Prioritising health outcomes with patients and members of the public in the context of core outcome sets and National Institute for Health and Care Excellence guidance

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Abstract

Thesis Title: Prioritising health outcomes with patients and members of the public

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Introduction: Core outcome sets (COS) are agreed minimum sets of health outcomes that should be measured and reported in all relevant trials. COS development with patient and public input can help ensure the resulting COS reflects their needs and priorities. Similarly, patient and public input in health outcome selection of clinical guideline development can help ensure the resulting guidance is relevant to patients. This thesis investigated methods and perspectives surrounding patient and public input in COS and clinical guideline development and identified pointers to support future research in this area.

Methods: A survey of COS developers mapped commonly used methods of patient participation. A qualitative interview study explored participant experiences of the COS development methods. An ethnographic study investigated patient and public influence on health outcome selection in clinical guideline development. Discussion with a range of early stage researchers (ESRs) and European consultants enabled reflection on the roles of patients and members of the public in health research.

Results: Survey responses indicated that patient participants were included in 87% (141/162) of published, completed or ongoing COS. The Delphi survey was used singularly or in combination with other methods in 85% (119/140) of projects. The survey findings also highlighted the increasingly global nature of COS development. I interviewed 24 patients and health professionals about their experiences of participation in COS Delphi studies. Some interviewees struggled to understand the purpose of COS and aspects of the Delphi survey. Interviewees differed in how they interpreted and subsequently used the written documentation provided to COS participants. They wanted guidance regarding the use of the scoring system and stakeholder feedback. My ethnography included 230 hours of observations and 18 interviews. This identified the need for continued support and guidance for patients and the public by the committee, specifically, the chairperson, during guideline development. Specific recommendations include the use of plain language, specifically inviting patient and public input, and alternative methods of facilitating involvement including the use of COS previously developed with patient input. Discussion with ESRs and European consultants in combination with the other data in this study identified different perspectives including perceived challenges surrounding the role of patients in methodological health research and health outcome prioritisation. Further international conversation, collaboration and training in identifying and facilitating the various roles patients have in health research is needed.

Conclusions: There has been an increase in patient and public input in COS development, but a lack of parallel increased focus on how to optimise such patient and public input, internationally and across other methodological health research. The findings of this thesis will inform the development of guidance and research in these areas and help to improve methods. International collaboration is also needed to progress patient and public input in health research generally.

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Finally, I dedicate this thesis to my Mom and Dad, you have given me every opportunity in life. Your love and support has shaped me into everything that I am today, for that I am eternally grateful.

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Abbreviations

ABBREVIATION	Expansion
CADTH	Canadian Agency for Drugs and Technologies in Health
COMET	Core Outcome Measures in Effectiveness Trials
COS	Core outcome set
COS-STAD	Core Outcome Set Standards for Development
COS-STAR	Core outcome set standards for reporting
CROWN	Core Outcomes in Women's Health
EBM	Evidence based medicine
ECRIN	European Clinical Research Infrastructure Network
EMA	European Medicines Agency
EUPATI	European Patients Academy
EPITOME	Exploring Participant InpuT in Core Outcome Set DevelopMEnt
ESR	Early Stage Researcher
FDA	Food and Drug Administration
GC	Guideline committee
GIN	Guidelines International Network
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HOME	Harmonising Outcome Measures for Eczema
HP	Health professional
HTA	Health technology assessment
ICHOM	International Consortium for Health Outcomes Measurement
INVoLVED	Investigating Lay-members' Views in Clinical Guideline Development
IOM	Institute of Medicine
MiRoR	Methods in Research on Research
NHS	National Health Service

NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
OMERACT	Outcome Measures in Rheumatology
PCORI	Patient Centred Outcomes Research Institute
PICO	patient/problem/population, intervention, comparator and outcome
PoPPIE	People and Patient Participation, Involvement and Engagement
PPI	Patient and public involvement
RCT	Randomised Controlled Trial
WHO	World Health Organisation

Chapter 1: Introduction

1.1 Evidence- based medicine

Evidence- based medicine (EBM) has been described as the *"conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients"* (1). First described in 1991 as an approach in medical practice intended to optimise clinical decision making and subsequently patient care, EBM is characterised as the integration of individual clinical expertise with the best available clinical evidence from robust research studies (2). However, various writings indicate that EBM has a long history, with its philosophical roots found in mid-nineteenth century Paris and earlier (1). It includes major medical milestones such as William Cheselden's surgical research highlighting the importance of comparable treatment groups (3), James Lind's clinical trials into scurvy treatments (4) and John Snow's use of observational data to identify causes of transmission of cholera (5). According to a 2007 poll conducted by the British Medical Journal (BMJ), EBM was placed seventh among the fifteen most important developments that shaped modern medicine, ranking alongside milestones such as sanitation, vaccination, birth control and x-ray technology (6).

Practising EBM means that health research evidence is critically appraised to ensure its validity and trustworthiness. The practice of EBM hinges on five main steps (7):

1. Converting the need for information into an answerable question;
2. Searching for the best health research evidence;
3. Critically appraising the evidence for its validity, impact and applicability;
4. Integrating the evidence with critical appraisal, clinical expertise and patients' values, biology and circumstance;
5. Evaluating performance effectiveness and efficiency.

Searching for the best possible health research evidence (step 2) traditionally follows a ranked order of the available health research designs (8). Thus, a simple hierarchy of evidence was proposed to aid health professionals and researchers in evaluating health research evidence, Figure 1.1 (9, 10).

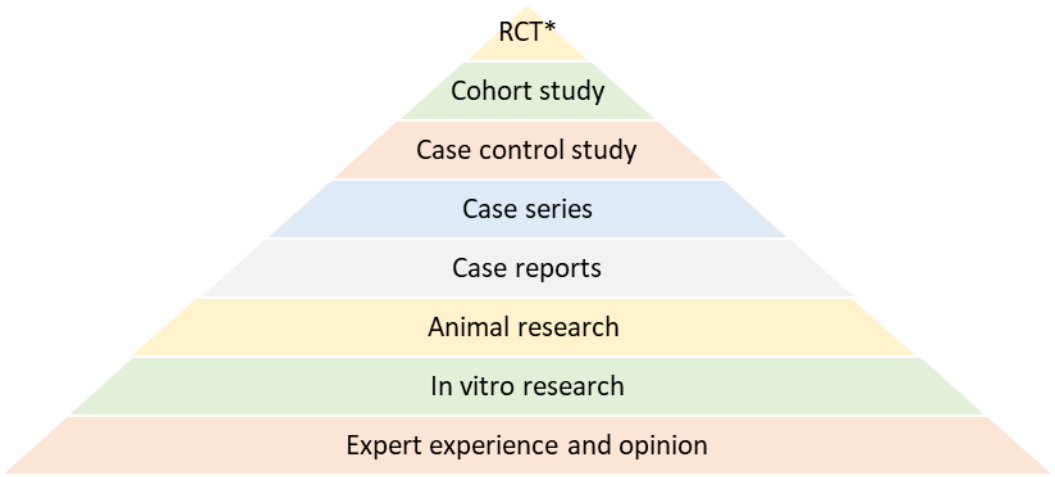

*Figure 1.1. The traditional hierarchy of evidence in clinical research design. Adapted from Djulbegovic and Guyatt (10) *RCT: Randomised controlled trial*

Since the original conception of the hierarchy of evidence was produced (Figure 1.1), it has been noted that randomised controlled trials (RCTs) can also be biased and do not immediately imply high-quality evidence (10). Thus, there have been many modifications of the hierarchy. Some of these modifications include systematic reviews, metanalysis and observational studies. By 2002 there were 106 systems to rate the quality of evidence (11). However, difficulties have arisen when researchers have applied these systems and considerable disagreement has emerged regarding how to assess the quality of various studies (12). In 2004, a group led by Atkins et al. evaluated six of the most prominent systems and reported that all had *"important shortcomings",* rendering them inefficient in informing decision making by patients, health professionals and policymakers (13). It has also been noted that most health professionals do not have the skills or the time to review bodies of evidence to inform their practice (14, 15). This led to a focus on increasing the availability of *"preappraised evidence based summaries"* (14) and the production of clinical practice guidelines (10) to ensure health care provision is rooted in high levels of evidence.

The realisation that *"i) traditional evidence hierarchies* (including that in Figure 1.1)*, ii) the importance of "processed" evidence for ensuring evidence-based practice and iii) the potential for clinical guidelines to improve practice and outcomes"*, led to a new system of rating evidence quality and grading the strength of recommendations (10). Known as the GRADE (Grades of Recommendation Assessment, Development

and Evaluation) system, this addresses all elements of a study including; design, risk of bias, precision, consistency, applicability, publication bias, magnitude of effect, and dose-response gradients. It provides a structured and transparent system for assessing the quality, credibility and validity of evidence (Table 1.1) (16). GRADE acknowledges the biases and limitations that can occur in RCTs and also enables the rating of high-quality observational studies, recognising their potential to provide definitive causal evidence (10). It is now in use by over 100 organisations including the World Health Organisation (WHO), Cochrane Collaboration and the National Institute for Health and Care Excellence (NICE) (17).

Study design	Quality of evidence	Lower quality if	Higher quality if
Randomised trial	High	**Risk of bias**	**Large effect**
		-1 Serious	+1 Large
		-2 Very serious	+2 Very large
	Moderate	**Inconsistency**	**Dose response**
		-1 Serious	+ 1 Evidence of a gradient
		-2 Very serious	
Observational study	Low	**Indirectness**	**All plausible confounding**
		-1 Serious	
		-2 Very serious	+1 Would reduce a demonstrated effect or
		Imprecision	
		-1 Serious	
	Very low	-2 Very serious	+1 Would suggest a spurious effect when results show no effect
		Publication bias	
		-1 Likely	
		-2 Very likely	

Table 1.1: Grading quality of evidence and strength of recommendations (GRADE) system to assess quality of evidence. Adapted from Guyatt et al., 2011 (16)

1.2 Health research studies

Health research studies are the main sources of evidence that informs EBM practice. These studies are undertaken with human participants to understand the impact of different tests, factors and interventions in preventing, detecting or treating disease. While the original hierarchy of evidence (Figure 1.1), indicates that the most reliable evidence comes from RCTs, later iterations of this hierarchy and the GRADE system

(Table 1.1) recognise non-randomised controlled trials and observational studies with comparison groups. RCTs, non-randomised controlled trials and observational studies fall into one of two main categories: observational studies or interventional studies.

Intervention studies typically include i) new drug treatments or new combinations of existing drug treatments, ii) new surgical methods or iii) behavioural interventions. All interventions have the aim of improving the prognosis, care and quality of life of patients and clinical trials are necessary to determine their efficacy and safety. Assessment of the results of a clinical trial determines whether the new intervention is to become a standard of medical practice. This assessment informs decision making at a population level via health policy and at an individual level by informing treatment decisions by patients and health professionals (18).

Intervention studies can be placed on a continuum, with *efficacy* studies progressing to *effectiveness* studies (19). Efficacy studies measure the performance of a new intervention under *"highly controlled conditions"* or optimum conditions which in turn restricts the patient sample and setting of the interventions' delivery (20). Effectiveness studies measure the performance of a new intervention under *"real-world"* conditions, such as in heterogeneous patient populations and in routine health care settings (21). In intervention studies RCTs are considered the gold standard in evaluating the effects of treatments, due to their robust methodological design (22).

In RCTs participants are randomised to one of two or more different groups; the test group receives the intervention being assessed and the control group receives either a placebo (*efficacy* study) or the current routine standard of treatment (*effectiveness* study) (19, 23, 24). Ensuring that RCTs focus on a specific *"well-built"* question is of paramount importance to the success of a trial and the best use of its resources (25). Thus, researchers typically follow the PICO (patient/problem/population, intervention, comparator and outcome) framework to focus their research.

1.3 Waste in the production of health evidence

As referred to in section 1.1 the production of health research evidence is not problem free. In 1757 James Lind described the *"need to remove a great deal of rubbish*" when introducing his review of various scurvy treatments (4). Over two hundred years later Doug Altman highlighted the *"scandal"* of waste in health research in a BMJ editorial (26), which is now considered one of the journal's most important articles (27). In it he pointed out that "*huge sums of money are spent annually on research that is seriously flawed through the use of inappropriate designs, unrepresentative samples, small samples, incorrect methods of analysis, and faulty interpretation"* (26). Since then there have been numerous publications, strategies and initiatives which aim to recognise and reduce waste in health research. In 2009, Chalmers and Glasziou estimated that 85% of all health research is wasted despite large financial investments, including public funding (28). They identified four linked stages within research practices that lead to waste in health research as outlined in Box 1.1

In 2014, The Lancet journal published a series of papers concerning waste in health research which advocated for greater consideration of research priorities (29), improved research design, conduct and analysis (30), obtaining appropriate regulatory and governance approvals (31), accessible research documentation (32) and appropriate research reporting (33). Other key milestones in recognising and reducing waste in health research are outlined in Table 1.2 (34). Health research should improve the care and quality of life of patients. However, as outlined above, flaws and bad practice within the research process render the research wasteful in many instances, leading to misspent investments and harm to patients. In 2018 Chalmers and Glasziou acknowledged that while progress had occurred *"research waste is still a scandal"* (34).

1. **Prioritising research questions that are irrelevant to health professionals and patients**
    - Irrelevant or low priority questions researched
    - Appropriate and important outcomes not considered or addressed
    - Health professionals and patients overlooked in setting research agendas
2. **Conducting unnecessary or inappropriate studies or study designs**
    - Failure to acknowledge existing evidence
    - Failure to reduce biases
3. **Failing to ensure accessible full publication**
    - Failure to publish full findings
    - Under reporting of negative results
4. **Selective reporting of research study information and findings**
    - Insufficient description trials interventions

Box 1.1. Four stages of waste in the production and reporting of research evidence. Adapted from Chalmers and Glasziou, 2009

Year	Type	Milestone
1966	**Publication**	"73% of research conclusions not justified" Schor and Karten (35)
1994	**Publication**	"Scandal of poor medical research" Altman (26)
1996	**Publication**	Consolidated Standards of Reporting Trials (CONSORT) statement (36)
1997-2000	**Initiative**	Foundation of ClinicalTrials.gov (37)
2006	**Network**	Foundation of EQUATOR (Enhancing the Quality and Transparency Of health Research(Centre (38)
2009	**Publication**	"Avoidable waste in research" Chalmers and Glasziou (28)
2010	**Initiative**	National Institute for Health Research (NIHR) launches "adding value in research" initiative
2012	**Publication**	"failure to replicate key preclinical cancer studies" Begley and Ellis, (39)
2013	**Initiative**	Launch of AllTrials campaign (40)
2014	**Publication**	Lancet series on "avoidable waste" (29-33)
2015	**Initiative**	Foundation of REWARD (Reduce Research Waste and Reward Diligence) Alliance (41)

Table 1.2. Various publications, initiatives and strategies, which aim to recognise and reduce avoidable waste in research. This table has been adapted from Glasziou and Chalmers, 2018 (34).

1.4 Ensuring patient-centred health research

Chalmers and Glaziou recognised the waste in health research that arises from the formulation of research questions that are irrelevant to patients (28). If done appropriately and meaningfully, patient and public input can help ensure research is patient-centred, consequently reducing waste in health research and ensuring results are valuable and credible (42). Patients and members of the public can be

included in health research via patient and public involvement and patient participation. In UK health research, a clear distinction is drawn between patient and public involvement (PPI) and patient participation (43).

PPI is defined as research *"being carried out 'with' or 'by' members of the public" not just "'to', 'about' or 'for' them*" (43). PPI contributors also known as patient research partners are often seen as members of the research study team and actively contribute to the design, conduct and dissemination of a health research study (43). In patient participation larger numbers of patients are typically recruited to contribute to research studies during the data collection phase exclusively.

It is important that the distinction between the two different roles is maintained, although it is often conflated and blurred. Patient participants and PPI contributors carry out very different activities and thus, have very different contributions to health research projects. There is a large, well-developed body of literature and guidance available to support contribution and input from both these roles. For researchers and patients to benefit from these resources it is important that their role within specific health research projects is clearly defined so the patients' input can be as meaningful as possible. The distinction is also important in terms of ensuring ethical research (44). Health researchers in some countries such as the UK, require ethical approval to conduct a research project with human participants, this helps ensure ethical standards and principles are upheld, such as risks and benefits assessments (45). However, PPI contributors are seen as equal members of research teams, thus, ethical approval is not required to facilitate their involvement (46). This difference in ethical requirements means the importance of researchers understanding the distinction between *involvement* and *participation* is paramount, so they can ensure that their health research project is ethical and appropriately supporting the patients and members of the public included.

1.4.1 Including patients in health research via involvement and participation

Researchers are increasingly subscribing to a patient-centred research system by actively seeking PPI contributors at various stages of their health research studies (47, 48). There are numerous reasons for involving PPI contributors in health research, from ethical standards, funding requirements, insight into patients'

experiential knowledge and reduction of waste in research (as outlined in section 1.4). PPI is increasingly seen by many as a moral and ethical imperative, as patients are the ultimate end users of health research, thus, they should be involved in guiding it (49, 50). Hutchinson et al. suggest that health research should be considered a social enterprise rather than exclusively *"knowledge production"* (51), in which patients are the ultimate consumer and thus, a fundamental and natural part of the research process. Furthermore, PPI contributors can be part of the mechanism which brings accountability and transparency to health research studies and practices (52).

PPI in health research is also a funding requirement in many countries. Funders in Australia, Canada, the UK, the USA and Europe encourage PPI in research and have various initiatives and funding organisations who have clear guidance to facilitate this. In the UK, the National Institute for Health Research (NIHR) established the national advisory group INVOLVE. The central aim of INVOLVE is to bring expertise together and lead the advancement of active PPI in National Health Service (NHS), public health and social care research. INVOLVE instruct researchers on how to involve patients and members of the public in the development of funding applications, research design and conduct of research (43). In the USA, the Patient Centred Outcomes Research Institute (PCORI) supports and funds research led by patients and members of the public (53). Promisingly, a 2016 survey of 50 research projects funded by PCORI indicated PPI in 90 % of the studies (54). Within Europe, the European Patients Academy (EUPATI) serves to connect PPI contributors with various health research projects in both academia and industry (55).

The insights gained from patients' experiential knowledge is also an attractive reason for researchers to involve PPI contributors in their health research projects. Within clinical trials, PPI has the potential to improve enrolment of patient participants, particularly if the PPI contributors also have lived experience of the specific health condition (56). Brett et al. argue that PPI contributors help build respect and relationships between health researchers and the public, thus increasing the acceptability of the research in the community (48). Brett et al. also suggest that by offering a patient perspective, PPI contributors can help inform the design of

appropriate recruitment strategies and the development of suitable data collection tools for patient participants (57).

Participation of patients in health research has long been common practice. As mentioned above patient participation to health research studies typically occurs during the data collection phase and usually occurs in larger numbers than PPI. It is the crucial participation of patients in studies, such as trials and cohort screening programmes, that has enabled the advancement of healthcare. Patient participants often provide data such as bodily markers to assess health outcomes, tissue samples or their bodies to health research. However, they were usually excluded from decisions regarding the research agenda and process or use of their data (44). In recent years, the importance of combining experiential data, gained via patient participation, into research on patients' health outcomes in studies is increasingly recognised. This experiential data is collected via a range of quantitative and qualitative methods designed to elicit information from patients about their experiences, needs and priorities (58). In turn this data can inform future research and help ensure it is centred on the needs of the patient. For example, Matza et al. conducted a series of qualitative interviews with patient participants with multiple sclerosis to gain patient experiential insight of relapse, to inform the development of new methods of identifying relapse episodes (59). Similarly, McCaffrey et al. conducted focus groups with patient participants who opted for integrative medicine approaches in their care plan to identify the motivations behind their decisions (60).

1.5 Outcomes in clinical trials

To make treatment decisions that suit the needs of the patient we require evidence that assesses the effectiveness and safety of an applied intervention (61, 62). This evidence is generated from the numerous trials that record and measure the effects that different illnesses, conditions and treatments have on components of a patient's clinical and functional status, through what are known as "outcomes" (61, 63). Examples of outcomes include quality of life, treatment costs, fatigue, white blood cell count, pain, mortality and adverse incidents or harms. These measurements or observations are the "outcomes" in the PICO framework, and usually refer to *"what*" is measured, and *"how"* it is measured (64). Within clinical trials, the *"how"* can be

defined as the measurement or observation used to capture and assess the effect of treatment such as assessment of side effects (risk) or effectiveness (benefits) and is referred to as the outcome measurement instrument (also known as an outcome definition) (61). It has been recommended that outcomes and outcome measurement instruments are defined at the time the trial is designed and should be specified in detail in the study protocol to avoid confusion and ambiguity (61, 65). However, doing so is complicated by confusion regarding the various definitions for outcomes and outcome measurement instruments (61, 66), as there is no internationally agreed standard, which is something future work could consider consolidating. The focus of this thesis is on the *"what"* is measured not the *"how"* it is measured.

Clinical trials are typically conducted in a series of early and later phase trials. Early phase trials usually investigate whether a drug is safe and the side effects it may cause, and subsequently provide an early assessment of the efficacy of the treatment. Later phase trials aim to test whether a new treatment results in overall benefit for the patient and is better than existing treatments or standard of care (referred to as effectiveness trials). Thus, the outcomes measured in the different phases will, and should vary, for example early phase trials in cancer may measure outcomes such as tolerability, toxicity, discontinuation and tumour response (67, 68), whereas later phase trials would measure outcomes such as overall survival (69). The focus of this thesis is on the outcomes of relevance in later phase trials that aim to inform the evidence base about treatment decision-making.

Typically, late phase clinical trials include multiple health outcomes of interest and usually the main health outcomes are those required for decision-making. The primary health outcome is typically the most relevant to stakeholders such as patients, health professionals, policy makers, funders and researchers. Usually, the primary health outcome represents the measure of greatest therapeutic importance (70) and sample size calculations for that measure are based on it (71). Researchers can suggest more than one primary health outcome if they are relevant to the research question. Secondary health outcomes measure other beneficial or harmful effects still important for overall decision-making and can sometimes explain

additional effects of the intervention (72). New interventions are assessed for safety and effectiveness by comparing the differences measured in health outcomes between groups.

1.5.1 Health outcomes measured and the link to waste in research

As noted in Box 1.1 in section 1.3, insufficient attention to the measurement of health outcomes in clinical trials can cause avoidable waste in the production and reporting of research (28). This leads to ineffective use of health care resources that are already limited (32). Problems arise due to i) inconsistency and heterogeneity across health outcomes measured (73), ii) health outcome reporting bias (74) and iii) the use of health outcomes that are irrelevant to end-users including patients (75).

1.5.2 Inconsistencies in health outcomes

Clinical trials within the same health condition or illness often include different health outcomes. Additionally, when the same health outcomes are measured different instruments are often used. Such inconsistency and heterogeneity gives rise to difficulties in summarising the evidence, as the results cannot be adequately compared and contrasted. The evidence is thus limited and this in turn restricts the decisions of end-users such as health professionals and patients. The problem of inconsistency and heterogeneity is evident across multiple health areas. For example, a 2013 review of oncology trials found that more than 25,000 health outcomes appeared only once or twice, with the authors stating *"the lack of a standard ontology as a major concern"* (76). Elsewhere, a 2016 review of the Cochrane Kidney and Transplant Specialised Register described the health outcomes as *"extremely heterogeneous"* noting the use of 6158 different measurements in 100 different outcome domains in 205 trials for paediatric chronic kidney disease. The authors further noted the lack *of "clinical and patient-centred outcomes*" in the reviewed studies (77). Similarly, a survey of 10,000 trials involving people with schizophrenia reported the use of 2194 different health outcome measurement scales (78).

1.5.3 Outcome reporting bias

Selective or biased reporting limits decision-making regarding the distribution of funds, research priorities, design and conduct of studies and crucially, patient

treatment and care. Within clinical trials the issue of selective reporting of health outcomes on the basis of the results, known as outcome reporting bias, is a recognised problem in published randomised trials (79, 80). It is defined as the publication of a selection or subset of the originally measured health outcomes based on their results (74), usually with a bias toward publishing health outcomes that are statistically significant (81). A 2004 systematic review of 519 randomised trials reported that in 33% of trials there was at least one unreported efficacy outcome, and in 28% of trials there was at least one unreported harm outcome (82). A 2008 review of study publication bias and outcome reporting bias demonstrated that 40-62% of studies had at least one primary health outcome that was changed, introduced or omitted (83). Outcome reporting bias has also been shown to negatively affect the conclusions of systematic reviews designed to collate the evidence and inform decision-making (84).

1.5.4 Relevance of outcomes to patients

It is critically important that appropriate and relevant health outcomes are selected, measured and reported. They need to include outcomes relevant to all end-users including patients, health professionals and policy makers. Selecting appropriate and relevant health outcomes increases the validity and credibility of the research question and resulting evidence. As patients are the ultimate end-users of research, it has been argued that there is a moral imperative to include their priorities (85). However, existing evidence suggests studies have used health outcomes that suit the priorities of researchers and pharmaceutical industries rather than those that are meaningful to patients or clinicians (86, 87). For example, a systematic review of health outcomes used in clinical trials of inhaled corticosteroids for children with asthma reported that the majority of studies mainly measured health outcomes relating to short term disease activity, whereas long-term outcomes such as safety of treatment, which is known to be important to patients, were largely overlooked (88). The authors suggest the potential reason for this mismatch was that the trials and their outcomes reflected the requirement of the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) (88). Crowe et al. also suggest mismatches exist between the research being undertaken and the areas patients and

health professionals want researched across a range of health conditions in their 2015 publication (86).

