	European Union
NIHR	National Institute of Health Research
ICU	Intensive Care Unit
CNS	Central nervous system
HEI	Higher education institute (e.g university)
NHS	National Health Service provider

Appendix 10. Interview topic guide for DECISION Study

Introduction

Introductions, reminder about purpose of the study, give details about the structure of interview, and explain about notetaking during the interview and audio recording. Reminder about pausing or stopping the interview at any time. Opportunity for any questions. Obtain consent.

Experience of involvement in a decision about a research study

Can you tell me about how you came to be X's carer?

Can you tell me how the question of X taking part in a research study came about? (Prompts: circumstances, people involved, details about the study)

What role did you feel you have/had in the decision-making process?

Factors involved in decision-making

How do/did you feel about being involved in the decision? (Prompts: comfort, confidence, burden)

What were your main concerns about making this decision?

Did you experience any difficulties?

Did you feel able/competent to make decision?

How did you involve others (if so who?), or did you make a decision on your own?

Basis for decision-making

So, thinking about what you based your decision on....

How did you come to a decision about whether X should take part in the study or not?

What factors do you think influenced your decision? (Prompts: features of the study, other options)

What do you think X's own view about the study would be? (Prompts: previous wishes, current preferences)

How much did your own views and what you know about X's views play a part in your decision?

How confident or certain did you feel about your decision?

Would it match their decision if they were able to say right now?

Would it be different if their wishes were clearly known?

How would you come to know? (Prompt: LPA?)

Thinking about X, their character, would it be important to X that they make their own decision?

Reflection on decision

What has happened since that time?

How do you feel about the decision now?

How does X feel about the decision? (If the person has since regained capacity) OR

How do you think they would feel (if not regained capacity)?

Reflection on ethical basis/concepts

Some people think that a decision like this should be based on what the person/patient themselves would have decided if they had been able to do so, but in other interview studies people have said that a number of other factors are involved.

What do you think of this? Do you feel the same or differently to what other people have said? (Prompt: reflect on previous answers and any tension between experiences and attitudes)

How do you see balancing what the person would have wanted alongside other factors/obligations?

Experience of role and making decisions

Have you been involved in making other decisions on behalf of X? (prompt: where live, medical treatment)

How do you see your **role** generally in relation to care of X? Is this different for decisions about research compared to others?

What did you feel about making **this decision** about a research study, compared to any other decisions about X you have been involved in? Did it seem the same or different to other decisions? (prompt: how? Basis for decision?)

Lasting Power of Attorney doesn't necessarily cover decisions about research, does that seem right to you, or not? Can you tell me more about why?

Ending the interview

Is there anything that you think would have helped you when you were involved in making this decision?

Is there anything else you would like to add that we haven't talked about?

Appendix 11. International Patient Decision Aid Standards instrument

Dimension	Item
Information	1. The decision support technology describes the health condition or problem (intervention, procedure or investigation) for which the index decision is required
Providing information about options in sufficient detail for making a specific decision	2. The decision support technology describes the decision that needs to be considered (the index decision)
	3. The decision support technology describes the options available for the index decision
	4. The decision support technology describes the natural course of the health condition or problem, if no action is taken.
	5. The decision support technology describes the positive features (benefits or advantages) of each option
	6. The decision aid describes negative features (harms, side effects or disadvantages) of each option.
	7. The decision support technology makes it possible to compare the positive and negative features of the available options.
	8. The decision support technology shows the negative and positive features of options with equal detail (for example using similar fonts, order, and display of statistical information).
Probabilities	1. The decision support technology provides information about outcome probabilities associated with the options (i.e. the likely consequences of decisions)
Presenting outcome probabilities	2. The decision support technology specifies the defined group (reference class) of patients for which the outcome probabilities apply.
	3. The decision support technology specifies the event rates for the outcome probabilities (in natural frequencies).
	4. The decision support technology specifies the time period over which the outcome probabilities apply.
	5. The decision support technology allows the user to compare outcome probabilities across options using the same denominator and time period.
	6. The decision support technology provides information about the levels of uncertainty around event or outcome probabilities (e.g. by giving a range or by using phrases such as "our best estimate is...")
	7. The decision support technology provides more than one way of viewing the probabilities (e.g. words, numbers, and diagrams).
	8. The decision support technology provides balanced information about event or outcome probabilities to limit framing biases.
Values	1. The decision support technology describes the features of options to help patients imagine what it is like to experience the physical effects.
Clarifying and expressing values	2. The decision support technology describes the features of options to help patients imagine what it is like to experience the psychological effects.
	3. The decision support technology describes the features of options to help patients imagine what it is like to experience the social effects.
	4. The decision support technology asks patients to think about which positive and negative features of the options matter most to them.
Decision Guidance	1. The decision support technology provides a step-by-step way to make a decision.
Structured guidance in deliberation and communication	2. The decision support technology includes tools like worksheets or lists of questions to use when discussing options with a practitioner.
Development	1. The development process included finding out what clients or patients need to prepare them to discuss a specific decision
Using a systematic development process	2. The development process included finding out what health professionals need to prepare them to discuss a specific decision with patients
	3. The development process included expert review by clients/patients not involved in producing the decision support technology
	4. The development process included expert review by health professionals not involved in producing the decision aid.
	5. The decision support technology was field tested with patients who were facing the decision.
	6. The decision support technology was field tested with practitioners who counsel patients who face the decision.
Evidence	1. The decision support technology (or associated documentation) provides citations to the studies selected.
Using evidence	2. The decision support technology (or associated documentation) describes how research evidence was selected or synthesized.
	3. The decision support technology (or associated documentation) provides a production or publication date.
	4. The decision support technology (or associated documentation) provides information about the proposed update policy.
	5. The decision support technology (or associated documentation) describes the quality of the research evidence used.
Disclosure	1. The decision support technology (or associated technical documentation) provides information about the funding used for development.
Disclosure and transparency	2. The decision support technology includes author/developer credentials or qualifications.
Plain Language	1. The decision support technology (or associated documentation) reports readability levels (using one or more of the available scales).
Using plain language	
DST Evaluation	1. There is evidence that the decision support technology improves the match between the features that matter most to the informed patient and the option that is chosen
	2. There is evidence that the patient decision support technology helps patients improve their knowledge about options' features
Test (for DSTs that are directed at investigations or screening tests)	1. The decision support technology describes what the test is designed to measure.
	2. The decision support technology includes information about the chances of having a true positive test result.
	3. The decision support technology includes information about the chances of having a true negative test result.
	4. The decision support technology includes information about the chances of having a false positive test result.
	5. The decision support technology includes information about the chances of having a false negative test result.
	6. If the test detects the condition or problem, the decision support technology describes the next steps typically taken.
	7. The decision support technology describes the next steps if the condition or problem is not detected.
	8. The decision support technology describes the chances that the disease is detected with and without the use of the test.
	9. The decision support technology has information about the consequences of detecting the condition or disease that would never have caused problems if screening had not been done (lead time bias).

Appendix 12. Acceptability tool for stakeholder feedback on the decision aid

Thank you for joining us today! We would like to know what you think about the decision aid and how it could best be used.

1. The length of the booklet is:

- Too long
- Too short
- Just right

2. The amount of information is:

- Too much
- Too little
- Just right

3. Do you think you would find this decision aid useful?

- Yes
- No
- Other

(comments):

.....

4. What did you think of the values clarification exercise in Part Four? Would it make the decision:

- Easier
- More difficult
- Other

(comments):

.....

5. What did you like about the decision aid?

.....
.....
.....
.....

6. What suggestions do you have that could improve the decision aid?

.....
.....
.....
.....