Patient reported outcomes are those directly reported by patients. Patient reported outcome measures (PROMs) are designed to capture the patient's assessment of how they function or feel regarding their health or treatment (89). For example, the Oswestry Disability Index (ODI) and the Roland Morris Disability Questionnaire (RMQD) are examples of PROMs used to measure the impact of low back pain on patients (90). PROMs have the potential to contribute significantly to clinical research provided they accurately and meaningful capture the patient's perspective (89, 91), as they provide a patient voice in evaluating healthcare(92). Patient inclusion in the development, application, evaluation and interpretation of PROMs is widely acknowledged as increasing the quality and validity of the measurement (93-96) and is supported by institutions such as PCORI (53). On the other hand, concerns have been raised that patient input in PROM development can be cursory and poorly reported (89). A 2016 scoping review of patient involvement in the development of 193 PROMs indicated that patients are not involved in all phases of PROM development. Their input is mostly sought during the item development and testing for comprehensibility phases (97). Further, the authors report that patient involvement in PROM development has not increased over time (97). It has also been suggested that there is a lack of guidance for developers on how patient input can aid development (98). However, there are continued calls for active collaboration between developers and patients (89) and a recent framework for incorporating PPI in PROM development offers further guidance to developers (98).

1.6 Standardising health outcomes

1.6.1 Core outcome sets

One potential answer to the problems of inconsistency, heterogeneity and outcome reporting bias in clinical trials is the development and application of agreed standardised sets of health outcomes, known as core outcome sets (COS) (99). A COS is defined as a minimum set of agreed standardised health outcomes, which should be measured and reported in all trials in a specific condition (100). It is considered a fundamental list of health outcomes (101), not an exhaustive list and researchers are

expected to measure additional health outcomes in their trials as they consider appropriate (102). As previously noted, there are two distinct aspects to measuring outcomes; *"what"* is measured and *"how"* it is measured. For example, taking the health condition of back pain, the *"what"* could include pain intensity, physical functioning and health related quality of life. A research team have a multitude of *"how"* instruments to measure it such as the Oswestry Disability Index (ODI) version 2.1a and Multidimensional Pain Inventory (MPI-PI) (103). When developing a COS, *"what"* health outcomes to measure are usually identified first, then *"how"* to measure these health outcomes can be determined, including the time points at which those measurements should be taken.

Uptake and implementation of COS will lead to higher quality trials, as COS will reduce heterogeneity and inconsistency between trials, as all trials would measure and report the agreed health outcomes. Thus, COS use should reduce waste in trial research and enhance the value of evidence synthesis (104). COS have potential for use in other areas of health research, including systematic reviews of relevant trials, clinical audits (105) and, more recently, in routine care and practice (106).

1.6.2 Core outcome set initiatives

There have been coordinated efforts in various disciplines to standardise health outcomes. In the 1970s the WHO Handbook of guidelines recommending the minimum requirements for data collection in cancer trials was a result of over 30 different trial groups coming together to form consensus on what should be measured (107). More recent initiatives that focus specifically on particular areas of health include the work of the Outcome Measures in Rheumatology (OMERACT) collaboration, which promotes the use of consensus based COS in clinical trials in rheumatology (108). Similarly, the Harmonising Outcome Measures for Eczema (HOME) Initiative, is an international group developing COS for use in eczema trials (109). While the Core Outcomes in Women's and Newborn Health (CROWN) Initiative, is a consortium of obstetrics, gynaecology and neonatal journals which promote the development and reporting of COS within women's health research (110). There are also initiatives to promote the development and uptake of COS for routine practice. One such example is the International Consortium for Health

Outcomes Measurement (ICHOM), which organises international collaborations between health professionals, outcomes researchers and patient advocates to standardise COS in a range of medical conditions for use in clinical practice (111). Increasingly, COS are developed to be used in both research and clinical practice, recognising the overlap that exists between the two areas (112).

1.6.3 COMET Initiative

Complementing the various initiatives outlined above is the Core Outcome Measures in Effectiveness Trials (COMET) Initiative. It was founded in 2010 as a non-disease specific organisation to bring together people interested in the development and application of COS. COMET's aim is to *"collate and stimulate relevant resources, both applied and methodological, to facilitate exchange of ideas and information, and to foster methodological research in this area*" (73). The COMET Initiative uses several ways to achieve that aim including the development and maintenance of the COMET website and database (104), the development of the COMET handbook to promote methodological guidance (100), hosting international conferences which include training workshops (113-115) and the development of the DelphiManager (http://www.comet-initiative.org/delphimanager/) software tool which can be used in the development of COS. In 2014, COMET set up the "PoPPIE (People and Patient Participation, Involvement and Engagement) Working Group" to ensure patients and members of the public are considered in COS development.

The COMET database is publicly accessible and searchable; it contains a comprehensive catalogue of COS developments that are published, ongoing and planned. It is updated every year via a systematic review. The first review was conducted in 2013 (73) and four updates have since been conducted in 2015, 2016, 2017 and 2018 (112, 116-118). COS developers are encouraged to register their planned or ongoing studies for free on the database. The database allows COS developers to search for other relevant COS, thus reducing the potential for duplication of effort. It also enables trialists and researchers to search for COS relevant to their trials. The website contains other resources such as plain language summaries, COS protocols and systematic reviews of health outcomes measured in trials.

COMET also conducts methodological research regarding the design, conduct and reporting of COS developments. The content of the COMET handbook ranges from the explanation of the history and need for COS, to methods, techniques and considerations for developing COS and advice for implementing and updating COS (100). In addition, COMET has published recommendations for COS protocol documentation (119), minimum standards in COS development (106) and COS reporting (120). Ongoing work includes assessing the uptake of completed COS by trialists (121) and PPI in COS development, design and conduct (122).

COMET encourages inclusion of all relevant stakeholders in COS development, comprising researchers, health professionals, patients and members of the public (106), thus increasing the measurement of health outcomes measured relevant to the end-user. Thus, a role of PoPPIE is to oversee the PPI, patient participation and engagement activities of COMET to help ensure meaningful input of the patient voice in COS through appropriate methods of development and dissemination (123) .

1.6.4 Methods for developing core outcome sets

COS development is facilitated by a number of qualitative and quantitative methods, which are used singularly or in combination to enable the participation of all relevant stakeholders including patients and members of the public. These methods include Delphi surveys (124, 125), nominal group technique (NGT) (126), consensus meetings (127), focus groups (128), questionnaires, and interviews. The characteristics of these methods are outlined in Box 1.2. The 2016 COMET systematic review update indicated an increase in the proportion of studies using literature/systematic reviews and the Delphi survey (116). The 2017 update highlighted an increase in the use of mixed methods, including Delphi surveys (118). The 2018 update highlighted the continued high use of mixed methods including the Delphi survey (112). Examples of studies that have used a combination of methods include Harman et al. (127) and Blazeby et al. (129), with each using the Delphi survey followed by consensus meetings. COS has also been developed by systematically reviewing the relevant literature, both as a standalone method which resulted in recommendations on health outcomes to measure (130) and more recently in combination with other methods (131).

	Individual responses from all participants	Group interaction	Non face-to-face (Telephone, email)	Face-to-face	Participant anonymity
Focus group	No	Yes	No	Yes	No
Individual interview	Yes	No	Yes	Yes	Yes*
Nominal Group Technique	Yes	Yes	No	Yes	No
Questionnaire	Yes	No	Yes	No	Yes
Delphi survey	Yes	No	Yes	No	Yes
Consensus meeting	No	Yes	No	Yes	No
Systematic review	No	No	No	No	No
Stakeholder discussion	No	Yes	No	Yes	No

*Box 1.2 Characteristics of methods used in COS development. * The participant is known to the interviewer, otherwise it is anonymous*

Qualitative Approaches

As noted above, qualitative approaches such as interviews and focus groups have been used in COS development (132). These methods enable in-depth exploration of known and unforeseen participant priorities without the constraints of more structured methods like questionnaires which have fixed answers. Usually the qualitative approach is used to develop the long list of health outcomes which is then used to inform the Delphi survey (133). This approach helps developers ensure that the list is more patient-centred rather than simply relying on systematic reviews of the literature which may prioritise health outcomes important to researchers only. Keeley et al. further note that qualitative approaches to COS development can help developers understand patient prioritising of health outcomes, the scope of health outcomes and crucially the language used by patients which can then be used in the Delphi survey to further ensure it is patient-centred (133).

Nominal Group Technique

Nominal group technique (NGT) is a commonly used formal consensus development method (134, 135) used to draw out the priorities of different stakeholders and achieve consensus in a face to face environment. By using pre-determined, structured questions, NGT seeks to elicits responses and ideas from each individual. These are then discussed by the entire group. By collaboratively reviewing and discussing individuals' responses the group can reach consensus on priorities by voting or rating each idea. The process of discussion and voting can occur a number of times before the final group opinion is complied. The key feature of NGT in comparison to other methods is that it aims to allow the expression and collation of disparate ideas, with a view of reaching consensus. If conducted and facilitated well it enables full immersion in decision-making while preventing domination of one area of discussion over another. It also aims to ensure the inclusion of each participant's view and minimises the influence of power differentials between individuals. It has been argued that the collaborative nature of NGT can increase the participants' sense of ownership and accountability (135).

Delphi Survey

The Delphi survey is the most frequently used method for stakeholder participation in COS development. The Delphi survey was originally developed by the Rand Corporation in the 1950s (136). The survey has since been modified to suit consensus development across a range of disciplines from health research to financial forecasting. Within the COS development framework, it is used for achieving "*convergence of opinion from experts*" (stakeholders) on the importance of different health outcomes in sequential rounds of questionnaires (100). Participants rate a long list of health outcomes, usually on a numerical scale such as Likert scale 1-9, although other ranges are used. Participants can suggest further health outcomes if they believe something important is missing from the long list. Participants may also provide feedback on individual health outcomes listed. After each round (Delphi surveys in COS development typically involve two or three rounds, depending on the decision of the research team (137)), the rating responses are summarised and fed back anonymously so that stakeholders can consider the views of others before re-rating the same health outcomes. The number of outcomes in each round varies between COS projects, with some as low as 10 outcomes per round and others with over 100 outcomes per round (137). In the Delphi survey approach, participants maintain their anonymity and have no direct communication with each other, reducing the influence of power differentials between different stakeholders that can otherwise be problematic with direct communication between participants (138). Additionally, the survey is less resource intensive than other methods as it is conducted remotely thereby eliminating the costs associated with face to face research methods.

Consensus meetings

In many COS developments the Delphi survey is followed by a consensus meeting, in which stakeholders meet and review the Delphi survey results. They can also discuss the inclusion or exclusion of any health outcomes on which no consensus was reached during the Delphi survey. Alternatively, the consensus meeting can also be a stand-alone method. Consensus meetings can either follow formal approaches such as nominal group techniques or rely on informal fluid discussion. Both

approaches typically require the presence of a skilled facilitator who is not a member of the research team to ensure that all stakeholders have an equal opportunity to get involved. COS developers might invite all stakeholders to one meeting, whereas other developers might consider separate meetings for different stakeholder groups e.g. health professionals and patients, in an effort to reduce the influence of power differentials between health professionals and patients (139).

1.6.5 Patient and public inclusion in core outcome set development

The importance of including patients and members of the public in deciding *"what"* outcomes to include in COS development is increasingly recognised. For most conditions, many different health outcomes could be included in a COS. When patients have not been included in the COS development process, important health outcomes have been overlooked (140, 141). The most clearly demonstrated example of this is in the COS development for rheumatoid arthritis. Initially this COS was developed without input from patients and members of the public. However, at a subsequent OMERACT conference, a patient consultation identified fatigue as a health outcome of great importance to patients (140), a finding which was confirmed in further studies on patient perspectives(142, 143). Fatigue has since been included in the COS for rheumatoid arthritis.

Thus, the inclusion of patients and members of the public in deciding which core outcomes should be measured, reduces the danger of omitting important health outcomes. However, examples also exist where health professionals have identified areas that patients were reluctant to talk about in focus groups(144). While instances like this may be due to the specific methods of accessing patients' perspectives being unsuitable, rather than the patients not considering these health outcomes, it nonetheless highlights the need for multi-stakeholder approach to COS development. As outlined in section 1.6.3 the COMET Initiative recognises the expertise and crucial contribution of all relevant stakeholders in developing COS, and advocates for the inclusion of PPI contributors and patient participants (123) alongside researchers and health professionals.

COMET suggest that PPI in COS development can aid developers in recruiting relevant patient populations, pre-empting ethical issue that may arise, devising an

appropriate study design and supporting information, ensuring that the COS is relevant to patients and aiding dissemination of the study results (100). Examples of PPI in COS studies include Morris et al. who engaged and consulted with parents at various stages of the research process to design a plain language summary of the COS results (145). The COMET database has a list of useful PPI resources and methodological guidance for COS developers. Furthermore, there is ongoing research on PPI in COS development and the methods and processes surrounding it (122).

The value of including patients as participants in COS development has also gained recognition. While a 2013 systematic review found that only 16% (31/198) of published COS studies published up to August 2013 reported patient input (73), a 2018 update of this review indicated patient input in 28% (62/225) of COS developments published to March 2017 (118). Patient participants take part in COS development via a range of methods as described above. However, it is uncertain which are most suitable, accurate and efficient. This is likely to depend on several factors such as health condition, target population and the available resources. (146). This is especially important for COS studies concerning globally prevalent health conditions (147, 148), otherwise these COS studies will not contribute to improving global health or reducing waste in research (149). COMET's second systematic review update reported an increase in international stakeholder participation from continents other than Europe or North America, from 33% before August 2013 up to 55% in January 2016 (147), due to increased input from stakeholders in Australasia and Asia. The third COMET systematic review update found only 16% of COS studies published before March 2017 had input from stakeholders in low and middle income countries (150). From the COS reports, it is largely unclear whether these international stakeholders include patients and members of the public, and if so, how many. International health professionals can be engaged in COS development via professional organisations (151) or personal networks (61, 152), however the equivalent networks for patients and members of the public do not necessarily exist. COS developers have previously indicated that including international patients raises various difficulties including language, resource implication, ethics and recruitment

(61, 123, 153). Efforts to include international patients usually centres on small numbers based on personal networks (61, 154). Yet promisingly, novel approaches for international patient and public participation are emerging. For example, researchers are developing a COS with approximately 80 international patients in seven countries via interviews with trained health professionals who follow a standard protocol (155). Other COS developers have accessed international patients via patient organisations and invited them to participate in online surveys (156).

1.7 The role of outcomes in clinical guideline development

As referred to in section 1.1 the realisation that health professionals do not have the skills or resources to assess the quality of all relevant evidence to inform their practice has led to a focus on increasing the availability of *"preappraised evidence based summaries"* (15) and the establishment of organisations such as the Cochrane Collaboration to systematically review evidence (128). It has also led to an increased focus on the implementation of clinical guidelines (11), which are defined as *"systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances"* (157, 158). The increased focus on the use of clinical guidelines gave rise to the production of clinical guidelines by a number of national or professional bodies (129) such as the NICE (126), who develop clinical, public and social care guidelines for use in England. The role of the clinical guidelines is to reduce variation in the availability and quality of NHS treatments and care (159). Prior to the establishment of guideline development organisations such as NICE, clinical guideline development was largely based upon expert opinion and limited to reviews of the evidence (160). Nowadays, guideline development groups typically follow a standard method in which evidence, usually in the form of systematic reviews, is used in combination with the expertise of relevant stakeholders to assess benefits and harms (161, 162), thus establishing recommendations for clinical practice (163). There are numerous methods through which evidence is synthesised and discussed for clinical guideline development (163). This includes systematic reviews (164), meta-analysis (165), reviews of the cost effectiveness of health interventions (166), and formal and informal consensus methods (167). In 2011 the Institute of Medicine (IOM) published standards for

clinical guideline development (162). They stated that guidelines should be developed as follows (162, 168):

1. By committees with negligible conflicts of interest;
2. Every recommendation should be informed by a systematic review of the evidence;
3. Every recommendation should be explained and rationalised;
4. Recommendations should be described in a standardised manner;
5. Recommendations should be rated according to its strength and the committee's confidence in the quality of the supporting evidence.

The GRADE system (outlined in section 1.1) is a common method used to assess and rate recommendations in clinical guideline development (17, 159), but other systems also exist (169).

Clinical guidelines are important tools for improving patient care (170, 171). They are also used to inform patients about different types of treatment and care options, thus, the guidance must be presented in forms accessible to patients (159). For clinical guidelines to have their desired effects they must be implemented but reports suggest compliance with guidelines varies (172, 173), which is wasteful and puts patients at risk of substandard treatment and care. The production of health professional and researcher centred clinical guidelines has been identified as one of the potential barriers to clinical guideline implementation (174). Other barriers to compliance with clinical guidelines can arise within policy and decision making for healthcare systems. For example if a clinical guideline was developed without due consideration for cost effectiveness it may negatively impact other areas of the healthcare system, thus rendering the clinical guideline inefficient for use (175, 176). Difficulties in applying clinical guidelines to inform the care of patients also exist (177). Thus, there is growing recognition of the importance of including patients and members of the public in clinical guideline development, ensuring these are patient centred, address patient needs and preferences and are subsequently implementable (178). In recognition of this, numerous guideline development

organisations, including the Guidelines International Network (GIN) (179), and NICE (159), now place patient and public inclusion as a key component of their processes.

Much has been written about mechanisms and frameworks for engaging patients and members of the public in guideline development. A 2011 systematic review of PPI programs for clinical guideline development identified reasons for patient and public inclusion across the various programs. These included; incorporation of patient values, preferences and knowledge into the guideline and improving the comprehensiveness and implementation of the guideline (180). There are a number of methods for involving patients and members of the public in clinical guideline development. Boivin et al. used a typology devised by Rowe and Frewer (181) to categorise these methods, comprising *"direct participation", "consultation" or "communication"* (180, 182).

Within the UK, NICE relies on all three types of methods outlined above. NICE committees and other working groups must include at least two members who provide a patient/carer perspective to the guideline development (159). Within this type of direct participation it is recommend that patients and members of the public are selected based on their ability to consider the evidence objectively and make recommendations that depart from preconceived views or self-interests (183).

NICE also facilitate patient and public inclusion by *"consultation"* or indirect input. This includes patients and members of the public inputting to guideline development by focus groups, written testimonials and video-taped interviews that are then presented to developers. NICE further facilitates patient and public inclusion in *"communication"* as NICE guidance is produced in plain language versions and made available to patients, carers and the public. NICE works with patient organisations to disseminate this guidance and receive feedback (159).

Finally, guideline groups also host *"open forums"* or *"scoping workshops"* in which various stakeholders, including patients and members of the public, have an opportunity to comment on the guideline at various junctures including topic, scope, content, final recommendation and implementation (184, 185).

Importantly, the discrepancies in health outcome relevance outlined in section 1.5.3 also have an impact on clinical guideline development. Results from clinical trials are one source of data used to inform health technology assessments (HTA) of new treatments, other sources include observational studies and integrative methods in which data and information from existing sources is combined, such as in economic modelling. The results from HTAs generate information on the clinical- and cost-effectiveness of a technology or intervention and are then used to inform clinical guideline development for routine practice and care. Due to patients' unique lived experiences of disease and treatments, the importance of their inclusion in HTAs and clinical guideline development is increasingly recognised (186, 187). A 2015 evaluation on the influence patient insight had on HTAs for the Canadian Agency for Drugs and Technologies in Health (CADTH) Common Drug Review showed patient perspectives can be integrated into HTAs. However, a review of 30 drug assessments showed that from 119 health outcomes that patients identified as important, only 61 (51 %) were measured in trials (188).

A potential solution to these discrepancies is the active endorsement by guidance development organisations of the use of COS and the COMET database. In their methods manual NICE advocate using the PICO approach for developing questions about interventions and recommend searching for suitable COS via the COMET database (159). NICE further advise the use of COMET's published recommendations for minimum standards in COS development (106) and COS reporting (120) to assess quality and validity. Upstream of guideline development at NICE, the surveillance team assess the need for updating previously published guidelines. This team is currently conducting exploratory work investigating whether published COS can help ascertain if the health outcomes discovered during surveillance are important enough to require a guideline update (ref- personal communication, NICE surveillance team member- July 2018).

Along with other appropriate stakeholders, guideline developers are increasingly included in some COS studies. This further ensures that COS reflect the most important health outcomes to all groups and will result in more effective and efficient use of published research, from informing clinical trials to guideline development for

routine practice and care. Furthermore, guideline developments can often lead to research recommendations, particularly in areas where evidence is sparse or low quality. These recommendations can also flag important gaps in COS development (189) and so contribute to the evidence life cycle. Correspondingly, an increasing number of COS developers are developing their studies for use in routine health care and practice, as well as research. According to a June 2019 search of the COMET Initiative database of 235 ongoing studies, 53.6% (n=126) are COS for research and practice. As of December 2018, of 337 published COS 10.7% (n=36) were for both research and practice. Finally, the use of COS in guideline surveillance and development will ensure that health outcomes important to patients and health care professionals are considered, as they can support guideline developers in prioritising health outcomes for inclusion in their clinical guidelines.

1.8 Rationale for the thesis

The value of patient and public input in standardising and prioritising health outcomes to be measured in research is increasingly recognised. There has been a rapid expansion in the number of COS being developed in recent years, yet there is also a growing awareness of the need for attention to be given to the methods and processes used to facilitate patient participation. Further, there is growing recognition of the importance of internationally developed COS and thus the need to provide for the inclusion of patients from as many countries as possible There is also increasing cognisance of the role patients and members of the public have in developing clinical guidelines based on the review of relevant research, which may include COS studies. As highlighted in this chapter, it is important to identify methods and processes that allow international participants, particularly patients and members of the public, to contribute to choosing health outcomes for COS and clinical guidelines. This needs to be in a manner that is meaningful to them, thereby ensuring that the resulting COS and clinical guidelines are relevant and credible. There is currently no accepted gold standard method for facilitating patient and public input to COS development or in health outcome selection during clinical guideline development. Further work is necessary to explore which methods are

most suitable and what the priorities are for guidance and further research in these areas.

The focus of this thesis is on exploring the methods by which nationally and internationally based participants contribute, be it by direct or indirect methods, to COS development and clinical guideline development and their opinions on the processes used. In particular, the following questions will be explored:

1. What method(s) do COS developers use to facilitate patient participation?
2. How do participants experience COS development and the method(s) via which they participate?
3. How do patients and members of the public influence health outcome selection during clinical guideline development?
4. What are the priorities for guidance and further research in these areas?

1.9 Aims and objectives of the thesis

The central aim of this thesis is to explore how an international range of patients and members of the public are included in and experience prioritising and selecting health outcomes to inform research and practice. The research is guided by three main objectives which are to:

1. Map the methods of patient participation used by COS developers. This was achieved by surveying COS developers about patient participation, the number of countries involved and the methods used in their COS development (Study One).

2. Explore international participants' experiences of their input in COS development to understand their perspectives of their participation of health outcome prioritisation. This was undertaken using a qualitative approach with semi-structured interviews (Study Two).

3. Investigate how patients and members of the public experience and influence health outcome selection during clinical guideline development. This was undertaken using an ethnographic approach (Study Three).

The research was then brought together to make recommendations for practice, guidance and future research.

1.10 Thesis structure

The remainder of this thesis is structured as follows:

Chapter 2: presents a survey of COS developers, which mapped how frequently COS developers include patients as participants in COS development, the methods of participation they used and the number of countries represented in their COS studies.

Chapter 3: presents a qualitative study which explored participants, both health professionals and patients, opinions and perspectives of the methods used to facilitate their input in COS development.

Chapter 4: presents an ethnographic study which explored patient and public influence and experiences of input in health outcome selection during clinical guideline development.

Chapter 5: presents my reflections and conclusions on PPI in health-related methods research more generally, and international COS development. These reflections are underpinned by the studies described in chapters 2 and 3 and further discussion and interactions with Early Stage Researchers and European consultants. My overall conclusion is that more work is needed beforehand for preparing patients to participate in COS and also health outcome selection in guideline development is articulated within this chapter as are my recommendations for future research.

Chapter 2: Mapping the methods of patient participation used by outcome set developers: A survey of developers

Preface

Chapter 2 describes the methods and results of the survey I conducted as the preliminary step in exploring the inclusion of patients and members of the public in COS development. This survey examined how frequently COS developers include patients as participants in COS development, the methods of participation they use and the number of countries represented in their COS studies. Work arising from this chapter has been published in BMC Trials (2018; open access) (Appendix A1 Publications). Sections of this chapter include direct excerpts of the published manuscript. As lead researcher, I was responsible for the preparation and drafting of the protocol, survey creation, data collection and analysis (assisted by Ms Lucy Brading, PhD student). The survey also asked one question in relation to Ms Lucy Brading's research on patient and public involvement in COS development as distinct to patient participation. I did not analyse the involvement data nor document it in this thesis. I wrote the original draft of the published manuscript, which was edited by senior authors and has been subject to peer review.