7. How would you best describe your experience or role in relation to this topic:

- I am a researcher/health or social care practitioner
- I am a family member/member of the public/member of a relevant organisation

Appendix 13. Prompts for stakeholder discussions on acceptability of the decision support intervention

1. Introductions - including why you have come along today

2. First impressions on format

(Prompts: paper format, booklet, A5 size, alternatives)

3. How do you see this being used?

(Prompts: face-to-face, provided/sent out ahead of time, available online via a study-specific website or a general website like Alzheimer's Society, or the research registry 'Join Dementia Research')

4. Who do you think this will be most useful for?

(Prompts: different settings e.g memory clinics/care homes/GP, relationships e.g spouse/parent, or ages)

5. Who do you think it will be least useful for?

(Prompts: different settings, relationships, not all ages)

6. Do you see any potential barriers or burdens to using it?

(Prompts: time, resources, attitudes, skills)

7. Can you see how these could be overcome, or think of ways around them?

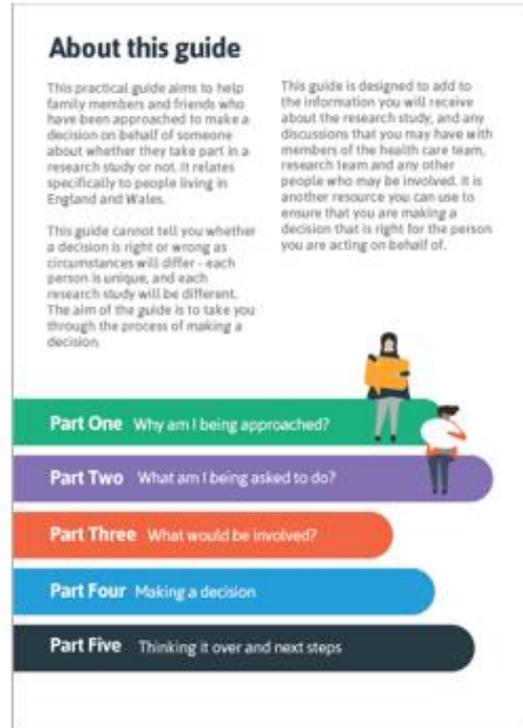
(Prompts: different way of delivering, training, resources)

8. How likely do you think it is to support family members?

(Prompts: do you think it will achieve its purpose, why?)

Do you have any other final comments?

Appendix 14. Decision aid for family members acting as research proxy



What if I need more information?

If feel you do not have enough information to make a decision please ask us, we will be happy to answer any questions. You can also consult others if you wish; this can include other family members or friends who may be able to advise what they think the person's wishes and feelings would be likely to be, or other care professionals.

Do I have to decide right now?

Take time to make a decision. Unless there are particular requirements for the study, you do not need to make a decision straight away. You may feel that you would like more time to consider the information and what it would mean to the person you represent to take part.

What's next?

If you consider that the person you represent would not want to take part, let us know. If you think that the person you represent would want to take part in the study, or would have no objection to taking part, we will ask you to record your decision on a special form. If you do not feel able to make a decision, or would prefer not to, let us know. You may be able to suggest an alternative person who could be approached.

Can I change my mind?

If you do decide that the person you represent would have wanted to take part in the study you can change your mind at any time. They will be withdrawn from the study without detriment to their care or treatment.

Next steps...



Part Five

Any questions?

What questions do you need answered to help you decide? You might want to show these questions to a member of the research or care team, or to others.

1. _____

2. _____

3. _____

4. _____

Part Five

Contact details of the person providing Guide...



Developed by
Victoria Shepherd,
Cardiff University, 2019



Appendix 15. Key messages for using the decision support intervention

Instructions for using 'Making decisions about research for others - a guide to decision-making' booklet

About the guide

This guide is intended for family members or close friends who have been asked to act as a consultee or personal legal representative on behalf of an adult who lacks capacity in accordance with the Mental Capacity Act 2005. It has been developed from research, including with families who have been involved in making decisions about research, and existing decision support aids. In addition to being evidence-based, it has been developed in accordance with the legal frameworks governing research involving adults who lack capacity in England and Wales. Different laws may apply in other parts of the UK.

How to use the guide

The booklet should be used in conjunction with the usual Patient Information Sheet for the research study under consideration. It is intended to provide information about the consultee or legal representative's role, and so to supplement the information about the study itself. It can be used to facilitate discussion with the consultee or legal representative as an interactive part of the consultation process, and also taken away and referred to at a later date.