2.1 Introduction

Evidence enables treatment decisions to be made according to the needs of the individual patient. This evidence comes from numerous studies that record and measure the effects that different illnesses, conditions and treatments have on patients. These measurements are known as “outcomes”. Health outcomes include such things as quality of life, treatment costs, fatigue, white blood cell count and pain. However, across different studies of the same condition or illness there is considerable variability in the health outcomes measured. This has given rise to difficulties in summarising the evidence, as the results cannot be adequately compared and contrasted (116). In turn the usefulness of studies in advancing research, informing clinical practice and empowering clinicians and patients with knowledge regarding interventions is limited (102), rendering the research wasteful in many instances (28, 29).

One answer to this problem is the development of core outcome sets (COS). A COS is a minimum set of agreed standardised health outcomes which should be measured and reported in all trials of a specific condition. It is considered a fundamental list of outcomes (101), not an exhaustive list and researchers can measure additional health outcomes within their trials if they wish (102). The same set may also be relevant to the systematic reviews of those trials. The Core Outcome Measures in Effectiveness Trials (COMET) Initiative recognises the issue of heterogeneity in reported health outcomes and aims to tackle it by bringing together people interested in the development and application of COS.

While the usefulness and importance of these sets is accepted, researchers need to include patients in the development of COS (123). For most conditions there are many different health outcomes that could be included in a COS. When patients have not been included in the COS development process, important health outcomes have been overlooked (190). This is because evidence indicates that patients and families can differ in the priority they give to certain health outcomes compared to clinicians (191). Including patient participants in deciding which health outcomes should be in a COS thus reduces the danger of omitting important health outcomes. More

broadly, patient participation in COS development enhances the value of research, as it helps to ensure that the health outcomes reported are relevant to patients.

When using the term 'patient' in this chapter I refer to patients, carers, health and social care service users and people from organisations who aim to represent these groups. Researchers are increasingly including patients alongside other stakeholders in identifying what health outcomes to measure in clinical trials. While a 2013 systematic review found that only 18% of published COS studies reported patient input (73), subsequent updates of this review in 2014 and 2015, indicated patient input in 59% and 61% of published COS developments, respectively (116, 117).

Two stakeholder groups who are important to all COS are clinicians and patients (100). However, the best methods for facilitating their participation is unknown. There are numerous challenges in enabling participation in a COS study and these will vary depending on the participants, the research team and the condition being researched. Challenges include selecting an appropriate recruitment method, finding the best way to explain the concept of a COS, using a suitable method to elicit perspectives of patients and health professionals, maintaining participant input over time, and enabling the inclusion of patients in face to face meetings with health professionals and academics (123). Previous COS studies have reported variable rates of recruitment of participants in the development of the COS (116), while COS developers have also reported limited experience of engaging with participants in the development of important COS (153).

To screen the relevant ongoing or recently published COS development studies, I sent a short survey to COS developers of recently published or ongoing COS developments. This allowed me to establish how frequently COS developers include patients as participants in COS development, the methods of participation they use and the number of countries from which COS developers sampled patients from. By describing the trends in the development of COS, the survey has helped identify areas for further improvement and study. This information also informed the next study of my PhD project while allowing me to build the appropriate communication network for future information and recruitment (detailed in Chapter 3).

2.2 Methods

2.2.1 Design

I thought a survey appropriate for this particular phase of the project as it is comparatively inexpensive and allowed me to engage with a large number of COS developers. Studies have shown that questionnaire length has a substantial effect on the number of non-responders (192), so this questionnaire was purposely kept short to avoid this issue and to not overburden any prospective respondents. Other factors thought to influence the overall response rate include readability of questionnaires, such as the number of syllables per word, words per sentence, typeface and font size. I therefore followed what is considered best practice in the literature (The National Institute of Adult Continuing Education guideline "Readability: How to produce a clear written materials for a range of readers") when building this survey.

I conducted the survey in English and included some brief demographic questions before enquiring about patient participation in COS development. Patient participation was defined as: "where patients or the wider public (family members, carers, health and social care service users and people from organisations who represent these groups) or both, take part in the development of a core outcome set by giving data on their opinions regarding what outcomes are important." If a respondent answered "No" to the use the patient participation they were redirected to the end of the survey and a thank you page. Any respondents who answered "Yes" to patient participation in their COS development continued on to six further questions in relation to this. A flow chart and full list of the questions is available in Appendix A2.1. I constructed the survey using the SurveyMonkey software (193), as it was more amendable to the purpose and design of the survey than other existing online survey software such as SurveySelect.NET or SurveyGizmo. The benefits of using SurveyMonkey include the facility to incorporate filter questions (whereby depending on the responses, respondents were automatically directed to the next appropriate question). The software was programmed individually for the study purposes and the responses were exported into a suitable database where I anonymised the responses by applying a specific code to each respondent. A password-protected codebook was held separately on the University of Liverpool

secure M-drive. While I acknowledged the contribution of COS developers in the subsequent write-ups, all survey responses were confidential and data was aggregated.

2.2.2 Participant selection and recruitment

I identified the COS developers via a search (02/02/2017) of all studies published from 2013 and ongoing COS projects in the COMET Initiative database. The COMET Initiative has created and maintains a publicly accessible database (www.comet-initiative.org) of planned, ongoing and completed COS work that have been registered with COMET and is updated annually with published studies that have been identified through a systematic review, as described in Chapter 1.

I sent the survey to the lead authors of the COS development as a link within a personalised email Appendix A2.2, inviting them to visit the SurveyMonkey website where the survey was hosted. Adopting a personalised approach and follow-up contact with those who do not respond to the initial email has been suggested to increase the odds of response by more than a quarter (192), therefore I sent personalised emails and I sent three further personalised emails to non-responders.

2.2.3 Analysis of survey responses

I validated responses relating to published COS projects by reading the appropriate publications where these were available and emailing COS developers for clarification where necessary. I analysed the data descriptively using Microsoft Excel.

2.2.4 Ethics

The study was approved by the University of Liverpool's Health and Life Sciences Committee on Research Ethics (Human participants, tissues and databases) ethics committee on the 16th of February 2017 (reference: 1339) (Appendix A2.3).

2.2.5 Informed Consent

I sent all participants involved in the survey a personalised email explaining the purpose of the study (Appendix A2.2). Participants had to follow a link in the email which led to the survey. By doing that and entering responses to the survey questions, it was assumed they had agreed to participate and their consent was presumed. Participants were free to withdraw their consent and leave the survey at any time without having to explain or provide reason.

2.3 Results

2.3.1 COS studies surveyed

I sent the survey to 192 COS developers. Some developers were involved in multiple COS projects and I asked them to complete the survey for each relevant COS. I contacted 59 developers for 59 published COS projects, 129 developers for 150 ongoing COS projects and 4 developers for 16 published and 19 ongoing COS projects. I collected responses from February until May 2017.

There were 146 respondents yielding a 76% response rate and providing data regarding 195 projects. Other comparable online surveys report response rates of between 31-53% (194-196). The breakdown of respondents and their projects is as follows: 37 responders for 37 published COS projects, 29 responders for 29 completed COS projects, 49 responders for 52 ongoing COS projects, 25 responders for 27 planned COS projects, 6 responders for a mixture of 15 published, 12 completed, 17 ongoing and 6 planned COS projects.

2.3.2 Patient participation- frequency, type and number of countries recruited from

Table 2.1 summarises the frequency of patient participation in 162 COS projects since 2013, from published, completed and ongoing studies, after excluding 33 studies still in the planning stage. Overall, respondents indicated that 141/162 (87%) COS projects had included patient participants in the development of their COS (Table 2.1).

Stage of COS development	**COS with no patient participants n (%)**	**COS including patient participants n (%)**
Published	14 (27)	38 (73)
Completed	3 (7)	38 (93)
Ongoing	4 (6)	65 (94)
Total	21 (13)	141 (87)

Table 2.1: Frequency of patient participation in COS projects by COS development stage

Survey responses for patient participation matched published information for 51 COS; in the remaining published study it was not possible to make this comparison as the developer did not provide their name in their survey response. Of 24 published COS for which no survey response was received or could be matched, five (21%) of the journal articles reported patient participation. Thus, non-respondents for the published COS projects had a lower patient participation rate than that of those who responded to the survey. This is likely to also be true for non-respondents of ongoing studies, resulting in an over-estimate of patient participation reported in the survey.

Table 2.2 summarises the year of publication and health area classification covered by the 24 published COS for which no survey response was received or could be matched and 51 published COS for which it was possible to match the survey responses to the publication. To protect the COS developers' anonymity I use the general health area classification as assigned on the COMET database to describe the health conditions covered by the 75 publications. The majority of these 75 COS were developed by researchers based in Europe, America or Canada or international steering committees. Table 2.2 shows that the published non-responders were more likely to be from older COS projects (2013 and 2014). This supports the finding that published responders more often included patient participants, since their projects were more recent and involvement of this stakeholder group has increased over time.

Year of publication	Published non-respondents (n=24)	Published respondents (n=51)
2013	8 (33.3%)	9 (17.6%)
2014	13 (54.2%)	12 (23.5%)
2015	2 (8.3%)	19 (37.3%)
2016	1 (4.2%)	11 (21.6%)
Health area classification*	**Published non-respondents (n=24)**	**Published respondents (n=51)**
Cancer	6	9
Child health	0	5
Eyes and vision	1	1
Gastroenterology	2	1
Heart and circulation	4	7
Infectious disease	0	1
Kidney disease	0	1
Lungs and airways	0	1
Neurology	3	5
Obesity	0	1
Orthopaedics and trauma	3	7
Other	1	1
Pain-chronic	0	1
Pregnancy and childbirth	2	4
Rehabilitation	0	1
Rheumatology	2	3
Skin	0	1
Wounds	0	1

*Table 2.2: Comparison of published respondents and non-respondents, based on year of publication and health area classification. * health area classification used as assigned on the COMET database*

Developers reported input from a variety of patient stakeholder groups (Table 2.3): 101 (72%) projects included both patients (healthcare patients, healthcare users, consumers, family members, spouse, carers, etc.) and patient organisations (patient support groups and patient charity representatives).

Stage of COS development	COS including patient participants (n=140)*		
	patients and patient organisations **n (%)**	patients only **n (%)**	patient organisations only **n (%)**
Published	23 (62*)	14 (38)	0
Completed	28 (74)	10 (26)	0
Ongoing	50 (77)	14 (21)	1 (2)
Total	101 (72)	38 (27)	1 (1)

*Table 2.3: Frequency of the patient participant groups included in COS projects by COS development stage * No further information was provided in relation to one published study thus it has been excluded from further analysis*

For projects including patient participants, Table 2.4 shows how many countries were involved in the 135 studies where a response was provided. Half of COS projects included patient participants from only one country, and this was usually the United Kingdom (41/70, 59 %). Where the study was international, typically COS developers involved participants from 5 or more countries (n=30/135, 23% of total COS).

Stage of COS development (n)	**1 country n (%)**	**2 countries n (%)**	**3 countries n (%)**	**4 countries n (%)**	**5+ countries n (%)**
Published (36)	21 (58)	5 (14)	1 (3)	1 (3)	8 (22)
Completed (36)	13 (36)	6 (17)	5 (14)	3 (8)	9 (25)
Ongoing (63)	36 (57)	10 (16)	2 (3)	2 (3)	13 (21)
Total (135)	70 (52)	21 (16)	8 (6)	6 (4)	30 (22)

Table 2.4: How many patient participant countries are included in COS development by COS development stage

2.3.3 Methods used to facilitate patient participation in COS development

Table 2.5 summarises COS developers' responses regarding the methods that they had used to facilitate patient participation. Developers responded via a fixed response option that included five commonly used methods (Delphi survey, questionnaire, focus group, qualitative interview and consensus meeting) and an

additional “other” option, which prompted respondents to state the method in a free-text box. All method combinations can be found in Appendix A2.4.

As Table 2.5 shows, the Delphi survey was the most popular method, having been used singularly or in combination with other methods in over 119 (85%) of the 140 projects with patient participation. A multiple methods approach was used in 110 (79%) of the 140 projects with patient participation, of which the most popular method of was the combination of i) Delphi survey, qualitative interviews and consensus meeting (22/140, 16%), followed by ii) Delphi survey singularly (21/140, 15%). In ongoing studies the most popular methods used were the combinations of i) Delphi survey, consensus meeting and qualitative interviews (16/65, 25%), followed by ii) Delphi survey, consensus meeting, focus group and qualitative interviews (9/65, 14%) and finally iii) Delphi survey and consensus meeting (7/65, 11 %).

Methods used	**Published n (%)**	**Completed n (%)**	**Ongoing n (%)**	**Combined n (%)**
Number of COS studies included	37	38	65	**140**
Delphi survey only	12 (32)	7 (18)	2 (3)	**21 (15)**
Questionnaire only	2 (5)	0	1 (2)	**3 (2)**
Qualitative interviews only	0	0	2 (3)	**2 (1)**
Consensus meeting only	2 (5)	0	0	**2 (1)**
Focus group only	0	1 (3)	0	**1 (1)**
Nominal group technique only	0	0	1 (2)	**1 (1)**
Mixed methods *(see descriptions below)*	21 (58)	30 (79)	59 (90)	**110 (79)**
Delphi survey and another method(s)	*15 (71)*	*26 (87)*	*56 (95)*	***97 (88)***
Consensus meeting and another method(s)	*6 (29)*	*2 (7)*	*2 (3)*	***10 (9)***
Qualitative interview and another method(s)	*0*	*1 (3)*	*1 (2)*	***2 (2)***
Focus group and another method(s)	*0*	*1 (3)*	*0*	***1 (1)***

Table 2.5 shows the methods used either singularly or in combination to facilitate patient participation. A full breakdown of the methods can be found in A2.4

2.4 Discussion

2.4.1 Main Findings

This survey indicated that COS developers are increasingly including patients as participants in COS project development, despite reports of COS developers finding patient participation difficult to facilitate in comparison to the participation of other stakeholder groups (153).

While many will welcome the increased inclusion of patients and patient organisations in COS development, it could also be argued that patient participants should exclusively be people who have personal experience of the condition or situation, as they are best placed to offer insight into what outcomes are important to someone living with a condition. This would exclude people working for patient organisations as COS study patient participants or others without personal experience of what it is like to live with a condition, as their perspectives may be closely aligned with that of a healthcare professional or researcher. However, it should be noted that some individuals within such organisations may also have direct patient experience themselves. Further research could examine what should constitute patient participation in COS development and explore the roles these groups have and the similarities and differences in the input they provide.

The principle behind the development of a COS is that all researchers working on the same condition, illness or treatment will use that COS in their research. Therefore COS need to be relevant for use across different countries if they are to improve the power of research to benefit patients (123). The findings of this survey are encouraging, with several COS projects being run in two or more countries with patient participants. However, the majority of COS projects mainly included patient participants from only one country, usually the UK. Previous research has indicated that COS developers have concerns regarding the practicalities and resources surrounding international COS development. Concerns were also raised in relation to the *"heterogeneity of views that might arise when participants are included from multiple countries"* (153). Future research could explore methods of developing COS with patients and health professionals from multiple countries in a practical and feasible manner.

A key challenge in patient participation is enabling patients to contribute their perspectives in ways that are meaningful and sustainable. It is vital that the methods suit the patient group concerned. Patient and public involvement where patients and the public are involved as active research partners in a COS project, can provide a patient and public perspective on the suitability of different methods from the design to conclusion of a COS project. The collaboration of researchers and patient and public involvement partners can help to ensure the appropriate design and conduct of a COS project. The survey responses indicated that the use of combinations of different methods, such as the Delphi survey, questionnaires, interviews, focus groups and consensus meetings, is not unusual. It was also evident that the Delphi survey was the most popular of all methods of participation in COS development. Delphi surveys can widen patient participation, promote transparency and offer anonymity. However, these surveys can be lengthy, and some believe these are intimidating for patient participants (123). COS developers have acknowledged a need for guidance on conducting Delphi surveys and consensus meetings (153).

2.4.2 Strengths and Limitations

A strength of this study was the relatively high response rate of 76%. However, non-response bias is a potential issue within this survey. My validation work shows non-respondents for published projects had a lower patient participation rate than that of those who responded. This is likely to also be true for non-respondents of ongoing studies, resulting in an over-estimate of patient participation reported in the survey. Full and accurate reporting of COS projects, including details of patient participation, should continue to improve if developers use the recently published COS-STAR reporting guideline (120). Initially I did not ask respondents to indicate which COS study they were answering in relation to. However, I later added this question once it became apparent that many developers can be involved in multiple projects at once and that raises difficulties in matching the developer to the COS study based on developer name alone. To address this, I matched initial responses from COS developers by thoroughly checking the COMET Initiative database and reading relevant publications. A further limitation is that any relevant COS developments that were not registered on the COMET Initiative database during the survey period were

not included in this survey. However, as the COMET Initiative update their database annually via a systematic review of the relevant literature, any omissions are likely to be minimal. A potential limitation of this study is that I piloted the draft survey with individuals associated with the research team and the COMET Initiative only and not with external COS developers.

2.4.3 Summary

The results from this survey demonstrate the ongoing inclusion of patient participants in the development of COS and the international approach that some developers are adopting, despite the literature suggesting there are barriers to be overcome in developing international COS projects. It also indicated that the Delphi survey is the most popular method for including patients and members of the public in COS development, either singularly or in combination with other methods.

The next step in exploring the inclusion of patients and members of the public in health outcome selection entailed examining participants' experiences of COS development via Delphi surveys. I addressed this in the EPITOME Study (Exploring Participant InpuT in Core Outcome Set DevelopMENt) which is detailed in Chapter 3. EPITOME was informed by the survey findings detailed in the current chapter and consisted of semi-structured qualitative interviews with participants who have taken part in international COS developments via the Delphi survey.

Chapter 3: Exploring Participant InpuT in Core Outcome Set DevelopMEnt (The EPITOME Study): A qualitative interview study

Preface

Following on from the work described in Chapter 2, I undertook a qualitative interview study as the next step in my PhD project. Using the survey findings detailed in Chapter 2, I devised a sampling framework to recruit participants from a range of COS studies to explore their experiences of participation in COS development via the Delphi survey. Chapter 3 presents the findings of these interviews and describes participants' perspectives and opinions of the Delphi survey method of participation. Work arising from this chapter has been published in the BMJ Open (2019; open access) (Appendix A1 Publications). Sections of this chapter include direct excerpts of the published manuscript. As lead researcher, I was responsible for the preparation and drafting of the protocol, data collection and analysis. I wrote the original draft of the published manuscript, which was edited by senior authors and has been subject to peer review.

3.1 Introduction

Inconsistency in outcomes measured in clinical trials is a major concern across a multitude of health conditions, limiting the synthesis of available evidence and ability to reach reliable conclusions (28, 77).

Core outcome sets (COS) are one potential solution to this problem. A COS is a minimum set of agreed standardised outcomes which should be measured and reported in all trials in a specific condition as a minimum (100). Three important stakeholder groups in the development of COS for trials are health professionals, patients and those who will use the COS in research, such as clinical trialists or industry (106).

Several methods are used to include stakeholders as participants in COS development, including interviews, focus groups, nominal group technique and Delphi surveys. Delphi surveys, used singularly or in combination with other methods, are the most popular method of facilitating participation (197). These involve iterative rounds of questionnaires listing outcomes and asking participants to score the importance of each outcome. Scores are subsequently summarised across the various stakeholder groups and fed back to participants in the following round. This allows participants to consider the views of others before re-scoring each item. Furthermore, participants' individual views are anonymised which minimises the influence of power differentials between different stakeholders that can be problematic with direct communication between participants (123, 138). The creation, administration and analysis of Delphi surveys is relatively inexpensive. The availability of online Delphi survey platforms allows large samples and facilitates international development of COS, thus, ensuring they are relevant globally.

However, Delphi surveys have been described as potentially intimidating for some patient participants (123) and COS developers have acknowledged a need for guidance on conducting Delphi surveys and the consensus meetings which typically follow them (153). While recent surveys of COS participants indicate that their experiences of Delphi surveys have been generally favourable (198, 199), no research, to the best of my knowledge, has explored in-depth the perspectives of patients and health professionals on participating in COS Delphi surveys. I therefore

explored their opinions and experiences of participation to identify ways to enhance Delphi surveys for future participants in COS development studies.

3.1.1 Aims and justification of qualitative approach

The results of the survey mapping methods of patient participation in COS development (Chapter 2) demonstrated the popularity of the Delphi survey as a method of participation. However, Delphi surveys have been described as potentially intimidating for some patient participants (123) and COS developers have acknowledged a need for guidance on conducting Delphi surveys and the consensus meetings which typically follow (153). While recent surveys of COS participants indicate that their experiences of Delphi surveys have been generally favourable (198, 199), no research has explored in-depth the perspectives of participants of COS Delphi surveys. I therefore explored participants' opinions and experiences of participation to identify ways to enhance COS development via Delphi survey for future participants in COS studies.

I took a qualitative approach, as it enabled me to capture the holistic experiences of participants (200). Furthermore, qualitative studies are undertaken where the aim is to develop a deeper understanding of a phenomenon rather than to measure or quantify it (201). In this study, semi-structured interviews followed by thematic analysis allowed me to deepen my understanding of how participants viewed the Delphi survey within COS development. Unlike a structured interview or survey, which produces standardised responses, the semi-structured interview allowed the opportunity to adapt questions or probe further based on interviewees' responses, it also allowed interviewees to raise aspects that were important to them and voice their perspective in their own words (202).

3.1.2 Theoretical perspectives

A. My initial positioning

It is impossible for most individuals to be free from value or attain complete objectivity and as researchers it is important that we are aware of this and take the appropriate steps to ensure that we protect the integrity of the data we investigate. By being reflexive and open about our own identity, beliefs and thought-processes and the impact that may have on our research, we can create a level of distance

between us as researchers and the data (203). While it is beyond the scope of my thesis to offer a detailed debate on the relationship between researcher and theoretical perspectives, it is important to acknowledge my positioning and to offer some information on this, my worldview and my discipline.

Prior to commencing this PhD, I was a research assistant collecting health data directly from patients and members of the public. This allowed me to interact with numerous people in various states of health. It gave me insight into the many different ways in which people experience health systems, treatments and delivery of care. This exposure piqued my interest in the role of patients and members of the public in health research. I was intrigued by the value patients and members of the public could offer, the methods in which they could contribute and finally, the moral and ethical obligation we as researchers owe them. I believe that researchers, health professionals and patients should work collaboratively in setting the health research agenda, as it is the sum of all our experiences and knowledge that will enable progression of healthcare and health outcomes. Consequently, I started from a value position that patients and members of the public should be included in all stages of health research relevant to them and that if it is done well, their inclusion can increase the quality and validity of the results, thus having a positive impact.

B. Choosing my lens: research paradigms

The first point to consider in answering any research question is which methods you will use. The answer is largely determined by the research question itself, as different methods lend themselves to different questions and settings (204). The methods used are also dependent on numerous factors such as funding, resources, the worldview of the researcher and underlying philosophies that may exist (205, 206). The second point to consider is why choose and use those specific methods. Crotty suggests that the answer to this second point is more than simply needing a process capable of exploring the research question, that it is *"something that reaches into the assumptions about reality that we bring to our work"* (207). These research methods and how they produce knowledge are embedded in particular political and ideological positions, known as *"research paradigms"* (208). Research paradigms represent our basic beliefs and the lens through which we view the world as

researchers, thus they offer the pathway through which researchers conduct their research (207, 209). Some of the most prominent paradigms in health research includes critical realism, social constructionism, interpretivism, phenomenology, positivism and pragmatism as outlined in Table 3.1.

Paradigm	Summary	Methodology
Critical realism	The real world exists independent to our knowledge, human perceptions, theories and constructions. We then interpret this reality by drawing on our perspectives and experiences of what is observable.	Participatory and emancipatory approaches
Interpretivism	Reality is constructed through meanings created by individuals and groups. It is the researcher who determines the value of all scientific inquiry from the research question, to the methods and analysis.	Qualitative approaches
Social constructionism	The world around us is not real in and of itself. Through social agreement we give reality to concepts models and theories. We continually test, expand and reimagine these constructions based on experience and information.	Interaction and synthesis
Phenomenology	Reality is constructed through the lived experience of humans, thus is interpreted subjectively by those involved.	Qualitative approaches
Positivism	Reality is knowable and driven by natural laws, thus the biases and values of the researcher must not influence outcomes and results.	Quantitative approaches
Pragmatism	Reality is the practical effect of ideas rather than the abstract. Individual researchers have the freedom of choice to select processes that best suit their needs	Mixed method approaches

Table 2.1 Summary of potential research paradigms. Adapted from Guba and Lincoln(210), with additional information from Bygstad and Munkvold (211) and Denscome (212).

Each of these paradigms rely on various methodologies, for example researchers who follow positivism typically use experimental and quantitative approaches in their search for a reality that is knowable and driven by natural laws (210, 213). Researchers who follow interpretivism are more likely to use qualitative approaches in their exploration of a reality that is created by individuals and groups (210, 213). Pragmatism enables researchers to draw on both positivism and interpretivism, as it places importance on the real-world rather than the abstract. Researchers who

follow pragmatism believe that reality is the practical effect of ideas and usually adopt a mixed-methods approach when exploring research questions.

Health research seeks to improve the care and treatment of patients, to improve their health outcomes and ultimately enhance quality of life. However, health is complex, thus health research is complex. Researchers need to be aware of this and have the flexibility to adopt quantitative and qualitative approaches to generate and synthesise knowledge. Further, researchers need a range of lenses through which data can be viewed, as Miles suggested *"researchers should be open to an ecumenical blend of epistemologies and procedures, and leave the grand debate to those who care about it"* (214). Thus, for many in health research, pragmatism offers a practical, context-driven solution which considers both objective-quantitative and interpretive-qualitative knowledge (215). Thus, I approached the work detailed in this chapter from a pragmatic paradigm.

3.2 Methods

3.2.1 Design

In this study, entitled EPITOME (Exploring Participant InpuT in Core Outcome Set DevelopMEnt), I used qualitative interviews to explore patients' and health professionals' experiences of participating in COS Delphi surveys. I elected to include health professionals in this interview study so I could broaden my understanding of similarities and differences in a range of participant perspectives.

3.2.2 Sampling strategies and recruitment

I used the responses of COS developers to a previous survey (197), described in Chapter 2, to inform purposeful sampling of host COS studies from which to recruit interviewees. Host studies were eligible if they had involved a Delphi survey, had patient participants, included participants from more than one country and had concluded no more than six months prior to the interview. The survey described in Chapter 2 indicated that some COS developers are taking an international approach to development. I was interested in exploring this further as previous research with COS developers has suggested there are barriers to overcome in developing international COS, including issues such as *"heterogeneity of views that might arise when participants are included from multiple countries"* (216). COS developers of

each host study distributed a recruitment advert (Appendix A3.1) to all stakeholders who registered for the first round of the Delphi survey. The advert invited interested individuals to contact me and I then provided a participant information sheet (Appendix A3.5). I discussed both the recruitment advert and participant information sheet with my PPI contributor who approved both documents before dissemination. I led all interviews conducted in this study. Thus, I sought to recruit interviewees who would be comfortable conversing in English, my native language. Both the recruitment advert and the participant information sheet were therefore disseminated in English only. Furthermore, all COS Delphi studies that I sampled were conducted in English. For each host COS, I aimed to interview up to two patients and two health professionals. After dissemination to two different host COS I decided to acknowledge the time and input of interviewees with a thank you card and £15 (or currency equivalent) shopping voucher. From exploring the literature I thought the voucher and amount were suitable, as it was not excessive to the point at which it could be viewed as coercion or undue inducements. Participants were informed that this voucher did not override the principles of freely given and fully informed consent and they were informed from the beginning of the interview that they could withdraw from the study at any point without losing their voucher.

The research team believed that the voucher and the amount attached to it would increase the recruitment rate (particularly amongst the harder to reach patient and public group), without introducing unnecessary bias. Moreover, the literature suggests that the potential dangers of giving such vouchers/payments/ tokens to the patients is outweighed by the gains, such as reducing bias and compensating for power differentials between the researcher and the researched (217-219). I contacted the interviewees who had participated in the interview study before the introduction of the voucher and thank you card and offered them both in acknowledgement of their time.

3.2.3 Data collection

As described in section 3.1.1 I considered a qualitative approach the most appropriate for this study. I chose semi-structured interviewing as opposed to other qualitative methods such as focus groups as it enabled me to explore interviewees'

experiences and opinions on a one-to-one basis, whereas focus groups would not necessarily have elicited individual responses. Furthermore, one-to-one interviews suited the international nature of this study, as focus groups would have been resource intensive and difficult to organise. Other qualitative research methods such as ethnography were not appropriate as COS Delphi participants are typically not in engaged in the participation in a common setting over a longer period of time, thus, it is not possible to observe their social interactions and behaviours. The semi-structured format allowed the opportunity to adapt questions or probe further based on interviewees' responses, it also allowed interviewees to raise aspects that were important to them and voice their perspective in their own words (202).

Due to the international focus of this study, I conducted interviews via telephone or email exchange, to maximise response rates and run a cost-effective study. Although telephone interviews can result in loss of some of the benefits of face-to-face interviews such as observing body language, research has shown the quantity, nature and depth of responses are similar (220). I collected the data between October 2017 and June 2018. At the time of interview, interviewees were between seven months and six weeks from having participated in the final round of the host COS Delphi. The interviews were topic-guided and semi-structured, using a conversational approach to explore issues that I anticipated to be important, while enabling interviewees to raise areas that were important to them. My topic guide was developed and informed by discussions with COS developers and my PPI contributor who had experience of COS development (Appendix A3.2), and previous qualitative research (221), Box 3.1. outlines the key areas that were explored. Email exchange interviews followed a similar format asking a range of open-ended questions across topics. If necessary, I followed up on responses with additional open-ended questions to further explore the interviewees' answers and comments. I tailored questions for each interviewee by reviewing available information on the host study before the interviews. This information included, for example: participant information materials such as guidance sheets and videos, the number of rounds, scoring systems used, numbers of domains and outcomes scored and examples of outcomes scored. For one host study a screenshot of the Delphi survey was supplied by the developers

which I used as a memory aid with interviewees from that COS Delphi study. Email interviews followed a similar format asking a range of open-ended questions across topics, if necessary, I followed up on responses with additional open-ended questions to further explore the interviewees' answers and comments. I transcribed the first two audio-recorded interviews the remainder were transcribed verbatim by a University of Liverpool approved transcription agency into Microsoft Word. I checked and anonymised the transcripts before analysing them. The data is currently held in password encrypted files on The University of Liverpool's secure server. I conducted all interviews in English. Before starting data collection, I received training in qualitative methods from the Health Experiences Research Group at the University of Oxford (Appendix 6).

Key areas covered during interviews
• Background To explore the interviewee's background and to elicit contextual information about how his/her experience of the COS development began. • Preparation To explore how interviewees prepared for the COS development, and how they described COS and Delphi surveys. • Engagement phase To explore the processes the interviewee engaged with during the study. From contact with the research team, to accessing study materials, taking part in the Delphi (and other processes if relevant), to follow-up information. • Reflections To explore how the interviewee now views their experience of participation, the methods used and the purpose of the study.

Box 3.1: Summary of the key areas covered during the interviews. A full list of questions can be found in Appendix A3.2

3.2.4 Data analysis

Data analysis drew on Braun and Clarke's six phase thematic approach (222). Analysis was initially deductive following the topic guides but became more inductive as the analysis progressed (222) and ranged from line-by-line coding, to considering whole transcripts. I initially read the transcripts and reflective fieldnotes that I made immediately after each interview to inform my interpretations. A codebook was developed for the content using open coding. By grouping the codes together, recurring patterns and themes were identified and organised into categories (222). As this study was part of doctoral research, I performed all the coding and identification of themes. However, transcripts, codes and themes were discussed and reviewed regularly throughout the analysis process with my supervisory team. The PPI contributors attached to this study was unable to participate in the analysis and discussion of the findings due to other commitments, unfortunately I could not find a second PPI contributor to ask for further assistance. With my supervisory team we frequently discussed the new data and whether it was continuing to contribute to the analysis and exploration of the research question. At approximately interview number 20 we agreed that no new relevant data was being collected. I decided to continue for an additional four interviews to check that saturation had been reached and that no new relevant data was coming up in interviews. We all agreed that data saturation (the point at which new data cease to contribute to the analysis) had been reached after twenty-four interviews. I used Microsoft Word to facilitate coding and analysis (223).

While accepting that quality procedures cannot promise quality (224), the reporting of this study was informed by relevant guidance (225).

3.2.4 Ethics

I asked the NHS Health Research Authority query line whether ethical review from the NHS Research Ethics Committee was needed for this study (see Appendix A3.3). They responded that NHS ethical approval was not needed as interviewees were being interviewed in regard to their experience of a previous research study and not about their experiences as a patient of a health condition(s). Subsequently, the Health and Life Sciences Committee on Research Ethics (Human participants, tissues

and databases) at The University of Liverpool, granted ethical approval on the 22/06/2017 (reference 1969) (Appendix A.3.4).

To protect interviewees' and COS developers' anonymity, I have not identified the COS Delphi studies I sampled from. I use the general health area classification as assigned on the COMET database to describe the COS Delphi studies in what follows. I believe disclosing further information such as funding source, national base of the research team and further study design information could allow for identification of the COS Delphi study and its participants.

3.2.5 Informed Consent

Prior to seeking their informed consent all potential interviewees were provided with a participant information sheet (Appendix A3.5), which I emailed to them at least 24 hours in advance of the interview. Due to the diverse and international nature of the study population, it was impractical to seek signed informed consent forms from all potential interviewees, as not all had access to computers with scanners, and relying on the postal service for the return of signed consent forms was impractical. Therefore, interviewees who opted to proceed via email exchange scanned and returned signed informed consent forms via email. Those who opted to participate via telephone interviews gave audio-recorded consent prior to proceeding with the interview, a decision which was approved by the ethics review board at The University of Liverpool. I explained the informed consent process before starting each interview (Appendix A3.6) and interviewees had time to ask questions and discuss the study. If the interviewee was happy to proceed, I audio-recorded their consent and started the interview. All interviewees could withdraw their consent and leave the study at any time without having to explain or provide reason.

3.2.6 Patient and public involvement statement

Patients and the public were involved in developing and reviewing the topic guide, recruitment advert and participant information sheets used in this study.

3.2.7 Definitions

In presenting the remainder of this chapter I use the term 'patient' to refer to patients, carers, service users and people from organisations who seek to represent these groups. I use 'health professional' to refer to clinicians and pharmacists.

Interview excerpts shown below were selected to demonstrate the findings and my interpretations. Health professionals are indicated by "HP" and patients by "P", the COS in which they took part is indicated by "COS" and a number e.g. HP1COS1; "[…….]" indicates text removed for succinctness.

3.3 Results

3.3.1 COS study sampling and interviewee characteristics

I initially identified 39 potential host COS studies via the survey (197) (Figure 3.1). Two further ongoing COS studies were brought to my attention by COS developers, which were not in the COMET database at the time of the survey, but were subsequently added. I contacted the developers of 20 of these COS studies in batches to inform purposive sampling to achieve maximum variation. Of these 20, I excluded 14 studies from further consideration (Figure 3.1). I distributed the recruitment advert, via the COS developers, to the participants in the remaining six COS studies, plus the two further studies brought to my attention, giving eight unique online COS studies. Of these I recruited participants from seven COS studies. In an effort to protect the anonymity of the COS sampled from and their participants, I have categorised the COS studies using the terms by which they are organised on the COMET database. These studies covered: geriatrics (COS1), dermatology (COS2), other (COS3), cancer (COS4), paediatrics (COS5), gynaecology and obstetrics (COS6) and otorhinolaryngology (COS7). They varied in terms of the number of outcomes they asked their original participants to score, the number of rounds, scoring system, and in the ways feedback was presented to Delphi survey participants.

Following distribution of my advert, forty participants from the seven COS studies contacted us. I did not interview 11 of these (6 HPs, 2 patients and 3 unknown status) as interview quotas for their COS study had been reached. Of the 29 participants invited for interview, 24 participated. Of the remaining five, two patients withdrew as they were unable to recall any details of their COS study whilst two patients and a HP did not respond after the initial contact.

Table 3.2 summarises the demographic characteristics of the 24 interviewees (eleven HPs and thirteen patients), two interviews were completed by email exchange, and the remainder were telephone interviews. Interviews by telephone lasted on average

approximately 75 minutes. Interviews by email exchange varied between the two interviewees. One interviewee sent very brief, succinct responses and we exchanged 3 emails. The second email exchange interview provided longer written answers and we exchanged 6 emails. Twelve (50%) were resident in the United Kingdom (UK), four in Ireland, three in Canada, and one from each of Australia, Italy, Singapore, Spain and the Netherlands. Twenty-two interviewees described themselves as having professional occupations, two patient interviewees were retired and did not disclose their most recent occupation. Ten interviewees (three patients and seven HPs) had prior to the COS study they were being interviewed about previous experience of COS, Delphi surveys or both. One of the three patients with previous experience was also the patient research partner (involved in the design and conduct) of the COS development about which they were interviewed.

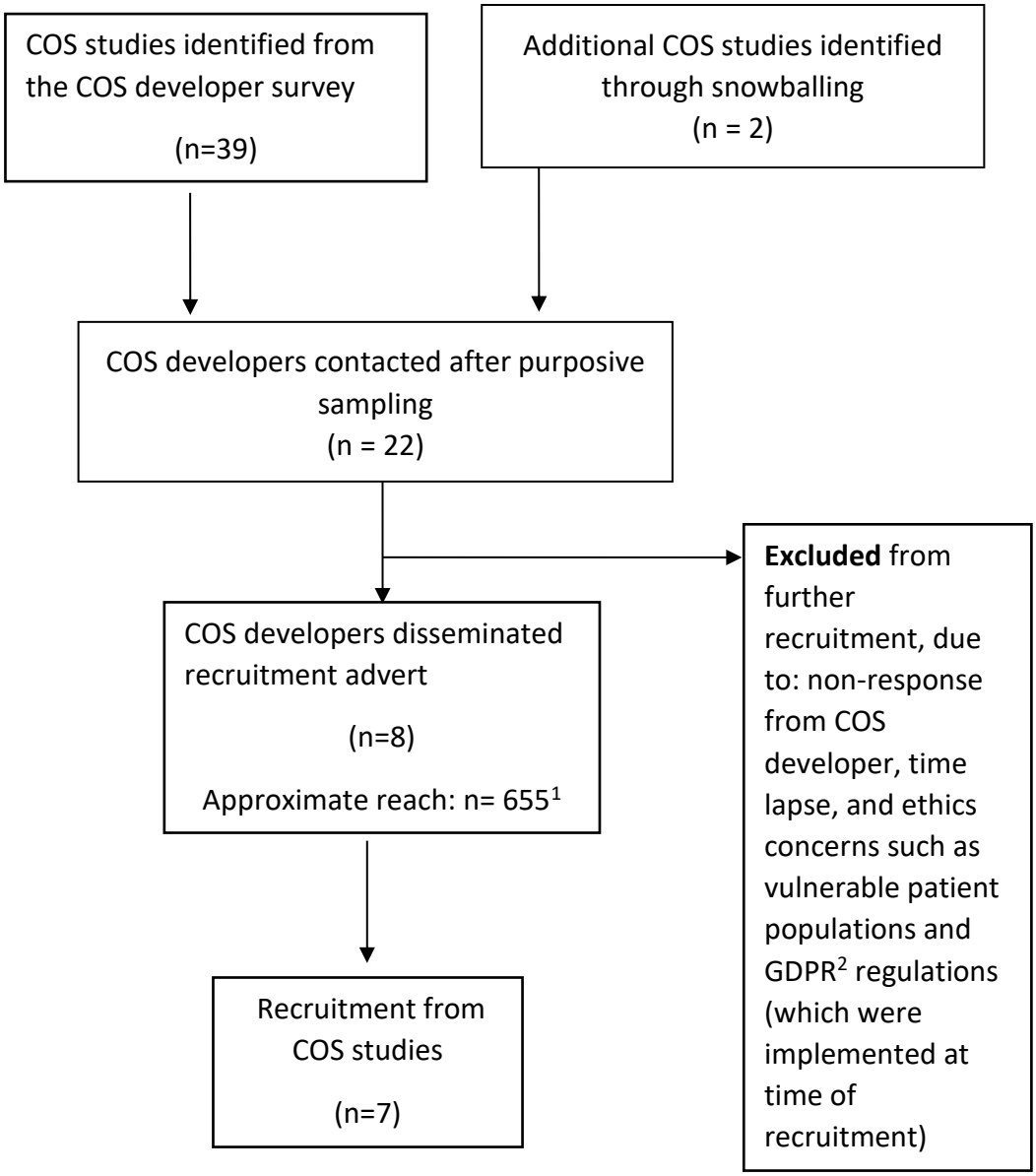

Figure 3.1: Sampling of COS studies that fit my sampling framework. [1]Reach of two COS studies is unknown, approximate relates to the other 6 COS studies. [2] General Data Protection Regulation (GDPR) is a European Union (EU) law regulation regarding data protection and privacy for all individuals within the EU and the European Economic Area (226)

Identifier	Gender:	Age range (years):	Country:	Prior participatory experience:	
				COS development	Delphi survey
P1COS1	Male	65-74	UK	No	No
P2COS1	Female	≥75	UK	No	No
P3COS2	Female	45-54	UK	No	No
P4COS3	Female	65-74	Canada	Yes	Yes
P5COS2	Male	45-54	UK	No	No
P6COS3	Female	55-64	Canada	Yes	Yes
P7COS4	Female	55-64	UK	No	No
P8COS4	Female	55-64	Netherlands	No	No
P9COS5	Female	35-44	Ireland	No	No
P10COS6	Female	45-54	Ireland	Yes[a]	Yes
P11COS7	Male	55-64	UK	No	No
P12COS7	Female	65-74	UK	No	No
P13COS2	Female	55-64	UK	No	No
HP1COS1	Female	45-54	Canada	No	Yes
HP3COS4	Male	45-54	Spain	Yes	Yes
HP4COS2	Female	35-44	Singapore	Yes	Yes
HP5COS4	Male	35-44	UK	Yes	Yes
HP6COS5	Female	55-64	UK	No[b]	No
HP7COS5	Female	25-34	Ireland	No[c]	No
HP8COS5	Female	35-44	UK	No[b]	No
HP9COS5	Female	65-74	Ireland	Yes	Yes

HP10COS6	Female	35-44	Italy	No	No
HP11COS6	Male	55-64	UK	Yes	Yes
HP12COS6	Female	55-64	Australia	Yes	Yes

Table 3.2: Interviewee demographic characteristics. [a] Interviewee was also the patient research partner of the COS study they were interviewed in relation to. [b] Two HPs stated awareness/knowledge of COS and Delphi survey but had not participated previously. [c] One HP was involved in an earlier phase of the COS study for which they participated in the Delphi survey.

3.3.2 Findings from interviews

For most interviewees, taking part in an online Delphi survey several months ago had not been a particularly salient or memorable event. Therefore, some interviewees, particularly patients, at times struggled to recall details of the host COS and so the interviewer had to provide them with brief prompts or reminders throughout the interviews. For example, P9COS5 had "*signed up to a lot of studies"* during the same time period and asked the interviewer to remind her of what the study was about. On explaining the topic of the Delphi survey and giving some reminders of the process such as the number of rounds and the process of reviewing and scoring outcomes, P9COS5 commented that she could recall filling out only one round of the Delphi survey. Thus, I interviewed her interview in relation to that round only.

While all participants in each of the seven COS studies had access to resources such as information sheets (and to online videos for two of COS studies), which explained the purpose and format of the study, interviewees differed in how accurately and fully they understood the purpose of COS and the process of the Delphi survey.

In what follows I present five thematic findings from the interviews as follows: i) how previous experience helped interviewees understand COS Delphi studies, ii) the differences in how participants understand the processes and purposes of Delphi surveys, iii) the question of who is being represented in the COS Delphi studies, iv) the motivational and emotional aspects of COS Delphi participation and v) how the scoring system used in Delphi surveys are understood by participants.

Previous experience helped interviewees understand COS Delphi studies

As indicated in Table 3.2 several interviewees had previous experience of COS and Delphi surveys. In comparison to those without such experience, these interviewees generally showed a better understanding of the purpose of COS and indicated greater satisfaction with the Delphi survey. HPs with previous experience (n=7) praised COS for their importance and usefulness in research, and the Delphi survey method for its simplicity. HP5COS4 said, *"That's the beauty of it, it is just not a difficult, all the hard work is done by the people that analyse the data. It is just like answering a customer service survey from Sky isn't it? Click next, next, next you just do it don't you, but I would put more effort to this than I would do a customer survey from Sky because it is more important to me."*

HPs without previous experience talked about having about read up about COS and Delphi surveys or of seeking advice from colleagues and peers to enhance their understanding of the study and prepare for their participation. For example, HP7COS5 took part in an earlier event for the same COS study at which the developers had been present; *"it made me think more fully about the bigger picture of research going forward and how these processes like the Delphi survey feed into that"* and that otherwise she *"would have approached it in a less informed way."*

The three patient interviewees with previous experience also spoke about the impact of this. Over the course of these prior studies, they described their experience evolving from one of confusion during their first study to one of enjoying the process and better understanding the purpose of a COS with each subsequent study "*once you get the hang of it, I really enjoy doing them because I like where it takes you*" (P6COS3). P10COS6 spoke of not having a *"bull's notion what is going on"* in earlier studies with regard to both the purpose and method of COS development and had *"to do a lot of online research myself to learn",* despite receiving information sheets for each study. Reflecting on this evolving experience of COS and Delphi surveys during her interview, she suggested that providing participants with a visual synopsis of the purpose of COS and Delphi survey method from the outset of a study would be helpful: *"I would have assimilated the message much quicker."*

Patient interviewees (n=9) with no previous experience, varied in their understanding of the purpose of the Delphi survey. With the agreement of the research team, I defined understanding the purpose of the Delphi survey as understanding that the multiple rounds were designed to a) reach consensus amongst various expert stakeholders and b) allow for reflection on the scores assigned to each outcome. The comments of some interviewees showed that they understood the Delphi survey's purpose was to reach consensus on which core outcomes to include. For example, P7COS4 explained the study was *"looking at how people felt with their recovery […] what they went through and what they were left with and how important those were to the person involved*." In contrast, others such as P8COS4 described the Delphi survey's purpose more vaguely as to gather a *"broad base of information on how many different people experience the treatment."* Moreover, she did not talk about the process in terms of prioritising the outcomes listed or reaching consensus amongst stakeholders. P1COS1 was confused about whether his study was complete or if he should expect further rounds of the survey: *"I don't even know that you could say a line had been drawn under it*." P11COS7 reflected on whether he *"could have done more to understand how the process worked earlier on. Particularly with the […] expert involvement, I now understand so next time I shall be even better at it"* and suggested *"a practice run"* would have been useful before entering the actual study. In a few cases participants indicated that their lack of understanding had influenced their overall experience of participation, "*I think one of my real concerns is that I didn't really contribute anything to the research because I really wasn't sure what I was doing"* (P2COS1).

Helping participants understand the purpose and process of Delphi surveys - one size does not fit all

The findings indicate that interviewees had different needs for support to aid their understanding of the purpose and process of COS Delphi surveys. P3CSO2 and P4COS2 were two first-time patient participants. They both received the same study documentation and said they reviewed it. However, their accounts indicated that they differed in their understanding of the documentation, and these differences influenced their contributions to and experiences of the study.

P4COS2 thought the study documentation he received was *"appropriate",* elaborating *"I have worked in the past in IT, in pharmaceuticals, in politics[…]so I am quite happy to see text that is fairly technical in nature or fairly clinical in nature and you know that is something I find easy enough to get to grips with."* He thought that the study "*was a very constructive thing to do. And I could see personally, something like that being done prior to any clinical trial, so that the end points of the clinical trial […] look at, you know how beneficial say a product is from the patient's perspective*."

In contrast, P3COS2 who worked in marketing commented that she *"didn't understand the terminology"* in the documents and as a result described being *"switched off from the process element […] psychologically I was just focussed on taking part and having my say."* She wondered if the study and its data would get *"stored away somewhere in a filing cabinet and forgotten about ….] I think what was lacking in the communication is how this is going to actually practically inform future research. And maybe that is my lack of understanding of how these sort of surveys work, and how these outcome surveys work, I don't really get, how that will translate into future treatments."* In response to P3COS2's comment, the interviewer explained that COS were used as minimum sets of outcomes in clinical trials so that evidence can be compared across studies and inform decision making regarding treatments. The interviewer added that the Delphi survey was a method to develop the COS by seeking consensus amongst relevant experts including patients. In response, P3 recalled that she had received information to that effect in the study documentation before adding, *"I really wish that had been captured in the communication a bit more clearly […] maybe I'd have done things differently*."

Representation in the Delphi survey- who and when

Both HP and patient interviewees raised the issue of "who they should be representing?" when completing the Delphi survey. They questioned whether they should try to think or imagine what outcomes fellow patients or HPs would likely prioritise when scoring the outcomes study, or whether they should focus only on their own opinions and priorities. None reported receiving guidance on this.

P4COS2 thought *"it can only be a genuine result if everybody says what they personally feel"* and "*trying to guess* [how others feel]*"* would defeat the objective.