It is not intended to tell the consultee or legal representative whether a decision is right or wrong. The aim of the guide is to take them through the process of making a decision. It provides a structured approach to decision-making, clarifying the patients' values and applying those values to the decision about participating (or not participating).

What the guide contains

The guide starts with **Part 1 Why am I being approached?** This provides some background information about why they are being involved in the decision-making process.

It is important that they understand whether they are being asked to provide informed consent on behalf of the person (for clinical trials of medicinal products) or to provide advice (other types of research). **Part 2 'What am I being asked to do?'** can be used to indicate this by ticking which of these the person is being asked to do.

The key message is that the consultee or legal representative should remember that they are not making a decision for themselves but need to think about what the person they represent would want, which may be different from what they would choose.

Part 3 What would be involved? encourages the consultee or legal representative to consider the possible advantages and disadvantages. There is space available for them to write down what they consider to be some of the relevant advantages and disadvantages to be.

Part 4 Making a decision breaks the decision down into 6 steps and contains a 'values clarification exercise' to help them to clarify how these relate to the wishes and preferences of the person they are representing.

The person acting as consultee or legal representative may still be unable to make a decision having received information about the study and their role in the decision. **Part 5 Thinking it over and next steps** has more information about what to do next.

Appendix 16. List of conference presentations and workshops given as part of PhD

Title	Format	Conference	Date
Deciding for others - informed consent and proxy decision-making for research involving adults lacking capacity	Poster	South West Society for Academic Primary Care meeting, Oxford	March 2017
Mental capacity and research – a researcher’s perspective	Oral	Mental capacity – action in research event, Cardiff	March 2017
Informed consent and proxy decision-making for research involving adults lacking capacity: a systematic review (framework synthesis)	Poster	International Clinical Trials Methodology Conference (ICTMC), Liverpool	May 2017
A review of the empirical and normative ethical issues in proxy decision-making for research participation: convergence and disjuncture	Oral	Post-graduate Bioethics Conference (PGBC), Oxford	September 2017
Research involving adults lacking capacity to consent – health and social care professionals' knowledge and understanding of the legal frameworks	Oral	PRIME Centre Wales annual conference, Swansea	October 2017
Involving people with dementia in research -who decides?	Invited workshop	Wales School for Social Care Research annual conference (WSSCR), Cardiff	February 2018
Mental capacity and consent for research	Invited workshop	Health and Care Research Wales support and delivery event, Cardiff	March 2018
Research involving adults lacking capacity to consent – health and social care professionals' knowledge and understanding of the legal frameworks	Oral	South West Society for Academic Primary Care meeting, Plymouth	March 2018

Managing consent for research involving adults who lack capacity – Population health trials	Oral	Population Health Conference, Cardiff	June 2018
Deciding for others: family members' experiences of decision-making for research involving patients who lack capacity to consent (<i>work in progress</i>)	Oral	International Conference on Communication in Healthcare (ICCH), Porto	September 2018
'You are being asked to advise': written information provided to representatives of patients lacking capacity to consent to research <i>*Winner Best Research Poster Award*</i>	Poster	International Conference on Communication in Healthcare (ICCH), Porto	September 2018
Research inequalities in health and social care: how can we address the exclusion of adults who lack capacity to consent? <i>*Winner Best Poster Award*</i>	Poster	Health and Care Research Wales annual conference, Cardiff	October 2018
Capacity and consent - Research in Care Homes	Invited workshop	Health and Care Research Wales annual conference, Cardiff	October 2018
Different ethics? Research involving adults who lack capacity to consent	Invited workshop	CASCADE ExChange practitioner workshop, Cardiff	November 2018
Ethical aspects of surrogate decision-making for clinical trials: a systematic review of empirical research	Oral	Society for Clinical Trials meeting (SCT), New Orleans	May 2019
Surrogate decision-making for clinical trials: a qualitative exploration of surrogate decision-makers' experiences	Poster	Society for Clinical Trials meeting (SCT), New Orleans	May 2019
Development of a complex intervention to support informed decision-making by family members acting as proxies on behalf of adults who lack capacity to consent to trials	Oral (accepted)	International Clinical Trials Methodology Conference (ICTMC), Brighton	October 2019