This contrasts with P7COS4, a female who described trying to answer the outcomes section of that was applicable to males only: "*I just thought well if I was in that situation I will answer it as if I was that person maybe you know. […] Yes maybe I shouldn't have done that."*

In COS3, both patient interviewees were also advocates in a relevant patient organisation, and both had previous experience of COS Delphi studies. P6 described how she *"learned very early on"* to answer from her own perspective. Conversely, P4, who had her own personal experience, as well as an advocacy role, drew on her knowledge of the perspectives of other patients from discussions she had had through her work with the patient organisation *"I do try to work in their concerns and the issues that they have."* She added that COS developers should consider how the different phases in a patient's journey and their life could affect the way they scored outcomes: *"my priorities are different now, than they were when I was diagnosed over 30 years ago […] you know different things would have affected me. […] over the years with the chronic disease you learn to live with it and adapt to it, so […] yes I think that can affect your responses too."*

HPs touched on similar issues regarding who to represent when scoring outcomes, although compared to patients, this was less prominent in their accounts. HP1COS1, was an academic, a service provider and a policy maker. Referring to both her experiences as a professional and her personal opinions, she explained that she drew on *"a bit of both"* when scoring outcomes. Similarly, HP11COS6, an academic and service provider, explained *"it was a mixture of, of relating it to myself and relating it to patients. But I was, even when I was relating it to myself I was relating it to me thinking of myself as a patient or the father of a patient or something like that."*

Motivational and emotional aspects of participation

A few patients and HPs talked about the motivational and emotional aspects of their participation when asked about their feelings and thoughts surrounding their decision to participate.

HPs praised the Delphi survey method of COS development for its consensual and collaborative approach and cited the opportunity to learn from international

colleagues as one of the motivations for participating. They also spoke of their belief in the importance of COS in their field and their desire to contribute.

Patients described being *"happy"* that they could contribute their experiential knowledge and have input in research studies relevant to them. Some saw the COS study as one of the few research projects relevant to their condition and this was a motivating factor in their participation. P8COS4 talked about how her illness was *"rare"* and how information and research on the illness was limited "*so it was great for us* (other patients) *and for me specifically you know to fill in something that was specifically to do with my* (illness)", she further elaborated that the COS study *"made us feel someone was listening or someone was going to help us."* P3COS2 talked about how she felt *"happy"* to be included in research relevant to her, as she was outside the age range that was typical for patients with the health condition concerned. Similarly, P5COS2 *"thought it was quite exciting the fact that they would ask regular kind of sufferers of particular problems what do you think should be included in a trial. What outcomes do you think are important and everything and getting feedback from people outside the scientific community. I thought was quite cool and as somebody who suffers from various medical conditions the ability for me to give my input on what I think is important to a patient."*

P6CO3 had participated in multiple COS Delphi studies. She described her enthusiasm for the Delphi survey as a motivation to participate: "*every time I do them, I enjoy them more I really, really like the process"* and her willingness to participate in studies that used the resulting COS: "*you might have a preconceived notion of what something should be, or perspective on what something should be, or what the final product should look like, and it takes you in a different direction and if you just kind of you know let go and let it take you where it takes you through the questions and the feedback and everything I think it is a really interesting way of coming up with a list and I think it is a really true list."*

Two patients and one HP indicated that reviewing the list of outcomes had affected them emotionally. Speaking of when she reviewed the scores provided by fellow participants in the second round of P8COS4 commented that she had: *"changed some of my answers on the second round, when I was thinking about having a*

possible (intervention removed) *then I was like oh, I wouldn't want that at all […] I was sort of realising that I was grateful for where I was basically."* HP7COS5 said that when reviewing the fellow participants' feedback *"there were definitely moments of almost insecurity I suppose because you are aware, […] you are in amongst a group of other people who are very familiar with this field and experts […]"* She described initially feeling uncertain about her answers: *"it is ok to obviously be encouraged to check back on yourself and to be really thoughtful when you are kind of giving those sorts of answers [….] so I think there was a little bit of both an awareness of needing to stay objective but there was certainly a more subjective, emotive aspect to seeing how other people were answering."*

P2COS1 spoke of how reviewing the outcomes as part of the COS study had made her aware of outcomes that she had not previously realised were associated with her condition and treatment: "*A lot of the outcomes I would never have thought of those as outcomes from the sort of medication I am on if you see what I mean."* She described how this had affected her: *"I am seriously worried about that. […] I was given no indication* [by healthcare provider] *[…] that I need to be careful."*

Scoring system

Examination of the published reports and/ or protocols showed scoring systems in the seven host COS studies used either a 9- (n=6) or 5- (n=1) point Likert scale. In five of the COS that used a 9-point Likert, scores were further differentiated as: 1-3 'Not important' (n=4) or 'Limited importance' (n=1), 4-6 'Important but not critical', 7-9 'Critical'. In the sixth, the anchor descriptions were 'not at all important' (1) and 'extremely important' (9). In the COS that used a 5-point Likert scale, participants were asked to rate their level of agreement on a series of statements regarding potential outcomes, with scores labelled: 1 Strongly disagree, 2 Disagree, 3 Ambivalent, 4 Agree, 5 Strongly agree.

Several interviewees did not comment on the scoring system during their interview. Those who did comment varied from praising or indicating satisfaction with the scoring system, to wanting a system with fewer categories and further guidance on how to apply the scale, although the majority of interviewees were positive about the

scales used in COS Delphi studies that they had taken part in. Those who expressed satisfaction with the 9-point scales, indicated that they were familiar with using these: *"I am usually happy with Likert scales so, fine"* (HP12COS6), while another interviewee summed up her experience of the scales as *"not a big deal"* (P4COS3).

Interviewees who took part in a COS that used a 9-point scale and liked it praised the wide range of options and the three distinct bands as helpful. For example HP9COS5 commented *"I liked the way they set it out in that they were, you know while it was 9 it was important, not so important and least important so that even within those categories one could actually subdivide them, and I actually think I liked that. Sometimes you know you are asked you know, should something be important, and there are kind of gradations within importance, and so I think that for me I liked that subdivision. It gave me a little bit more flexibility."* P7COS4 noted *"grading it you know, systematically up from 1 to 9 so yes that was useful because it give you, although a lot of my scores were up on the higher range there were a couple of lower ones so I think the having 1 to 9 was a good idea."*

Other interviewees had a preference for fewer categories. Speaking of the 9-point scale in her study, P2COS1 commented "*I really don't think a score from 1 to 10 is realistic. […] maybe if you are a very skilled researcher yourself you might be able to deal in that level of gradation but I don't think the vast majority of us can. I think, you know, a 5 point rating scale is the most that most of us could do. You know with any degree of accuracy."* Similarly, also speaking of the 9 point scale HP8COS5 said "*what is the difference between a 6 and 7, you know what I mean if it is just sort of all in the middle of the road […] so whether or not it could have been less numbers to help make a more definitive answer."* However, like other interviewees who had a preference for a scale with fewer categories she acknowledged *"there might be reasonings behind why you have got 0-9 and that type of thing*." While some interviewees found the three bands on the 9-point scale helpful, responses from some HPs and patients indicated that further guidance and support is needed to help them use the 9-point scale. Similarly P11COS7, a first time patient participant, raised the difficulties he experienced in *"connecting physical sensations with a numerical value"* when relating

his physical symptoms to scoring outcomes. He added that this *"produces a certain anxiety between whether you pick 5, 6 or 7."*

HP6COS5 was the only interviewee who compared the scoring system to other methods of prioritisation when she flagged her overall preference for a numerical scale when scoring a long list of items in comparison to ranking them *"if I had been given the list and said you know rate these 1 to 20 it would have been harder to do."*

3.4 Discussion

3.4.1 Summary of findings

As previously described in section 3.1.2.1, my value position before beginning this PhD work and specifically the project detailed in this chapter, was of the importance of collaboration between all relevant stakeholders in improving health research. In particular I believe in the importance of engaging with patients and members of the public in manners and methods that enables participation which is meaningful to them, so that they can contribute as fully as possible to the research. Furthermore, I believe the onus is on us, as researchers, to ensure that the appropriate processes and procedures are in place to enable patient and public participation alongside other stakeholders. It is while reflecting on that value position and the context surrounding it that I discuss the findings from the EPITOME study in what follows.

I found that while some interviewees understood the purpose of COS and the Delphi survey, others struggled to understand the purpose and aspects of the Delphi survey method which in turn influenced their contribution and experience of the study. The accounts of the interviewees indicate that COS participants would benefit from further guidance and support.

Interviewees could be broadly separated into two categories; those with and without previous experience of COS development and/or Delphi surveys. The accounts of those with previous experience, both HPs and patients, showed they had a good understanding of the purpose of COS and were satisfied with the Delphi survey as a method of participation HPs without previous experience reported engaging with relevant literature and colleagues prior to and during participation, thus enhancing their understanding and experience. In contrast, the accounts of patients without

previous experience indicated considerable variation with some showing good understanding, while others understood little of the study and its purpose. Aspects that the latter group struggled with included understanding that the Delphi survey aimed to achieve consensus amongst stakeholders, applying the scoring system and knowing whose views to represent when participating. This limited their engagement and interpretation of the documentation they had received from COS developers, and their input and experience of COS development.

The importance of representing of all relevant stakeholder groups including patients in COS development (106, 123) is increasingly recognised, as it is in wider health research (227-229). There is also growing appreciation of the importance of supporting their participation in ways that are meaningful, thus avoiding tokenism and enhancing the credibility and validity of the resulting research (230, 231). However, my findings suggest that not all the interviewees thought their participation in COS development was meaningful, as the purpose and process of the study was communicated in ways that were not accessible for them. Theory surrounding health literacy describes its role in patient empowerment and advocates for information to be made accessible to all patients in appropriate formats (232-235) This is particularly important for patient participants in COS development, most of whom will not have taken part in this type of research previously nor have access to the literature or colleagues to illuminate the process. A few patient interviewees in this study indicated that they saw understanding COS Delphi studies as their personal responsibility or felt uncomfortable with their limited of understanding. However, when asking patients to participate in COS studies developers are inviting them to the world of research (123), thus, it is the responsibility of the COS development community to ensure the guidance and support is in place to allow meaningful participation. There has been a rapid expansion in the number of COS being developed, with an associated rapid increase in the number including patients in Delphi surveys. My findings indicate that this expansion has perhaps outpaced the development of relevant guidance for Delphi studies to enable meaningful participation for all.

Delphi surveys have been used across multiple fields from military settings to financial and business fields, project management and health research (136, 236). The method has been modified across all fields to serve a variety of purposes (236), including within COS development. Much of the wider literature surrounding Delphi survey documents the experiences and reflections of research teams and the methodological modifications they have used (123, 237-242). To the best of my knowledge there is no literature which directly documents the experience of Delphi survey participants in EPITOME's in-depth manner. However, recent surveys of COS Delphi participants focussed on improving recruitment and retention indicated that the participants were generally satisfied with their experiences of Delphi surveys (198, 199). This study points to specific areas where further guidance and support is required to communicate the purpose of COS and the process of the Delphi survey which I summarise as pointers for COS developers to consider in Box 3.2. This complements the findings of two recent surveys of COS Delphi study participants which indicated that they benefit from repeated guidance on principles of core outcome set development during the rounds, that reminders about these principles were acceptable (199), and that recruitment and retention of participants is more likely with personalised communication (198). To date the most common way of providing participant information regarding a research project is via written documentation. Much research has indicated poor health literacy is prevalent (243-246), thus the importance of ensuring plain language communication cannot be underestimated. However, this study's findings suggest not only is plain language communication required, but also further consideration of how to explain the purpose of COS in ways that are relatable and salient to patients. This explanation and delivery could make use of visual, written and auditory methods, such as analogies, infographics, visual metaphors, digital stories and other narrative forms. The most appropriate method or combination of methods is likely to depend on the population and health condition to which the COS will be relevant. The use of visual resources have been documented in other healthcare areas such as health promotion (247), patient education (248) and nursing training (249). In COS development demonstration videos of the Delphi survey enhanced participant retention to the study (198). The COMET website provides resources to help

developers facilitate participation, including documents explaining COS in plain English and an animation video (http://www.comet-initiative.org/resources/PlainLanguageSummary), co-produced with members of the public.

This study also indicates areas in which further research and direction would be useful. The issues raised by interviewees regarding how to apply the scoring system, point to the need for better communication. The 9-point Likert scoring system where items are graded in accordance to their level of importance is a common method, recommended by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group (250). There are statistical considerations in support of using a longer scale including the ability to calculate variance in scores. Thus, it is important that participants in COS Delphi studies have the information and support they need to apply this system. Involving patients and members of the public as active research partners would provide a patient perspective on the suitability of different aspects of the COS study from design to conclusion, including helping with the development of appropriate documentation, resources and support (123, 198).

Interviewees also raised the issue of whose perspective to take into account when scoring outcomes. Pending further research, I would recommend that in the first round of the Delphi survey COS developers ask participants to score according to their own individual perspective, not score according to the perspective of others. In the second or subsequent rounds participants should be asked to reflect on the scores of other participants, while being clear that they do not have to change their own scores. Having reflected participants should be asked to score according to their current view of what a COS in that specified health condition should include (251). Participants can be encouraged to score outcomes they have no experience of to date, but may experience in the future, although an "unable to score" option or equivalent should also be provided for each outcome. A key exception to participants scoring from their own individual perspective is when carers act as proxy respondents in COS studies. In health research on certain patient populations there is often no alternative to using proxies (252, 253), yet there is evidence of discrepancies in how proxies prioritise outcomes compared to patients themselves

(254, 255). During the first round of COS Delphi studies proxies should score according to what they anticipate is the perspective of the patient and not from their own perspective as a carer, and follow the same advice as other participants in subsequent rounds. Thus, COS developers should consider which proxies can provide a valid opinion on the anticipated perspective of the patient and how best to support this type of participation.

Some interviewees described the motivation and emotions associated with their participation. Understanding that participants are motivated to engage in COS development out of desire to contribute to the research topic and satisfaction with the Delphi survey's collaborative and international approach will be useful to COS developers when advertising and recruiting participants to their study. The emotional impact of participation requires consideration from developers and researchers when designing and conducting their COS studies to optimise the experience of participants and minimise any negative impacts on them.

3.4.2 Strengths and Limitations

This study has provided insights into COS development via Delphi surveys from the perspective of participants. As previously noted, participation in the COS Delphi studies was not a particularly salient event for interviewees, however during their interviews they were provided with tailored prompts and reminders as needed.

This study only describes the experiences of participants who agreed to be interviewed, recruited from seven COS studies and limited to English-speakers. Those interviewed, including patients, mostly described themselves as having "professional backgrounds". Thus, while saturation was reached within our sample we note that interviewees' experiences and perspectives may not but typical of the wider patient population. However, by purposively sampling across a range of COS studies, we anticipate that our findings will be broadly transferable to other COS studies. Moreover, our interviewees were international, reflecting the increasing international development of COS.

Pointers
• COS developers should consider the most appropriate medium(s) to communicate their COS Delphi studies information and guidance *Points to consider: Language used, target audience, health condition* • COS developers need to ensure that the scoring system used is explained in ways that participants can understand. • COS developers should explain to participants whose perspectives they should consider when scoring in different rounds • COS developers should explain to participants that in the first round of the Delphi survey they should score outcomes according to their own individual perspective. *Proxies: In the first round, COS developers should ask proxies to score according to what they anticipate is the perspective of the patient and not from their own perspective as a carer* • COS developers should ask participants in second or subsequent rounds to reflect on the scores of other participants, while also being clear that participants do not have to change their own scores. *Proxies: should follow the same advice as other participants in second or subsequent rounds* • COS developers can encourage participants to score outcomes they have no experience of to date, but may experience in the future, although an "unable to score" option or equivalent should also be provided for each outcome. • COS developers should consider the potential influence of their COS Delphi on participants and take appropriate steps to minimise negative effects. • By understanding what motivates participants into COS Delphi studies, COS developers can devise appropriate recruitment and retention strategies

Box 3.2: Summary of the pointers and recommendations COS developers should consider when designing and conducting their COS Delphi studies

3.4.3 Summary

The results from this interview study contribute to the growing evidence base on participation in COS development. The identification of areas where participants need enhanced guidance and support will be useful to future COS developers when planning their studies, enabling them to recruit and support participants towards a meaningful and positive experience of COS Delphi studies.

COS developers are increasingly including international patient participants in their studies. Thus, the work described in Chapter 5 details consultations I had with a range of European experts on whether patients in the experts' respective countries would participate in COS Delphi studies. This enabled reflection on how we as researchers can facilitate and support international patient participation in COS development, detailed in Chapter 5. Future research recommendations to further enhance patient participation in COS development and the prioritisation of health outcomes are also detailed in Chapter 5.

Chapter 4: Exploring patient and public input in clinical outcome selection during guideline development

Preface

This chapter describes the methods and results of an ethnographic study I undertook to explore the involvement of patients and members of the public in clinical guideline development, with a specific focus on how patients and members of the public influence health outcome selection. The research investigated the support and processes surrounding patient and public involvement in clinical guideline development and explored the perspectives of the individuals involved. Work arising from this chapter will be submitted for publication at a peer-reviewed, open access journal. Sections of this chapter include direct excerpts from the ongoing manuscript. As lead researcher, I was responsible for the preparation and drafting of the protocol, data collection and analysis. I wrote the original draft of the ongoing manuscript, which was edited by senior authors and will undergo peer review.

4.1 Introduction

Clinical guidelines are *"systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances*" (256). If successfully designed and implemented, clinical guidelines should standardise practice by reducing variation in care across health care settings (257, 258). However, poorly developed clinical guidelines can compromise the quality of care provided by health professionals to patients, resulting in suboptimal, ineffective or even harmful practices (176). Generally speaking, clinical guideline development follows rigorous methodology involving systematic reviews of relevant evidence. To ensure that the evidence is translated into meaningful clinical guidelines, it is essential that the evidence is contextualised to the everyday realities of healthcare service use and delivery (159, 259). Thus, the involvement of all appropriate stakeholders, including patients and members of the public, in the clinical guideline development process is important to ensure that guidelines are applicable to all those who will access, use or be affected by them.

Patient and public involvement (PPI) is understood as a cornerstone in enhancing the value and impact of healthcare research and delivery (260), including clinical guideline development (183). However, PPI is an evolving area, and there is still much debate about its definition, methods, operations, integrity and ethical standards (261). There is a need to ensure that patients are equal stakeholders in an expert-dominated environment, and that their lived experience and knowledge is integrated into the research and development process (262-264). One key area of clinical guideline development which patients and members of the public are likely to have an interest in, is health outcome selection. Health outcomes concern changes in the health status of an individual or population that are attributable to an intervention (265); examples include quality of life, fatigue, white blood cell count and pain. Health research in some areas has shown that health professionals have overlooked, or deemed insignificant, health outcomes that were later identified as important to patients (190, 191). If health outcomes deemed important to patients are disregarded in clinical guideline development, it renders the clinical guideline inappropriate to the needs and wants of the patients receiving healthcare.

Within clinical guideline development there are reports of the positive impact of PPI in health outcome selection (259, 266). Both Tong et al. and del Campo et al. facilitated PPI in their respective clinical guideline developments. Via a mixture of qualitative and quantitative methods they elicited the perspectives and needs of relevant patient groups and members of the public. The findings were subsequently fed into the clinical guideline development leading to a number of contributions to the overall clinical guideline development, including suggestion of relevant health outcomes (259, 266).

While PPI is recognised as an important component of clinical guideline development and is recommended or required by numerous guideline development organisations (159, 161, 162, 179) problems with its incorporation into the process can arise. In health research, failure to engage meaningfully with patients and members of the public can lead to tokenism, which is described as the inclusion of small numbers of patients, with limited involvement and impact on the process (267-270). The tokenistic involvement of patients can, in turn, limit the influence of clinical guidelines in improving the delivery of quality healthcare. In recent years, social scientists have focussed on understanding the processes of clinical guideline development and implementation. Their work has explored what goes into the production of clinical guidelines, such as the social organisation of knowledge within guideline development processes (271), and how guideline development is managed when evidence is absent for some key areas of the guidance (272). However, to the best of my knowledge there is yet to be any exploration of how different stakeholder opinions are integrated into guideline development, particularly during the health outcome selection phase. In light of these gaps, I undertook an ethnographic study entitled the 'The INVoLVED Study' (Investigating Lay-members' Views in Clinical Guideline Development), in which, I aimed to explore the involvement and influence of patients and members of the public within clinical guideline development at the National Institute of Health and Care Excellence (NICE) (159). NICE develops guidelines for clinical practice and social care for use by the National Health Service (NHS).

My PhD secondment to NICE provided an invaluable opportunity to explore patient and public involvement in health outcome selection during the clinical guideline development process. NICE plays a vital role in the development of evidence based clinical guidelines for practice and care in England via expert committees of health professionals, care providers and *"lay members"* (273) that review evidence. Lay members are individuals with personal experience of using health or care services, or from a community affected by the guideline. In what follows, I use the term *"lay member"* as defined by NICE: it refers to patients, carers, service users and people from organisations who represent these groups. I use *"health professional"* to refer to clinicians and clinical academics.

Lay members are typically recruited to NICE guideline developments via adverts on the NICE website. The lay member position is open to all patients and members of the public who have experience of the relevant health condition and can contribute patient and public perspectives to a committee's work. Lay members therefore include patients, family members, carers and employees of patient charities or organisations. Recruited lay members are invited to attend a training session delivered by PIP, where attendance is encouraged but not compulsory.

Procedurally, lay member input in health outcome selection during NICE clinical guideline development can occur at two junctures: i) scoping workshops, where the remit and scope of the guideline is discussed and agreed upon by the relevant stakeholders including patients and members of the public and ii) committee meetings, where the guideline is developed, based on a series of review questions set to answer the remit and scope of the guideline as agreed upon during scoping. During the early committee meetings, the technical team, which comprises systematic reviewers and technical analysts employed by NICE, devise evidence review protocols for each review question in conjunction with the committee members. To populate the various evidence review protocols with appropriate search terms, the technical team follow the PICO framework (patient/problem/population, intervention, comparator and outcome, previously described in Chapter 1). Thus, it is during these early meetings that the selection of health outcomes is made. The evidence review protocols are then used to search for

relevant literature and evidence surrounding each review question, which is then discussed and contextualised at subsequent meetings. In theory, all members of the committee can be involved in each step of the guideline development process.

In what follows, I report specifically on my findings in relation to how patients and the public influenced the selection of outcomes when determining the PICO framework in the context of NICE guideline development.

4.1.1 Aims and justification of an ethnographic methodology

I took an ethnographic methodological approach to meet the aims of this study, as it facilitated my objectives *"to 'get inside' the way each group of people sees the world"* and to *"document the culture, the perspectives and practices, of the people in their settings"* (274). Ethnography is a popular methodological approach used across multiple sectors including health services research, where it has a research history spanning over sixty years (275-278). It is particularly useful in health services research as it allows researchers to study social interactions, behaviours, and perceptions within and across groups, teams, organisations and communities. During clinical guideline development patients and members of the public are engaged in an interactive process involving numerous stakeholders that can be observed in a particular setting (30). By taking an ethnographic approach, I was therefore able to understand how patients and members of the public got involved in the clinical guideline development process and how this process was understood and experienced by patients, members of the public and other stakeholders present.

As a methodology, ethnography facilitates researchers in eliciting rich, holistic insights into peoples' views and actions in their everyday worlds, through the use of multiple, usually qualitative, methods (279). Qualitative methods enable researchers to develop a deep understanding of a phenomenon without measuring or quantifying it (201). Observation, both participant and non-participant, is the most recognisable ethnographic method (280). Other common methods include formal and informal interviews (281). Conducting in-depth observations of clinical guideline development meetings enabled me to understand how input from patients and members of the public is negotiated in practice. By subsequently interviewing the various patients and members of the public involved, I was able to also explore their experience and

understanding of the clinical guideline development process. These two methods allowed for triangulation, a hallmark of an ethnographic approach, which enables the researcher to gain different insights into peoples' perspectives, behaviour and interactions (224, 282). Furthermore, ethnographic approaches can facilitate openness and flexibility as it enables the researcher to respond to the research findings as they unfold (282) and adapt to unforeseen events in the research process. This was particularly useful in this study, as it allowed me to add extra observations in other relevant settings, such as scoping workshops and lay member training sessions, which are further detailed in section 4.2.2.

4.1.2 Theoretical perspectives

A. My initial positioning

As I discussed in Chapter 3 (section 3.1.2), it is impossible for most individuals to be free from value or attain complete objectivity in the research process. This acknowledgment is particularly important in ethnographic research, as it is a methodological approach which draws on the interpretations of the researcher. The researcher describes the phenomena they are observing and puts their interpretations into the context of other data and evidence to draw conclusions, or in the case of the study described in this chapter, to make recommendations. Researchers must take appropriate steps to ensure the integrity of the findings, this includes methodological considerations in data collection and analysis, which I will detail in the methods section of this chapter. Other steps include recognising one's own positions and values, so that one can be reflexive and open about how these may influence the studies conducted, from conception through to dissemination.

In Chapter 3 (section 3.1.2), I described my value position as the belief that patients and members of the public should be included in guiding research that is relevant to them and that, if it is done well, their inclusion can increase the quality and validity of the results thereby having a positive impact. This is a position that I extend to the study detailed in this chapter, with regard to patient and public involvement in clinical guideline development.

B. Choosing my lenses

In Chapter 3 (section 3.1.2), I offered my description and discussion of the different lenses and paradigms through which researchers can conceptualise, design and conduct their studies (Table 3.1). In quoting Miles (214), I described my view that in clinical research, researchers need a range of lenses through which data can be viewed. Thus, while I approached the work detailed in Chapter 3 from a pragmatic paradigm, the interpretivist paradigm was a more fitting lens for this ethnography.

Within the interpretivist paradigm, multiple realities exist and are dependent on other systems, such as individuals and groups, for meaning and understanding (210, 283). Interpretivism readily lends itself to the ethnographic approach as the goal of interpretivists is to understand and interpret the meanings of human behaviour and how people make sense of their actions, by exploring motives, meanings, reasons and other subjective experiences (284). Thus, interpretivist researchers usually rely on research processes and methods that follow a flexible and iterative approach (283). This was particularly pertinent in this study as it enabled me to capture many meaningful interactions between individuals and groups (285).

A limitation often associated with ethnography is the challenge of separating the ethnographic subject and the researcher's analysis (286). However, interpretivism accepts that the researcher and their study population are interdependent and mutually interactive (287). The interpretivist researcher is intertwined with the data collected and the results produced (288). Therefore, interpretivist researchers are expected to clarify their position and biography (289), as I did in section 4.1.2 Aabove. Furthermore, I reflect on my position and surrounding influences while discussing the findings of this work in section 4.4.2.

4.2 Methods

4.2.1 Sampling and data collection

The sampling of the guidelines in this study focussed on those being developed for clinical practice within NICE, rather than social care or public health practice guidelines. Within these, I sampled clinical guidelines that I could observe fully (from start to conclusion, or as close as possible). Initially, I selected three guidelines for in-depth observation. I selected these guidelines pragmatically as they were clinical in

nature, were about to start development and their proposed timelines coincided with the timelines of my PhD and so I anticipated that I could observe them from the first meeting and as close as possible to the final meeting. I thought the opportunity to observe these guidelines from the first to concluding meeting if possible was important to the ethnographic nature of this study. During the sampling period these three guidelines were the only possibilities that fit the above criteria. I approached the chair and guideline development manager of each guideline and explained the purpose of the study. An example of my request can be found in Appendix A4.1. I was granted permission to study two of these guidelines. One guideline development manager declined my request for observations, after discussion with the chair, due to the sensitive and somewhat controversial nature of the health topic. A number of weeks after beginning dating collection I learned of another guideline due to commence development in the following weeks, which suited my timeframe and again requested permission to observe. However, after some initial discussion and clarifications with the guideline development manager and the chair of the committee, who happened to be a lay member, I decided against pursuing the guideline and instead used my resources on additional observations. Thus, I progressed with two guidelines for in-depth observation. I later added in extra one-off observations at other clinical guideline development meetings, scoping workshops and a lay member training session. These extra observations were added to aid my understanding and exposure to the clinical guideline development process, subsequently helping put the data and interpretations into context. The details of the observations can be found in Table 4.1.

Data collection was conducted over a 12-month period from October 2017 to September 2018 and comprised in-situ observations of clinical guideline meetings, scoping workshops and lay member training sessions (Table 4.1). In total, I observed twenty-two different meetings which equated to over 230 hours of observational fieldwork, as detailed in Table 4.1. During these observations I conducted ethnographic interviews (spontaneous, informal conversations in the field which were directed around the focus of the research) with various committee and technical team members. I provided all committee and technical team members

from the two guidelines that were followed in-depth with a participation information sheet (Appendix A4.2) and they subsequently gave written consent (Appendix A4.3) for the observations. I reassured all committee members that the focus was on the processes around lay involvement and not on individuals' performance or the guideline content. I recorded the observations and ethnographic interviews through fieldnotes made during (*in situ*) and soon after the time of observation. Best practice states that *in situ* the fieldnotes must be orientated towards the aims and central research questions that need to be addressed, while being as inclusive as possible toward all events and interactions that may not be immediately understood, but whose relevance will become apparent later (221). The fieldnotes consisted of jotted notes including direct quotes and short notes which aided my later recall (290). I then wrote these initial jottings out as full fieldnotes in Word files. I did this as soon as possible after leaving the site. I included detailed descriptions, analytic notes, observer comments about the setting and subjective reflections. I also included brief diagrams and schema of the physical setting, as studies show that this can assist recall at a later date (291). I clearly and accurately labelled the data as I collected it with the date, time, location, length of observation, who was present (using code and pseudonyms) and keywords (292). I also collected relevant documents such as agendas, minutes and reports and used them as a memory aid when writing up the fieldnotes.

Number of observations	Setting	Focus of observations	Breakdown of observations
15	*In- depth guideline committee observations*		*All full day meetings* *9.30am- 5pm*
8	Cancer (GC4)	The inclusion of lay members in developing the guideline and the interactions and processes surrounding their inclusion	8/8 meetings 12 full days*
7	Obstetrics (GC9)		7/13 meetings 8 full days*
3	*Additional guideline committee meetings*		*All full day meetings* *9.30am-5pm*
1	Cancer (GC6)	The inclusion and interactions of lay members within the specific meeting.	1
1	Cardiovascular health (GC5)		1
1	Gynecology (GC1)		1
3	*Scoping workshops*		*All half-day meeting* *3 hour meetings*
1	Dermatology	The inclusion of lay members in scoping of the guideline. The interactions and processes that occurred.	1
1	Mental health		1
1	Rehabilitation		1
1	*Training workshops*		*All full day meetings* *9.30am-5pm*
1	Lay member training session	Training and advice NICE provided to lay members and their interactions on the day	1
22 meeting	Total hours	230 hours approximately	

*Table 4.1. The setting and focus of the in-situ observations, including the number of observations made in each setting. * A number of meetings occurred over two days.*

These observations and ethnographic interviews were further supported by eighteen in-depth semi-structured interviews with lay members, health professionals and committee chairs who were involved in clinical guideline development at NICE over a five-month period in 2018 (Table 4.2). Semi-structured interviews allowed for further exploration of committee members' experiences and understanding of the guideline development process and their involvement in it. The open-ended nature of such interviews enabled interviewees to talk about unforeseen areas which were important to them (221). I interviewed: lay members from nine different clinical guideline committees (n=14) this included two lay members who were exclusively from relevant national patient charities, health professionals from two clinical guideline committees (n=2) and committee chairs from two different clinical guideline committees (n=2). In the two clinical guidelines that I observed I approached the chairs, health professionals and lay members in person and asked them if were willing to be interviewed, in total eight interviewees were recruited from these two guidelines. I recruited the lay members from guidelines I had not observed via the NICE Public Involvement Programme (PIP), who are responsible for developing and supporting the involvement of people who use services, carers and members of the public, along with the organisations that represent their interests. PIP asked a selection of lay members from guidelines that had recently concluded or were ongoing if they were willing to be interviewed and were happy for their contact details to be forwarded to me. I then contacted these lay members directly, provided the relevant information (Appendix A4.4), and if they were happy to proceed, set up an interview. In total, I contacted 24 potential interviewees; six never responded, while eighteen responded and agreed to be interviewed.

In these interviews I explored lay members' understanding and experience of the guideline development process and the role and influence of the lay members. The topic guide was informed by qualitative research best practice guidance (221), and discussion with guideline developers and members of PIP (Appendix A4.7), the key points covered by the topic guide can be found in Box 4.1. This comprised open-ended questions and prompts to stimulate a conversation and allow for unanticipated topics to be discussed. The topic guide was tailored for each

interviewee depending on their role within the committee (chair, health professional or lay member) and stage of the guideline development (recently concluded or currently in development). I conducted interviews face to face (n=11) or via telephone (n=7), and all interviewees gave informed written (Appendix A4.5) or oral (Appendix A4.6) consent prior to the interview beginning. Interviews, which lasted 75 minutes on average (range 40-90 minutes), were audio-recorded, transcribed verbatim by a University of Liverpool approved transcription agency and pseudo-anonymised before being analysed. I also made reflective fieldnotes immediately after each interview.

Key areas covered during interviews

- Background

To explore the interviewee's background and to elicit contextual information about how his/her experience of the clinical guideline development began

- Preparation

To explore how interviewees prepared for the clinical guideline development

- Engagement phase

To explore the key processes the interviewee engaged with during the guideline development. Experiences they had, contact with others (committee, NICE, technical teams etc.)

- Reflections

To explore how the interviewee now views their experience of participation, the methods used and the overall guideline development process

Box 4.1: Summary of the key areas covered during the interviews. A full list of questions can be found in Appendix A4.7

	Pseudonym	*Gender*	*Committee*	*Committee Role*
1	Joan	Female	GC1	Lay member (patient)
2	Antonia	Female	GC1	Lay member (patient)
3	Grace	Female	GC2	Lay member (carer and associated with relevant patient charity)
4	Eve	Female	GC3	Lay member (senior employee of relevant national patient charity)
5	William	Male	GC4	Committee chair
6	Richard	Male	GC4	Lay member (patient)
7	Lisa	Female	GC4	Lay member (senior employee of relevant national patient charity)
8	Henry	Male	GC4	Health professional
9	Greg	Male	GC5	Lay member (patient)
10	Julian	Male	GC5	Lay member (patient)
11	Ben	Male	GC6	Lay member (patient)
12	Dylan	Male	GC6	Lay member (carer)
13	Ann	Female	GC7	Lay member (patient)
14	Mary	Female	GC8	Lay member (patient)
15	Cecilia	Female	GC9	Health professional
16	Andrew	Male	GC9	Committee chair
17	Ruth	Female	GC9	Lay member (carer)
18	Jennifer	Female	GC9	Lay member (carer)

Table 4.2: In-depth, semi-structured interviewee demographic characteristics.

4.2.2 Data analysis

Following Braun and Clarke's thematic analysis approach, I coded the data inductively (222). The analysis focussed on understanding patterns and structures of lay member input in clinical guideline development committees and how this process was shaped, alongside understanding the challenges of lay member input. I specifically looked at the guidance, processes and experiences surrounding the selection of outcomes within the PICO framework. I initially read and annotated the fieldnotes and interview transcripts to gain an overall impression of the data. I then coded the data and grouped together codes to identify and organise recurring patterns and themes into categories (222), which were applied and refined across the data (293). When I needed clarification or further understanding about various points or processes that I was observing, I followed-up with the appropriate individuals, or sought guidance from my supervisory team or contacts at NICE. As this study was part of doctoral research, I performed all the coding and identification of themes. However, transcripts, codes and themes were discussed and reviewed regularly throughout the analysis process with my supervisory team, who each read a sample of the fieldnotes and transcripts and reviewed reports of the developing analysis. We all agreed that data saturation (the point at which new data cease to contribute to the analysis) had been reached after 230 hours of observation and eighteen interviews. I used Microsoft Word to facilitate coding and analysis (223).

4.2.3 Ethics

The study was reviewed and approved by the Health and Life Sciences Research Ethics Committee (Psychology, Health and Society) at the University of Liverpool in October 2017 (reference: 2025) (see Appendix A4.8). Furthermore, the study was approved by NICE who provided access to all observation sites and supported interviewee recruitment.

4.3 Results

NICE acknowledge the importance of lay member involvement in guideline development (159). As an organisation they have developed various processes and mechanisms to enable and support lay member involvement. In what follows, I present my findings in relation to one specific aspect of the clinical guideline

development process, namely lay member influence in selecting health outcomes within the PICO framework. In this study I show that while most lay members were likely to become involved in other aspects of the clinical guideline development, they were not easily able to get involved in selecting health outcomes. I show that the reasons behind this include: perceived role of the lay member, the timeline of the clinical guideline development process, and the medical and scientific technicality of the guideline content. However, in presenting the findings I draw on four instances where lay members were involved, either directly or indirectly, in health outcome selection and use these instances to suggest potential solutions to facilitating lay member involvement in outcome selection. These include that guideline developers need to contextualise the clinical guideline content and provide lay members with enhanced opportunities to engage in the process. By identifying aspects of the guideline development process which hindered lay involvement in outcome selection, I hope that future lay involvement can be improved. Furthermore, at various points of the guideline development process, health professionals had the same limited involvement as lay members. Thus, in some instances which follow, I report my findings in relation to the committee as a whole, rather than lay members exclusively.

4.3.1 Outcome selection and lay member involvement

During my observations of a lay member training session, lay members were introduced to the guideline development process. This covered topics such as, what scientific evidence is and how it is collated and used, what outcomes are and the lay member role in the guideline development process, including how and when to get involved. Lay members were also advised of the various resources and support available regarding guideline development, and the PIP members facilitating the training session provided examples illustrating the impact of lay members in previous guideline developments. When interviewed, lay members largely described these training sessions as *"helpful"* and *"empowering"*, praising the explanation of their role, the process and the scientific terminology.

Specifically, during the training I observed, lay members were told by members of PIP facilitating the training about the importance of their input in directing health outcome selection for the evidence review protocols:

> *There was some time dedicated to explaining "outcomes" and how the "lay member voice and input is needed" in deciding what outcomes to search for in various review questions. A slide on the PowerPoint presentation read: "Protocol stage is a good opportunity for lay members to identify outcomes of the treatment, activity or care that are important to people using services or carers." Further to that the lay members were advised to "be specific, evidence reviews are resource intense", and that "usually there are 3-4 main outcome measures." PIP also provided some examples explaining what outcomes are. Lay members appeared to be actively taking notes directly onto their handouts during this session. (*Fieldnotes from the lay member training session.)

However, despite lay members finding these sessions positive in generally providing information and support, they largely did not recall the emphasis placed during sessions on the importance of the lay member role in health outcome selection. No lay members interviewed said the training session had influenced their involvement in health outcome selection. Moreover, during the observations lay members rarely participated in discussions about health outcomes or their selection. When interviewed, most lay members did not mention health outcomes as an area in which they were, or even wanted to be involved with. When asked who he thought was most involved in setting the evidence review protocols (which is where outcome selection occurs through the PICO format as outlined previously), Andrew, the chair from GC9, said:

> *"I think probably the NICE technical team, followed by probably the health professionals with specific expertise on the committee would probably be the ones who had the most influence on PICO, […] the lay members get involved in the later discussion."* Andrew, GC9

Echoing Andrew's description above, observations of GC4 and GC9 meetings found that the technical team led most of the early phase meetings by introducing prepared drafts of evidence review protocols for each review question and asking the committee to comment. For most evidence review protocols discussed during these observations, as noted above, lay members rarely got involved and even health professionals only became involved when their specific expertise was relevant to the review question. Frances, from GC3, was the only lay member who recalled learning about evidence review protocols and health outcome selection at the lay member training session. She characterised the protocol setting and thus, health outcome selection, as a: *"system the technical team would go through".* According to Frances, lay member and health professional involvement did not occur until the later phase when they started looking "*at the* (resulting) *evidence statements and use those to decide what the overall recommendation was."* Health professionals and lay members observed or interviewed as part of this study expressed the sentiment that it was not their role to get involved in this stage of the clinical guideline development and indicated a belief that they had different roles during different stages of the guideline development.

Lay members in particular understood the early phase meetings, where health outcome selection occurred in clinical guideline development, as something that was outside their remit. They described the process as one that was reserved for the expertise of the technical team. Lay members described their role and involvement as occurring at later meetings, as I describe in the following section.

Lay members' views on their role

While lay members mostly reserved specific health outcome selection, and the processes surrounding it, as a decision process for the expertise of the technical team, they did describe having a role in the clinical guideline development process more generally. They perceived this role as one involving them presenting the feelings and perspectives of patients for whom the clinical guideline is relevant. For example, Richard a lay member from GC4 and I spoke on multiple occasions about his *"motivation"* for joining the committee, with Richard commenting that:

> *"The whole* (patient) *journey through the cancer thing […] I thought there was a colossal void with a lot of very excellent stage posts during the process, during the treatments, during the investigations and so on, but there were big gaps in-between and it is a pretty desolate landscape when you are on the other* (patient) *side."* Richard, GC4

Thus, his hope in joining the committee was to explain this *"void"* to the committee from a patient perspective, thereby helping ensure that the content of the guideline would improve the *"journey"* for future patients. As with other lay members in this study he was describing his aim to humanise the resulting guidance by emphasising the importance of their patient experience. Performing their role in this way could guide health outcome selection, even if the lay members themselves did not comment on the direct link or specifically suggest a health outcome themselves. For example, during one interview, Joan a lay member from GC1, described how her experiential patient knowledge offered an alternative perspective and understanding of an intervention to that of health professionals:

> *"The clinician said oh it is just a simple test [...] And I said excuse me it is not a simple test and so* (technical team member) *said ok explain to us and so I gave the graphic detail of what it is really like, and the clinician was saying yes actually that is true. So, I thought oh gosh straight away I have got something to add here. Not to make it dramatic but to, it is all very well for a clinician they do it all the day but for a patient it is not like that. So, for the researchers to understand precisely perhaps even visualise I think that was helpful for them trying to weed out quite what the key search terms should be to get a bigger understanding of what we are trying to say."* Joan GC1

Joan was the only lay member interviewed to have discussed her role in this early phase of the clinical guideline development. Other lay members in the study only commented on their later involvement in the process. For example, when referring to evidence review protocols during his interview, Ivan, a lay member from GC5, described it as a section for the technical team and highlighted his own involvement in providing a patient voice in later meetings:

> "*I think that* [setting evidence review protocols including determining the PICO framework] *is more for the technical team […] the things that are relevant for a patient and their feelings and their journey, then yes […] I would have contributed to some of the later discussions we have had like that, how does this impact on the patient, or does it impact on the patient."* Ivan, GC5

However, several lay members felt that their involvement during the later phases was also restricted due to the nature of the clinical guideline. While all guidelines were clinical, some had more technical content or were more scientific and intervention driven than others. In one of the more technical guidelines lay members described feeling constrained in their ability to contribute a patient perspective at any point of the process. As a result, they negotiated alternative roles for themselves. Jennifer a lay member from GC9 described this alternative role as *"safeguarding"* the process;

> *"I do find it difficult to feel like I have a role in influencing that output* (the guideline)*, I am obviously not a doctor. I think it would be unrealistic for anyone to expect me to put my hand up and say oh actually I think you should use* (intervention) *because that is not what my role is. But, I think I can be there to see that the way that the committee make their decisions make sense, [...] to, to see that we are playing by the rules if you see what I mean and not so… rather than have that input in terms of the medical side, so I do still have a role but it is different."* Jennifer, GC9

These *"safeguarding"* roles arose when the lay members felt they could not get involved in the guideline due to its technical nature. Thus, they created an alternative role for themselves: to act as overseers of the committee and the development process. In doing so, the lay members directed their efforts towards trying to ensure the other committee members remained focussed on the topic and followed the appropriate procedures and timelines, instead of offering a patient perspective and input.

4.3.2 Understanding the challenges surrounding lay involvement

As described above most lay members in this study found it difficult to consider health outcomes as part of the scope of their involvement and therefore most did not participate in their selection during clinical guideline development. Below, I suggest based on observations of the processes and reflections potential reasons as to why lay member involvement in health outcome selection was limited.

Timeline of the process

Clinical guideline development has to conclude within a specified timeframe. Thus, there are specific targets and milestones for each phase of development, including the timing of committee meetings. This means clinical guideline development follows a largely linear process, as there is little time for revisiting tasks and items once discussed initially.

Both interviews and observations indicated that lay members and health professionals had little time or opportunity to familiarise themselves with the process and with each other during the early phases of clinical guideline development. Consequently, their involvement in influencing the clinical guideline was restricted, including in relation to health outcome selection. For example, during observations at GC4 and GC9 the involvement of committee members was mainly during discussions that took place in the later phases of guideline development:

> *A number of health professionals became quite animated and involved in discussion, they had been largely silent in the meetings up to this point. A number of dynamics have changed i) we are now into the evidence discussion phase so they can offer their interpretations, ii) committee members are visibly more comfortable with the process and with each other, they are now chatting together more regularly during meetings and break time, during discussions they appear to engage more with each other, challenging and supporting what has been said.* Fieldnotes from GC4, meeting 5

At later meetings in the clinical guideline development process committee members became more vocal and involved in proceedings as they became familiar with the process and its content, as well as becoming comfortable with each other. Various committee members verbalised this as *"finding their feet"* in the process as time

passed. Grace, a lay member from GC2 further elaborated this point when she said, *"I felt a bit lost in it all and it took me probably a good 9 months before I really understood how the process worked"*. For Grace, this meant that she only felt able to get involved during later phase meetings. Similarly, health professionals described during interviews and observations, that the early phase meetings were *"a learning process."* Cecilia, a health professional from GC9 further elaborated on the impact this had on later meetings when she reflected:

> *"Some things probably could have bared repeating. […] a lot of the time, silence is taken as an indicator that yes you are fine with everything but it can often mean I am not really sure what is going on but I am just going to just keep on listening, see if I can pick it up."* Cecilia, GC9

As the early phase meetings were when lay members learned about the process and became familiar with each other, they were often silent and did not get involved in setting evidence review protocols. Thus, the need for different avenues of enquiry or search terms only became apparent in later meetings. This became an issue when, during subsequent evidence discussions and recommendation writing meetings, committees requested evidence which differed from what had been originally agreed in the earlier evidence review protocols. Joan a lay member from GC1 was one of the committee members to describe her *"difficult"* experience of this:

> *"We have asked for another review that has been rejected and I find that NICE can be quite inflexible and in fact quite aggressive about saying well those were your search terms* (including outcomes)*, so that is the end of it."* Joan, GC1

As Joan mentioned, the technical team sometimes responded inflexibly to requests for further evidence searches. My interpretation from observing various meetings was that the technical team were unable to respond to such requests due to resource limitations on time and personnel. In GC9 and GC4 I observed similar points of tension and disagreement between the committees who required further evidence, yet the technical team could not facilitate this as they were limited by resources. In these instances, the committee were usually tied to the original search terms and

protocols agreed upon during the early phase meetings. In turn, lay members were limited in their later involvement, if the resulting evidence was not relevant and clear to them.

Technical content of guidelines

As already noted above, lay members sometimes felt inhibited from participating in discussions because of their lack of understanding of the technical nature of the clinical guideline content, including review questions and committee discussions. For lay members this technical content comprised terminologies, abbreviations and topic content which they believed were largely only accessible to health professionals or those with specialised training in the field. The technical nature of the clinical guidance development work is illustrated by one of the review questions, which asked *'what is the optimal dose and fractionation schedule for people with localised* (type removed) *cancer* (cancer grading and staging removed) *who are treated with radical radiotherapy?'*

Most lay members therefore found such guidelines challenging to become involved in. When interviewed they often made statements such as, *"half the time I have no idea what they are talking about"* (Joan, lay member, GC1) while some expressed feelings of "*frustration"* or commented that their involvement amounted to "*tokenism"* (Richard, lay member, GC4). Committee meeting observations further point to this*:*

> *"Ruth, a lay member was invited to speak and I was struck by the change in her body language from earlier in the day, she looked annoyed, no longer smiling and or trying to engage with the other committee members. She talked about the difficulties the lay members had that morning and in previous meetings in understanding the review questions and related terminology and discussion content. She said that their lack of understanding means "they can't contribute as might be expected". Rebecca a health professional replied that "it is very difficult" to talk about the content in other terms as they are the questions that they have to review, to which the other health professionals nodded in agreement."* Fieldnotes from GC9, meeting 4.

Speaking on behalf of herself and the other lay members Ruth noted the recurring difficulties they had in understanding the clinical guideline topic and content, which in turn limited their input and involvement. During interviews several lay members questioned their role in technical discussions and whether alongside their lay experience, they also needed clinical knowledge and expertise regarding treatments. As Ben, a lay member from GC6 reflected in his interview: "*it would be interesting to know what NICE expect of a lay person going into this very technical, very medical orientated process.*"

However, one sub-group who did not appear to struggle with the technical content were lay members who were representatives from relevant national patient charities. They seemed to have a more in-depth understanding of the technical content than lay members with direct lived experience (patients or carers). Thus, these *"professional"* lay members were able to engage frequently throughout the process, including the early phase meetings and health outcome selection. For example, Lisa, a lay member from GC4 who worked for a relevant national patient charity, explained her position:

> "(my perspective is) *very different to other lay members because I have had to develop an unbelievably detailed knowledge of* (disease)*, its treatments, its diagnosis and all the rest of it […] If I didn't have that I would be lost in that process […] if I was just a member of the public I have no idea how I would necessarily get to grips with all the information that is presented. Or sometimes even understand the discussion."* Lisa, GC4

During observations, Lisa often suggested certain search terms including health outcomes in early meetings such as various adverse events associated with the treatments reviewed in GC4, asked questions or discussed points with other committee members. She was also active in later meetings. Nevertheless, like others, Lisa predominantly focussed her interview reflections on her involvement in the later phase of clinical guideline development and did not explicitly mention her contributions in earlier meetings about health outcome selection. However, she did distinguish between her knowledge, developed through her work, and that of a 'member of the public'. She therefore had insight on how her professional role and

background enabled her to be actively involved throughout the clinical guideline development process.

Perceived differences in priorities

In one particular clinical guideline development, GC9, I observed that lay involvement can be limited by the differences of opinion and priorities between health professionals and lay members. In GC9 these differences pre-emptively restricted lay member involvement in health outcome selection.

Within the healthcare setting related to GC9 the patient population is highly vulnerable and typically needs urgent intensive care. These patients are unable to represent themselves and thus a *"proxy"* such as a family member acts as the patient's representative. Family members with experience as proxies made up the lay membership of this particular committee. During observations of GC9, health professionals talked frequently about the *"moral and ethical obligation"* they felt with regard to treatment and care of patients. When developing the clinical guideline they frequently mentioned this sense of obligation, particularly when discussing the quality of evidence and the reality of practice. Furthermore, they regularly drew on their clinical opinion and experiences. However, whilst health professionals voiced their perspectives and asked each other questions, they rarely asked the lay members for their opinions and perspectives. For example, during meetings health professionals spoke about the vulnerable patient population, the need for intensive high-level care and their legal and moral obligations to patients which they referred to as their "*duty of care"*. This motivation was always posed around the need to focus on the wellbeing of the patients. Cecilia a health professional on the committee explained this "*duty of care* "in the context of GC9 as *"proxies often are having to make decisions for (the patient) but the proxies aren't the actual patients […] sometimes the duty of care is more to the patient, independent of what the proxy might believe."* This prioritising of the patient meant that the health professionals on the committee did not, therefore, see the views of lay proxies as relevant to the scope of the clinical guideline as the importance of health professionals' role and duty to the patient.

An example of this occurred when discussing the search terms for an evidence review protocol:

> *"Doug (a health professional) was stressing "it has to be clinically important outcomes and outcomes that will not heal with time, lay members won't know about those, they don't care." The other health professionals appeared to concur with this statement as they nodded and murmured their agreement. The lay members continued to sit in silence."* Fieldnotes from GC9, meeting 4.

Doug here restricted the involvement of lay members before they had chance to express an opinion or suggestions regarding health outcomes, as he proposed in this instance that their priorities and understanding differed from what the clinical guideline and the patient population needed.

When interviewed, Cecilia, a health professional in GC9, reflected that it was *"tricky"* for health professionals to include lay members as they *"have different concerns or interests."* Other health professionals from GC9 echoed these views, suggesting that while health professionals understood the presence and importance of lay member involvement, they struggled to involve them in GC9 in a meaningful way. Discussions with health professionals in this guideline indicated that they believed that the content was too clinically driven for lay members to understand. Furthermore, they suggested that the interests and needs of the patients differed from those of the lay members.

However, immediately after Doug's intervention as described above, the chair of the committee asked Jennifer, the lay member present, for her opinion. Having been silent to that point Jennifer suggested a health outcome. One of the health professionals then translated Jennifer's suggestion of a health outcome into a clinically recognised term relevant to the health intervention under discussion. During her interview Jennifer praised the chair of GC9 and the support he provided:

> "*I think Andrew is a great chair, [...] he is respectful and he can keep everybody in check. He knows when to bring people in, and he recognises you know when people have something to say, he went out of his way to come and meet me on*

the first day and involve me, and always makes time to come and talk to me sort of during the breaks and make sure if I want to fill that lay member slot and he will have a chat with me to see if there is anything that we need to get out of it."

Other lay members interviewed also praised their chairs for their support and guidance. This included how chairs ensured the use of plain language amongst the committee, provided the opportunity for lay members to get involved and contextualised the clinical guideline content in a patient relevant manner. This praise highlights the important role the chair has in facilitating the involvement of lay members throughout the process.

Achieving lay member input

As outlined in three instances described in the sections above (Joan, Lisa and Jennifer), it is possible to achieve lay involvement in health outcome selection. With the exception of Lisa, these examples were underpinned by lay members being given the opportunity and support by other stakeholders involved in the process to speak their opinion.

In what follows, I present a fourth instance in which lay involvement occurred and thus, indirectly led to relevant health outcome selection. This further illustrates how lay members can be involved with the appropriate support, guidance and collaboration, particularly from other stakeholders within the clinical guideline development. This final example involved Richard a lay member in GC4 who had direct patient experience of the health condition. By Richard's own admission he struggled with various aspects of the clinical guideline development process and at times questioned the influence of his role within the committee. He was mostly silent during both early and late stage meetings and usually only spoke when invited to do so by the chair of the committee, the technical team or other committee members. It was following such an invitation and Richard's input in response, in which provided his perspective and experience as a patient, that the committee resolved a dilemma regarding what search topics to include in an evidence review protocol:

> *The discussion returned to "self-management strategies" and if it should be included in the evidence review protocol. The health professionals who were engaging in this discussion were divided, with some completely for its inclusion and others opposed to it completely. At this point Richard was asked for his opinion by the chair of the committee. He spoke in favour of "self-management strategies" and the positive aspects they carried for patients like himself. After some follow-up questions to Richard from various health professionals and some group discussion it was agreed to include "self-management strategies.* Fieldnotes from G4, meeting 3

While Richard did not suggest any health outcomes directly, his perspective resolved a point of conflict between other committee members. By inviting him to share his opinions in a language that he could associate with his experiences, the chair signalled that Richard's perspective was important. In turn, this encouraged the other committee members to be receptive to Richard's *"lay"* opinion. Richard's input provided the impetus to include *"self-management strategies"* as an intervention in the evidence review protocol. Subsequently, the health professionals and technical team members then determined search terms, including health outcomes, in line with the focus on self-management. While Richard himself did not directly suggest health outcomes or other search terms, his patient perspective about the impact that intervention can have helped the health professionals and technical team determine the PICO framework.

Richard's case echoes the dynamics that occurred in two of the instances described earlier, in which lay member perspective, experience and opinion were invited by either the chair, technical teams or health professionals and supported by various members of the committee. These inputs were subsequently translated into meaningful search terms for the evidence review protocol.

In the discussion below, I summarise the results and argue that there is a need for further guidance and support to facilitate enhanced lay involvement in health outcome selection during clinical guideline development.

4.4 Discussion

4.4.1 Summary of findings

Lay involvement in health outcome selection during clinical guideline development is achievable, despite being limited within my sample. The findings from this study indicate that continued guidance and support could enhance lay involvement, not only in health outcome selection, but also in the overall clinical guideline development process.

Health outcomes are important for patients and members of the public, thus lay involvement in their selection is important in ensuring the clinical guideline is relevant and patient centred. NICE recognise this and encourage guideline developers and technical teams to search the COMET Initiative database for relevant core outcome sets (COS) studies to consider during clinical guideline development (159). However, COS were not used for the two clinical guidelines observed in-depth during this study (GC4 and GC9). Ten COS exist specifically for the health condition discussed in GC4. Within the COMET Initiative database, the scope of 8 of these COS are for clinical trials or clinical research and two are COS for practice, however only three of these COS included patient stakeholders in development. Seven COS studies developed for clinical trials or clinical research are listed in the COMET database in relation to the patient group discussed in GC9. While these COS may not be of direct relevance to the health condition and specific treatment within GC9, it is possible that they could provide a starting point for discussion and adaption by the committee. In both instances, it appears that the relevant COS were not identified by the technical teams. As described below, the use of relevant COS studies developed with patients and members of the public may help to ensure important and patient relevant health outcomes are considered during clinical guideline development.

The guideline developments sampled in this study could be divided into early and later phases. Health outcome selection predominantly occurred in the early phase meetings, however lay members did not feel like they could get involved in this early phase, meaning their involvement was largely limited to later phase meetings. For most lay members interviewed, health outcomes and their selection were not a prominent or memorable part of their experience. Instead, lay members largely saw

outcome selection in the early phase as part of the technical team's responsibility and focussed their own involvement on providing experiential knowledge during later phases. Previous work has investigated the development of teams or committees and the influences on their collaboration (294, 295). Findings from my work suggest that confidence to participate in committee discussions progressed over time, however, it was often too late to influence outcomes. These findings reflect previous research and theory on how the teams, groups and organisations go through different stages of growth and development as they come together and familiarise themselves with each other and their context (296-298). Work by Tuckman categorises this development process into four stages "forming–storming–norming–performing". His work suggests that these phases are needed for teams to grow, tackle challenges and problems, discover solutions, take action and deliver results. (298). While, NICE lay member training does stress the importance of lay member input in health outcome selection (and throughout the wider guideline) and emphasises the need for committees to work together, the findings of this study indicate that additional processes are needed to support lay members when considering health outcomes that are important to them and to support them in the clinical guideline development process sooner.

Previous research suggests the technical nature, content and language of clinical guidelines can be a barrier to patient and public involvement, not only in health outcome selection but in the clinical guideline development more generally (299, 300). This study supports these findings, in that, when lay members engaged, they usually spoke about their personal experiences and opinions, which did not require technical language. This was in contrast to the technical and scientific language of the health professionals, *"professional"* lay members and the evidence under discussion. The proliferation of the use of this type of technical content and language led to frustration amongst lay members as they felt it restricted their involvement and it led to some feeling that their roles were tokenistic.

Clinical guideline development is centred on reviewing scientific research and evidence, which naturally increases the technical content and language used. A few lay members in this study indicated that they saw understanding the scientific

research as their personal responsibility or felt uncomfortable with their limited understanding. It has been suggested that a lack of training and understanding of scientific methods and processes can limit lay member involvement (180, 301). However, caution should be exercised when considering further training as a potential solution. Lay members are invited to committees by virtue of their experiential knowledge (302) and should not be expected to have highly scientific and technical knowledge. When involving lay members, guideline developers are inviting them into the world of research. Thus, it is the responsibility of the clinical guideline development community to ensure that we support and understand lay members' lived experience. Furthermore, we need to actively consider appropriate support and guidance alongside the relevant methods and processes to integrate lay member input meaningfully into the clinical guideline, rather than relying solely on training lay members in scientific processes and language.

Instead of using *"scientific"* language, lay members offered their perspectives and experiences within the context of the clinical guideline development. On three occasions in this study when lay members became involved in health outcome selection the other stakeholders present acted as translators who put the lay input into clinically relevant term(s) suitable to the context of the review question. In some instances, this extended beyond simple translation of terms and instead relied on actively listening to the lay member's perspective and experience and subsequently drawing out the elements that were relevant to the context of the review question. This highlights the importance of ensuring all stakeholders involved in the process are aware of the importance of lay member input and encouraged to support it. It also raises the question of how guideline developers can best facilitate the interpretation and translation of *"lay"* outcomes into clinically relevant search terms.

By drawing on examples in this study where lay members did influence the health outcomes selected, we can identify several processes which help to facilitate and support their involvement. This includes collaboration between stakeholders, the use of plain language, contextualisation of the topic and meaningful guidance. It is likely that a combination of these are required to provide lay member involvement in health outcome selection and clinical guideline development more generally (183,

299, 301). Three of the examples of lay member involvement in health outcome selection in this study were achieved via the support of, and collaboration from, the health professionals and the technical team. The findings also showed how the chair of a committee can serve as a bridge between the interests of lay members and health professionals by inviting and facilitating input from the lay perspective. Thus, it is essential that guideline developers understand the significant role committee chairs have and provide appropriate support and training to chairs, so that the chairs are fully aware of and equipped to seek and support lay member input at all stages of guideline development. This is particularly important during early phase meetings when the health outcomes for evidence review are determined. Further areas where the chair's guidance could be beneficial include contextualising the topic content to a patient perspective and ensuring the use of plain language by the committee (303).

This study also indicates areas in which further research and procedural change would be useful. Guideline development via committee discussion and consensus is ideally an iterative process. However, the procedures and processes currently in use are linear, with set timelines and targets in place to contain resources (304). This linearity seemed to restrict not only lay member involvement, but also health professionals, particularly in the early phase and in health outcome selection. This suggests that guideline developers need to consider more flexible timelines and methods to support committee members from the earliest point of the process. Ensuring all lay members receive their training session before the first guideline development meeting could potentially encourage earlier consideration of health outcomes and lay member involvement in their selection. Furthermore, this training could introduce lay members to the concept of COS from an early stage so that if relevant COS studies are found, lay members have the opportunity to critically appraise them along with the rest of the committee. Currently, patients and members of the public are represented at NICE scoping workshops, thus, these scoping workshops may be an additional opportunity to ensure patient relevant health outcomes are sought and forwarded to the committee for consideration.

Facilitating proxy lay members also present unique challenges when involving lay members in clinical guideline development. For specific patient populations there is

often no alternative to using proxies (252, 253), who are legally charged with making decisions about a patient's care (305). When involving proxies in clinical guideline development they are being asked to consider a wide range of health issues and decisions. Evidence suggests there are discrepancies in how proxies prioritise patient reported outcomes compared to patients themselves (254, 255). Furthermore, it is important to consider that health professionals and proxies have distinct differences in their roles, duties and relationship to the patient. Despite all stakeholders likely having the patients' best interest as their motivating factor, these differences represent a point of tension as highlighted in GC9. Guideline developers should be aware of the unique difficulties that may present when involving proxies as lay members and consider how best to facilitate their input.

Alongside the importance of continued guidance and support between committee members, especially from the chair as described above, there are several processes which could also be considered in addressing the challenges outlined in this study. As already noted, the use of relevant COS studies developed with participation from patients and members of the public to inform the evidence review protocols offers a unique opportunity to consider health outcomes determined important by a wider range of patients and members of the public. Using such COS studies during the PICO determination stage in evidence review protocols could help ensure a range of patient voices are considered beyond the lay members present on the committee. As the number of COS studies developed with participation from patients and members of the public increases (197), it is likely that they will serve as another useful method of ensuring that patient and public perspectives on important health outcomes are considered during clinical guideline development. Thus, technical team members should be encouraged to continue searching the COMET database during guideline development for suitable COS, which they can then appraise with the clinical guideline development committee. Critically appraising the COS in collaboration with the full committee is important so that all members can provide expert experiential knowledge on whether the health outcomes identified are relevant to the remit and scope of the guideline development. Other methods of facilitating further lay input could include written patient statements as used in

health technology assessments (302) which provides the opportunity for patients to give their testimony or stories which can deliver "insight" for committees to consider. The use of other qualitative methods such as focus groups and individual interviews could provide the opportunity to elicit patients' priorities in a more holistic setting. The findings from these could subsequently be presented in the committee to provide context and perspective (180, 266, 299) via a trained patient liaison or representatives if needed.

4.4.2 Reflexivity

Throughout the data collection and analysis period I took steps to ensure my interpretations and analysis stayed grounded in the data. In particular, it was important to consider how my time spent collecting data and the relationships I built with various technical team members and committee members may have influenced my opinions surrounding lay member involvement and the process of clinical guideline development. This is particularly true for GC4 and GC9 where I spent the most time. I also engaged with various individuals at NICE from both PIP and the methods team in an effort to ensure I was understanding the various processes and procedures they had in place as fully as possible. This engagement included formal and informal meetings, summary reports and in-house presentations. At the same time, I endeavoured to maintain a relative independence from NICE in an effort to maintain an outsider's perspective on the procedures. It would be remiss not to consider how my presence may have also influenced those I was observing and whether there was any change in activity and behaviour because of me (306). By integrating myself as fully as possible into GC4 and GC9 by attending most meetings, I hoped that the committee would become familiar with my presence and no longer view me as 'the researcher', thus limiting the impact of my presence (306, 307). I also reassured all those involved in study that the purpose was not to examine or evaluate individuals but the process as a whole. It was my hope that by reassuring the committee members about the purpose, rationale of my study and my presence in meetings they would feel at ease with my observations and not as if they were being evaluated or examined in how they behaved or engaged as a committee member.

This study was supervised by Dr Jessie Cooper and Professor Bridget Young both of whom are experts in qualitative methods and patient centred research. Their knowledge and experience of the wider field undoubtedly shaped my views and understanding of the phenomena I was observing. I discussed both my analysis and interpretations with them, they helped me to consider and refine my thinking surrounding them. This in turn helped ensure that the findings remained grounded in the data.

As previously described in section 3.1.2.1, before beginning this PhD work, I believed in the importance of meaningful collaboration between all relevant stakeholders in improving health research. Thus, as with EPITOME, it is from that value position and the context surrounding it that I discussed the findings from the INVoLVED study in the above sections.

4.4.3 Strengths and weaknesses of the study

This study has provided insights on how lay members influence clinical guideline development, particularly health outcome selection. As previously noted, health outcome selection was not a particularly salient for interviewees, nor particularly visible during observations. However, by sampling from a range of clinical guidelines we identified aspects of the process that increased or reduced lay member involvement.

This study only describes the experiences of participants who agreed to be interviewed and observations from clinical guidelines and other meetings that we could access. Thus, while saturation was reached within our sample, we note that interviewees' experiences and perspectives and insights gathered from the observations may not be typical. However, by sampling from a range of clinical guideline meetings and lay members, we anticipate that our findings will be broadly transferable to other clinical guidelines. Furthermore, while this study sought to explore lay member involvement, our findings will also benefit the involvement of other committee members such as health professionals.

4.4.4 Summary

This study's identifies challenges to lay member input in health outcome selection during clinical guideline development, but it also found that such input is achievable.

Support and guidance at various junctures, including continued collaboration amongst the various stakeholders on the committee can enhance lay member input in health outcome selection. Guideline developers and technical team members should consider use of relevant COS which have been developed with patients to inform outcome selection during guideline development. Other methods of engaging lay members in guideline development should also be considered, along with the development of further resources to translate lay input into clinical guidelines at different points of the process. These findings will be useful to future guideline developers when planning their guidelines in identifying methods and mechanisms that will enable them to support their committee members towards a meaningful and engaged experience of clinical guideline development and health outcome selection. Further, this study points to areas in which further methodological research will be useful in informing future guideline developments.

Chapter 5: Reflections and Conclusions

Preface

Chapters 3 and 4 presented the methods and results of two individual studies I conducted regarding patient and public input in health outcome selection in two different settings within the course of this PhD project. Furthermore, through my PhD framework I was afforded the opportunity to manage a journal club with fellow PhD students about patient and public involvement (PPI) in methodological research. From this I gained an understanding of Early Stage Researchers' knowledge and experience of PPI in health-related methodological research generally. Furthermore, I consulted with European experts to gain an international perspective on how to include patients in core outcome set (COS) development, which was important due to the findings in Chapter 2 of this thesis indicating that the development of COS is increasingly including international patient participants.

These opportunities in combination with the formal studies detailed in Chapters 3 and 4 exposed me to different attitudes, questions and behaviours surrounding the different roles patients have in health research.

In what follows, I reflect on these various interactions and the aims of my overall thesis, highlighting various issues I believe we should consider as researchers. Finally, I offer my conclusions on what this thesis offers and my thoughts on future research opportunities that I have identified from my work.

In addition to the manuscripts already detailed in their respective chapters, this chapter also draws upon a commentary published in BMC Research Involvement and Engagement (2019; open access) (Appendix A1 Publications). Along with Ms Maria Olsen, PhD student, I was responsible for developing the original concept (under the guidance of Professor Paula Williamson), the data collection and analysis. Along with Ms Olsen, I wrote the original draft of the published manuscript, which has been subject to peer review.

5.1 Summary of main findings

The principal aim of this thesis was to explore how patients and members of the public prioritise health outcomes in core outcome set development and within clinical guideline development. Previous research has shown us that including patients and members of the public in health research has the potential to reduce waste and ensure credible, reliable findings. One area in which patients and members of the public are likely to have a specific interest in health research and delivery of healthcare is the selection of health outcomes. Health professionals have overlooked, or deemed insignificant health outcomes that were later identified as important to patients (190, 191). If outcomes deemed important to patients are overlooked in health research and healthcare delivery it renders the results inappropriate to the needs and wants of patients, and thus it becomes less relevant and more wasteful.

To enable meaningful inclusion of patients and members of the public in health outcome selection it is important that the most appropriate methods are used. Several different factors determine the processes surrounding the selection and prioritisation of health outcomes. This includes: the clinical setting, whether the aim is COS development or clinical guideline development; and finally the availability of resources. There are several methods of facilitating patient and public input in the prioritisation of health outcomes.

In this thesis, I first sought to explore what method(s) COS developers are using to facilitate patient participation in the development of COS. Understanding the landscape surrounding patient participation in COS development led to the question of how do participants, particularly patients, experience COS development and the method(s) via which they participate. In parallel, I also explored how patients and members of the public influence health outcome selection during clinical guideline development. Finally, from this work I aimed to develop priorities for communication, guidance and future research in these areas.

Within Chapter 2, I mapped the methods of patient participation used by COS developers. I achieved this by surveying COS developers about the frequency of patient participation in their COS development and the method(s) they used to

facilitate this input. I found that patient participants were included in 87% (141/162) of COS in the published or completed stages, and over 94% (65/69) of ongoing COS projects. The Delphi survey was used singularly or in combination with other methods in 85% (119/140) of projects. Via the survey I also identified the increasingly global nature of COS development, with a growing number of studies having stakeholder representation from two or more countries (65/135), and 22% (30/135) including patient participants from five or more countries. Thus, the survey provided an up to date insight into the current trends within COS development regarding stakeholder involvement and the methods used.

Chapter 3 describes participant input in COS development from the perspective of patients, members of the public and health professionals. It was important to consider health professionals alongside patient and members of the public, as they are equal stakeholders in the development of COS. This qualitative work showed that interviewees who had previously participated in two or more COS or Delphi surveys generally understood the purpose of COS and were satisfied with the Delphi survey. However, some interviewees who were first-time participants struggled to understand the purpose of COS and aspects of the Delphi survey method, which limited their contribution and satisfaction with the study. Interviewees differed in how they interpreted and used the written documentation provided to COS participants, which points to the need for different mediums of communication. Findings also indicate the need for additional guidance regarding whose perspective to take into account when scoring health outcomes across the various rounds, particularly from round 2 onward, and on how to apply the scoring system. Furthermore, a few interviewees reported experiencing negative emotional impacts arising from reviewing health outcomes and stakeholder feedback, something COS developers must aim to avoid in future.

Chapter 4 comprised an ethnographic study investigating the influence of patients and members of the public in health outcome selection in their role as committee members in clinical guideline development. This identified how and when patients become involved in the clinical guideline development process and their role in determining health outcomes. It showed that patients and members of the public

were not always meaningfully involved throughout clinical guideline development. My findings point to the need for researchers to further support and provide guidance for patients and members of the public on what health outcomes are, avoiding technical language and empowering patients to speak. With further action on these points it should be possible to enhance patient and public involvement throughout the clinical guideline development process. I also recommend considering other methods of facilitating patient and public involvement in clinical guideline development particularly qualitative approaches such as interviews and focus groups to elicit in-depth insight on their needs and perspective, including prioritisation of health outcomes which could subsequently be fed back to other stakeholders. Furthermore, I suggest that guideline developers search for relevant COS studies which have been developed with patient participants and develop ways to use such COS to guide health outcome selection in clinical guideline development, subsequently ensuring input from a range of patients.

5.2 Reflecting on the patient role in research

As discussed in Chapter 1, there are numerous reasons for advocating for the importance of patient and public input in health research via both involvement and participation. These reasons range from ethical and political obligations, funding requirements, reduction of waste in research and the experiential insights patients can offer to research projects. Increasingly, health researchers across all fields and domains are responding to the growing patient centred research system, frequently by including patient and public involvement (PPI) contributors to input at the various stages of the research project from conception through to dissemination of findings. Patients have long been participants in health studies, in that they can contribute their data. However, this participatory role is now expanding into methodological research and helping set the research agenda and to inform other studies, for example within core outcome set (COS) development. In the COS development the role of patients as participants in helping prioritise health outcomes is growing (197), in a move that is replacing PPI contributors from inputting over health outcomes exclusively. Subsequently, the collaboration between patients and researchers has been described as reflecting, "*a fundamental paradigm shift in health and social care*

research, away from paternalism towards partnership" (308). Doctors know about the illness and research but patients know about the daily impact of living with the health condition.

There are some common threads that all researchers can consider before and during the research process when including PPI contributors in health research generally, patient participants in COS development (115) and patient and public input in health related methodological research. Researchers may wish to consider when to involve PPI contributors, who to involve as PPI contributors, how to recruit and keep people involved in projects, training and support mechanisms for PPI contributors, follow-up plans and dissemination approaches. When including patient participants, researchers might consider who to include, recruitment strategies, communication of scientific information, use of plain language, methods of participation and retention and follow-up plans. It is important that research teams carefully consider, understand and acknowledge each of these aspects. Failure to do so has the potential to lead to further waste in research. One example of such failure is tokenism, which is described as the *"superficial and disingenuous"* inclusion of small numbers of patients, with limited input and impact on the research (228, 267-270). This type of input can have a detrimental impact on patients and members of the public as it can result in patients' input being devalued by the research team and a poor experience for patients (57).

As demonstrated in Chapters 2 and 3, COS developers are including international patient participants in COS development alongside other relevant stakeholders. Predominantly through the Delphi survey either singularly or in combination with other methods such as qualitative interviews (197). Other COS related research, not discussed in my thesis, suggests COS developers are also involving PPI contributors as active members of their research teams (122). Meanwhile, in Chapter 4, I described how the National Institute for Health and Care Excellence (NICE) have a number of procedures and processes in place in an effort to involve patients and members of the public in clinical guideline development, which includes eliciting their input on health outcomes of importance. While EPITOME in Chapter 3 explored patient *participation* in core outcome set development and INVoLVED in Chapter 4

investigated the influence of patient and public *involvement* in health outcome selection during guideline development, both studies concerned patients and their role in prioritising health outcomes. Across both areas a number of common themes arose, including the questions of

1. How do researchers view involvement and participation?
2. Who is a patient and what is their role in research design?

Other work conducted during my PhD project, which I will describe in more detail below, also contributed to my reflection upon these questions and themes.

5.2.1 Tying the threads together; considering the role of patients

In the following reflections I draw my conclusions from four areas, including the following interactions;

- My experiences of speaking to expert consultants from different European countries (Part A).
- Attitudes discussed with fellow Early Stage Researchers (ESRs) when discussing patient involvement in methodological research (Part B).

Furthermore, in what follows I also draw on reflections from the INVoLVED (Part C) study described in Chapter 4 and the EPITOME study (Part D) described in Chapter 3.

A. European consultations

I engaged with nine consultants from six different European countries about their experiences and expertise regarding patient participation in health research within their respective countries. The aim was to explore how patients within their respective countries might understand participation in COS development via the Delphi survey. As COS are increasingly developed internationally (197), I believe it is important to gain some insight and understanding into how COS might be understood in a wider range of countries. A secondment to the European Clinical Research Infrastructure Network (ECRIN) during my PhD programme enabled these consultations. ECRIN is a *"public, non-profit organisation that links scientific partners and networks across Europe to facilitate multinational clinical research"* (309). Thus, they have built research and support networks across a range of European countries from which I was able to identify various consultants.

To find potential consultants I contacted ECRIN's "European Correspondent" within each country and explained my request. In total, the European Correspondents I spoke to introduced or provided the contact details of ten potential consultants from relevant networks or organisations across seven countries. I contacted these potential consultants via email, explaining my request Appendix A5.1, nine of whom responded favourably, the tenth did not respond (Table 5.1). These consultations usually lasted 60-90 minutes and were conducted via video-link or telephone. They covered the consultant's experience and knowledge of patient input in health research, societal and cultural facilitators and barriers within their countries and I specifically sought feedback on COS development and when possible the Delphi survey. To ensure a range of topics were covered, I used a topic-guide to help steer and navigate these conversations (Appendix A5.2). This topic guide was developed in collaboration with my PPI contributor, who along with my supervisory team approved the final version before the consultations. Typically, either on the video-link or via a prior email, I showed the "What is a Core Outcome Set?" video, developed by the COMET Initiative and displayed screenshots of the DelphiManager software (Appendix A5.3), to facilitate the COS specific section of the consultation. These were consultations with fellow researchers or patient representatives active in the field. The consultants took part in a professional capacity through which we discussed their expert opinion and experiences. As they did not contribute their individual or person data it is not considered to be a research study, thus ethical approval was not needed. Each consultant was made aware of the purpose of the consultation and were all happy to continue the discussion with me. I explained that the discussions would be presented in this thesis and potentially in other relevant domains such as publications or in-house reports.

Consultant number	Country	Role
1.	Denmark	European Patients' Academy (EUPATI member)
2.	Italy	EUPATI member
3.		Researcher in the field
4.	Spain	Researcher in the field
5.		Researcher in the field
6.	The Netherlands	Researcher in the field
7.		Researcher in the field
8.	Norway	Patient association research manager
9.	Switzerland	Researcher in the field
0.	*Czech Republic*	*No consultations undertaken*

Table 5.1 Country and role of expert consultant

B. Early stage researchers

My PhD project was undertaken within the Methods in Research on Research (MiRoR) consortium, a training programme in the field of methods in clinical research under the European Union Horizon 2020 initiative. In total, MiRoR is training 15 early stage researchers (ESRs), who are all undertaking PhD research, in numerous aspects of clinical research from planning of research, to conduct and reporting, including PPI and patient participation, via educational training from numerous international experts in the field. Some examples of the research areas these other ESRs are investigating include, the development of statistical methods for prediction of recruitment to clinical trials, improving peer-review processes and scientific reporting, evaluating the impact of collective intelligence, methods for identifying research gaps and improving current methods to evaluate research quality.

Interactive training in research methods is a key concept of MiRoR and it is achieved via biannual training events, webinars, online journal clubs, and writing exercises. In 2017, the MiRoR training event (event information can be found here) included sessions dedicated to PPI in research (content information can be found here) and communication of research (content information can be found here) to the wider public. Multidisciplinary teams, which included patient and public representatives, delivered both sessions. Applied training included the importance of PPI contributors to clinical trial research from design to conduct and dissemination of findings. Applied workshops dedicated to qualitative research skills including interviewing and focus groups, which can be used to enable patient participation in research were also provided.

In 2018, MiRoR invited a patient active in advocacy for PPI in research and a funder from the National Institute of Health Research (NIHR) to speak at the training event at the University of Split, Croatia. They introduced us, the ESRs and the wider MiRoR consortium to the merits and importance of including patients and the public in their research.

In 2018, along with Ms Maria Olsen and supervised by Professor Paula Williamson, I hosted an online journal club in which all the ESRs had the opportunity to reflect and discuss PPI in methodological research. We drew on our training events as outlined above and discussed a) whether it would have been possible to do things differently in our previous work and b) how we can implement PPI in ongoing and future work. The details of the published manuscript arising from this journal club is in Appendix A1. Ethical approval was not needed for this work as it arose from training events which were held in public forums, details of which are freely available online. However, the two speakers from the event in Split were informed of our idea for the journal club prior to their talks, they were both fully supportive of our work and reviewed and approved the final manuscript prior to submission. Similarly, ethical approval was not needed for the journal club with the ESRs as it was a discussion and exchange of knowledge amongst peers. However, all ESRs were advised of our intention to document the discussion and were happy to proceed. All the ESRs were

provided with the opportunity to review and provide comments on the resulting manuscript, their final approval was sought prior to submission.

5.2.2 Examining the threads; what can we learn?

Using a combination of the insights gained from the from the sources outlined above and in previous chapters, in the next section I will reflect and offer my conclusions on the following, previously outlined questions, in relation to patient involvement and participation in health research:

1. How do researchers view involvement and participation?
2. Who is a patient and what is their role in research design?

Question 1 How do researchers view involvement and participation?

As discussed in Chapter 1 section 1.4 of this thesis, the distinction between PPI and patient participation is important. The roles and activities of both are very different, thus, blurring them can have negative consequences and impact the validity of the research, as detailed in Chapter 1. Despite awareness of the distinction between involvement and participation (43, 44, 115) ongoing confusion and blurring of boundaries and conflation of the two roles exists. Some of this difficulty is likely to stem from the use of the terms *involvement* and *participation* interchangeably, across research fields, cultures and countries. It also arises when roles extend into each other, such as PPI contributors also providing participant data particularly in research following qualitative methodologies, which is mistakenly seen as *"collaborative"* (44, 115, 310). Furthermore, how clearly researchers define and support the roles and activities of patients and members of the public within their research studies can determine whether the roles are conflated or seen as separate yet complementary stages of research. Thus, it is important that research teams decide early on what role and activities their study requires and use the most appropriate guidance and support to facilitate this meaningfully.

A. European consultations

Most of the consultants I spoke to while at ECRIN focussed on PPI in research in their countries, despite my line of enquiry being centred on patient participation in their countries, firstly in health research generally and secondly the potential for patient participation in COS development. For example one of the consultants spoke about

her role in helping set patient experience surveys in hospitals or her input in study design for a pharmaceutical company as *participation*, whereas within the UK and following the INVOLVE statement her description would be closer to *involvement* (311). These consultations indicated that for the countries represented, the term *"patient participation"* is more closely linked to patients participating in decisions about their individual health, treatment and delivery with their healthcare provider; *"patient and public involvement"* is used to encompass patients who are included in any or all stages of the research process, either as active PPI contributors on the research team or as individuals who provide data. Some of the difficulty I experienced in explaining and discussing the various terminology with the consultants may also arise from the unique challenges posed by having patient and public input in COS development and health related methodological research. Within COS development in particular, this type of role may more traditionally and easily lend itself to PPI contributors rather than patient participants, adding to the challenge I faced in explaining and discussing the roles and terminologies during the consultations. This also presented challenges when discussing patient and public input in methodological research within the MiRoR journal club, which I describe later in this chapter.

Patient and public input in research in the various countries represented by the consultants I spoke to can also be viewed in context of the societal and research culture within those countries. With the exception of the Netherlands, the consultants I spoke to largely described patient-centred research as a *"new"* concept in their country. They described it as a growing concept that is largely driven by a combination of national patient associations and organisations, researchers in the field and funding requirements. However, the consultants from the Netherlands spoke to me about the more developed history of patient and public engagement and shared decision making in health care delivery and provision within their country. This stems from a 1950s movement called *"Nothing about us, without us",* a slogan used to communicate the idea that no policy should be decided by any representative without the full and direct participation of members of the group(s) affected by that policy (312). The consultants from the Netherlands described the levels of PPI and

patient participation in research there as more prevalent than in other European countries. All consultants acknowledged their continuing concern that the funders' requirements for PPI and patient participation in research have made it a *"tick-box"* exercise for some researchers, a sentiment which was also expressed during the MiRoR journal club, and acknowledged in the wider literature (313, 314).

B. Early stage researchers

Within the diverse group of MiRoR fellows, there were varying levels of understanding and exposure to PPI in health research. However, unlike primary clinical research projects where patients are recruited as participants, our projects covered methodological issues in different phases of research from planning, to conduct, reporting and peer-review. As a result, variation in applicability and implementation of PPI exists across the programme.

My own research as described throughout this thesis was the only project out of the 15 that had a PPI contributor involved. My PPI contributor was involved in the qualitative study outlined in Chapter 3 and the expert consultations outlined in this chapter. Furthermore, in Chapter 5 I present a future research recommendation which I developed through discussion with my PPI contributor. My project is the most prominent example of where there is a role for meaningful PPI in its conduct; the research directly investigates the perspectives of patients and members of the public and explores methodological aspects in an attempt to improve their experiences of and participation in COS development.

In the MiRoR journal club some of the other ESRs reflected on whether PPI earlier in their projects would have also been useful. The ESRs provided examples of where they thought PPI may have worked in their projects. However, after some discussion it became clear that they were confusing the juncture between *involvement* and *participation*. ESRs who had not considered PPI in their projects prior to the journal club, talked mainly in terms of how they could ask patients to participate in their research, rather than in terms of involvement.

Other ESRs, particularly those whose projects had a strong statistical focus, believed that PPI was not possible. However, after the training and discussion during the

journal club the ESRs acknowledged that various research projects have included PPI contributors in quantitative projects such as Hannigan et al. (315) and that with planning, training and partnership of both researchers and PPI contributors there is potential for successful collaborations. This in particular points to the need for ESRs and other researchers to be aware that PPI can and should start early in the research process, in the conception and design stage and does not need to be solely reliant on whether the research will include direct patient participation.

Question 2 Who is a patient? What is their role in research?

A recurring question throughout this PhD work and indeed widespread throughout the health research field is "who is a patient?" In turn this question raises its own issues and considerations, including "what is the role of a patient in research?" and "what is it we, as researchers, expect from them?" The counterpart to the second question should also be considered "what is it patients expect from us as researchers?", but that is outside the focus of this discussion.

A. Early stage researchers

From the discussion held in the journal club it appeared that many of the ESRs struggled to see the direct link or relevance of their methodological work to the patient population. For many of the ESRs it seemed that they saw their research as too far removed or upstream of where patients could be involved. However, after prolonged discussion during the journal club and in reflection after, it was obvious that the ESRs had started to consider where they could have PPI. For example, ESR 1's project is exploring methods for identifying and displaying research gaps. Post journal club, ESR 1 reflected that PPI in the planning phase to define the terminology used for shaping the project development may have been helpful:

> *"We consulted different experts in the field; looking back it would have been extremely useful to also ask patients and the public on what they thought about the term "research gap" to gather a comprehensive list on the different terms as understood by experts, patients and the public."* ESR 1

Furthermore, the journal club encouraged some of the ESRs to not only think about PPI involvement, which was the original purpose but also patient participation. An

example of this is ESR 13 who was investigating peer-review content and communication processes in biomedical journals. Subsequent to the journal club discussion ESR 13 started to consider how PPI and patient participation in data collection from patient peer-reviewers alongside the journal editors may have offered different input and insight:

> *"Patient peer reviewers are also part of the peer review process, I should have collected data from them as well in order to have a more complete, multi-faceted and holistic representation of peer reviewers in biomedical journals."*
> ESR 13

One of the greatest challenges discussed within the MiRoR journal club and perhaps the biggest barrier many of the ESRs saw in relation to PPI was the question of "who is a patient?", and how can they meaningfully be included in the research process. Concerns centred on the emergence of professional patients, patients who through training and continuous engagement achieve specific knowledge and profiles, and therefore may no longer be representative of the typical patient (262). While it was acknowledged that it is not conceivable to ask PPI contributors to represent all patients, concerns about being as inclusive as possible remained, in particular considering ways of reflecting the diversity of the patient community and including under-represented patient groups (316). Many ESRs questioned whether this issue could be overcome and whether they could satisfactorily involve patients in their own research.

In conclusion, the ESRs indicated a need for a wider discussion in the research community about how to find the appropriate balance between training and informing patients, while allowing them to retain and provide their unique perspectives and lived experience.

B. European consultations

Similarly, the consultants from across Europe also raised this issue when discussing PPI and patient participation in research in their countries. Consultants from Italy, the Netherlands, Norway and Spain spoke about the various training tools and workshops available in their countries to educate researchers and health

professionals on how to engage with and include patients in their research. According to the consultants I spoke to these tools and workshops are typically organised by various funding bodies. In each country represented, the consultants described national patient organisations as highly engaged in advocating for and driving the healthcare agenda, particularly in the Netherlands. According to the consultants I spoke to these organisations typically provide training to their members on how to be PPI contributors. Usually this revolves around preparing members to participate in committee and research processes. It is members of these organisations who are most likely to engage with all types of research, either via involvement or participation. While their work is seen as pre-dominantly centred around assessing health service delivery and patient experience and patient advocacy, their input in driving research is also growing. In the Netherlands, the consultants I spoke to believed that *"buy-in"* and support from patient organisations was essential in directing the research agenda and thus, *"expert and professionalised patients"* have an important role in progressing healthcare. However, all consultants that I spoke to expressed concern about the representativeness of patients from these organisations and questioned how we as researchers could engage with a wider population range, across all areas of health, from research to delivery. They described the biggest barrier to engaging with a wider sample is the concern that the general patient population have *"limited knowledge"* and an *"unscientific"* understanding of health research and clinical trials, restricting their input. Lack of public knowledge and interest in healthcare matters and a *"blind faith"* in decision making by health professionals was also cited as a barrier, particularly in Italy and Spain. Conversely, the consultants from Italy and to a lesser extent Denmark also suggested that the general public are sceptical of the healthcare industry, a problem exacerbated by *"fake news and sensationalism"* in the media, such as the *"anti-vax campaign"* in Italy (317). Consequently, these barriers have led to a reliance in some areas on patients or patient representativeness with a more advanced or "*specialist*" knowledge of the research process and the health condition in question.

C. Guideline Development

Within my work on the INVoLVED study (Chapter 4) the question of who is a patient (or a lay member within the setting of NICE) became an interesting line of

investigation. Two of the lay members in the ethnography were there due to their professional roles within relevant national charities rather than any experiential knowledge. NICE actively recruits both types of lay member to their committees. Despite their equal status to lay members with direct experience, within my study it appeared as though they were fulfilling a different role. By their own admission both believed they had a different type of knowledge and contribution to the committee than other lay members. Eve from GC3, one of the lay members from a national charity spoke about her feelings on this blurred status during our interview. She believed her skillset and knowledge were better suited to a different type of role, not currently available within the NICE process:

> "*My fundamental issue with how the system works is I don't consider myself a lay member. I am a professional. I am not a health professional but I am a professional and I am there as a professional, I am not a patient. My major recommendation to NICE […] is that I think they need to split people who are professional representatives, they are not health professionals and people who are actually patients."* Eve, GC3

She further elaborated her fear and frustrations that NICE guideline developers chose her based on her professional experience and background sitting on committees and meetings at the expense of patient's lived experience:

> "*When I applied one thing I was very aware of was that I was essentially going head to head with patients, and that felt it felt unfair for a number of reasons, you know for a lot of reasons because then we weren't being judged on the same things because I had no personal expertise to bring, but at the same time like I know how to do applications, I know how to do interviews, I have got experience of sitting on committees and meetings and things like that."* Eve, GC3

This raises the question of whether NICE need to focus their recruitment on recognising the different perspective that exist from various types of lay member and the bigger question of who are lay members? By exploring these issues in depth guideline developers can better facilitate meaningful input from lay members in

guideline development. Some of the potential methods for consideration have already been outlined in Chapter 4 section 4.4. While Lisa from GC4 shared similar sentiments to Eve with regard to how her experience and professional role differed from that of a lay member with patient experience, she did not directly express a need for a separate role for people with her profile. Both Eve and Lisa expressed concern that their fellow committee members, mainly the health professionals, did not seriously consider their input during meetings, instead viewing them as *"lobbyists"* or that their lack of lived experience was problematic.

Eve and Lisa were not the only committee members to comment on their role as *"professional"* lay members and what that meant in terms of committee involvement. For example, Richard, a lay member with direct patient experience was Lisa's fellow lay member in GC4. In conversation with him he frequently expressed his *"disappointment"* and *"isolation"* in being the only *"true lay member"* on the committee. He viewed Lisa as someone who was more closely aligned with the health professionals rather than an ally he could rely on. Other lay members interviewed during INVoLVED spoke about the importance of having the support and *"comradery"* of another lay member, a finding also reported in the wider literature (299). Observations of all GC4 meetings showed Lisa did more frequently engage in technical discussion and policy level issues, while Richard provided his experiential perspective and opinion. Interviews with lay members from other guidelines which had a '*professional*' lay member attached indicated similar feelings to Richard. GC4 provided an opportunity to speak to the health professionals and technical team about the two different profiles. The majority of those I spoke to agreed that Lisa and Richard were fulfilling two different roles, however value was seen in having input from both of them. Thus, there was general consensus that the presence of a charity representative should not be at the expense of a patient or vice versa. In GC9, both lay members were there due to their role as proxies. As previously, discussed in Chapter 4 there were times when they found it difficult to become involved due to the guidelines' technical content. During an interview with Ruth, a lay member from GC9 with experience as a patient carer, she reflected on whether the presence of lay member from a charity would have eased the difficulties she felt toward getting

involved in the technical discussions and suggested they would be better equipped to provide *"a more representative view of lay members"*.

D. COS studies

As I detailed in Chapter 3, having previous experience of COS studies and Delphi surveys influences the experience of the participant. Interviewees I spoke to acknowledged that it became easier and more intuitive with each study. A recurring discussion point in the EPITOME interviews and indeed in the wider conversations with various COS developers, was who can participate in COS studies and what types of patients are they accessible to. Questions such as what level of previous scientific research experience and understanding is required were raised by interviewees, who also speculated whether COS studies and the Delphi survey are too scientific and technical for patients without specific training or experience in health research. However, all interviewees did flag the importance of continuing to invite and support patient participation from a wide range of participants. Furthermore, a number of patient participants indicated that they would be happy to participate in a COS Delphi study again as they would be *"more prepared"* about what to expect in future. As previously stated, the original purpose of the consultation with the European consultants was to gain an understanding of whether COS Delphi participation from the general patient population in their respective countries was considered possible. From the group I spoke to, the majority thought this is currently unfeasible due to a lack of patient education and input in health research in their countries to date. For instance, while the feedback to the "What is a Core Outcome Set?" video by COMET was generally very positive, one of the strongest feedback points I received, particularly from the Danish and Italian consultants, was that many patients *"are not aware of what clinical trials are".* Thus, patient education and understanding needs to start from there before the concept and importance of COS can be understood and appreciated. All consultants stressed the importance of COS developers *"being very clear"* to patients about who they want in their projects and *"why their input is needed",* so that patients could fully understand that their experience and knowledge is *"enough"* and is *"important".* Furthermore, in relation to the Delphi Survey screenshots (Appendix A5.3), I showed the consultants they all flagged their concern that the Delphi is *"too high-level"* for the typical patient population in their countries.

The consultants thought that only "*selective*" or "*highly engaged*" patients would be able to participate in a *"meaningful"* manner, by this they meant the ability to follow the Delphi survey methodology appropriately. Specific concerns about where the general patient population in the various countries may struggle to participate in the Delphi survey included:

1. **Outcomes**

All consultants spoke about the need to explain health outcomes in a relevant and relatable manner and all agreed that patient relevant context is important. The consultants from the Netherlands further suggested that visuals or written explanations of the health outcomes could be useful. One of the consultants from Italy expressed a concern that if patients did recognise the health outcomes as relevant to them, then they may still struggle with prioritisation element of COS, as they do not usually consider prioritisation of health outcomes their routine healthcare: *"they do not typically have those conversations* (prioritisation conversations) *with their health professionals"*.

2. **Language**

All consultants stressed the importance of ensuring that the language used is as "*clear and readable"* as possible and that the wording was relevant and recognisable to the patients. This was in relation to not only the outcomes but also the purpose and process of the study. Some of the consultants suggested a "*glossary*" explaining key terminology and reminders of the purpose of the study throughout would be helpful to patients.

3. **Feedback**

A number of the consultants reflected on whether providing feedback would be "*leading*" for patients and encourage them to change their opinions *"to fall into line"*, with each other but particularly with health professionals. This was a particular concern for the consultants from Denmark, Italy and Spain; as previously mentioned they did not think there was a culture of patient and public input in decision making in their countries.

All consultants suggested that if I were to conduct a COS Delphi in their country in the current research climate, I should specifically target my recruitment toward '*professional'* and *'expert'* patient representatives, who can represent the wider population and understand the scientific research process.

5.2.3 Making sense of the threads; recommendations to consider

I have provided specific suggestions and recommendations for EPITOME and INVoLVED in Chapters 3 and 4 respectively. In the following section, I offer my suggestion that further awareness, education and research is required for both researchers and patients in order to further facilitate and enhance meaningfully the different roles patients can have in prioritising health outcomes and inputting in health research and health related methodological research.

Methodological research

Within the MiRoR journal club we concluded that providing ESRs with appropriate educational, interactive and real-world training, is a key step in introducing them to the various merits and challenges associated with PPI in early-stage research. In methodological research, implementing PPI can raise different challenges to typical health research in which direct links to patient relevance may be easier to understand by both researchers and patients. However, as training opportunities such as those provided by MiRoR showed, there are different steps researchers can take to incorporate PPI at various stages of methodological work. The MiRoR training events and subsequent journal club also encouraged the ESRs to consider the scope for patient participation within their projects. While initially there was some conflation between the two by the ESRs, explanation and discussion helped them see the distinction. ESRs also claimed to be more considerate of the impact their research would have on patients and the importance of communicating their findings appropriately. The ESRs indicated that the educational training had inspired thinking extending beyond PPI, as they also used the opportunity to reflect on how they could disseminate their current results and findings in plain language to a wide range of patients.

The journal club further recommended that future training should also stress the importance of researchers *"actively listening"* to PPI contributors. Understanding the motivations and logic behind a contributor's comments will enable researchers to ensure a more meaningful collaboration. As a number of ESRs pointed to uncertainty about how to implement PPI in research, future learning opportunities could look specifically at ways of implementing PPI. I note such guidance already exists for PPI in primary research (318). More investigation of the methods surrounding the training of PPI contributors receive in methodological research is also needed in order to improve the current practice (319). It is important to further note that such guidance and training will not only be useful for ESRs, but for researchers at all stages of their careers.

By ensuring researchers have the appropriate education, resources and guidance they can be enabled to consider and implement patient and public input in their projects. Other methods such as co-production (228) may also be advantageous to the researchers' work, depending on the research question and the resources available. Understanding the value the different types of patient and public input have in health research should also lead to a more standardised understanding of the various roles patients can have during the research process. Within methodological research we can ensure meaningful and beneficial patient and public input by striving to recruit individuals to roles appropriate to their knowledge, experience and skillset. Similarly, within guideline development it is also important to consider that different patients and their representatives may offer different contributions and insights. Thus, we need to consider how best to facilitate as many perspectives as possible and not exclude any. For example, based on the findings of INVoLVED, NICE may wish to consider including a third type of committee member alongside patients with lived experience and the health professional, the "third sector professionals". I believe that "third sector professionals" are individuals like Eve and Lisa who are not health professionals but equally they are not patients. Instead they are working professionals whose role is to understand the scientific literature in terms of policy and provision of services and support while representing the patients their organisations support. In my opinion this a third type of role within NICE guideline

development, that offers insight and perspective that is different to that of the health professionals and patient with lived experience. Thus, the inclusion of "third sector professionals" should be considered a separate position alongside other committee members.

COS development

COS developers need to consider who their target population is when recruiting participants and aim to recruit accordingly. Whether patients with direct experience of the condition or patient representatives with a more *"expert"* viewpoint are invited to participate will depend on the health condition and the scope of the COS. Having an understanding of these differences will also enable COS developers to better design their studies and provide support and guidance to participants, so that both parties know what is expected and what is feasible.

It is also important to consider how we as researchers can help the general public access and understand our work and to facilitate their input as fully as possible. The European consultants indicated that engaging patients as participants in COS studies would be difficult due to a general lack of understanding and education around health research. Thus, as researchers we need to consider how we can bridge this gap. Plain language dissemination of health research studies and their outputs is one potential answer. By informing the general public of health research that is relevant to them through appropriate language and mediums, we are inviting them into the world of research. This has the potential to stimulate their interest and understanding of health research generally and raise awareness that they are the most valuable stakeholder of the process. Furthermore, a number of educational and training campaigns exist which target both adults and children. These include EUPATI (55)as described in Chapter 1 and Ireland's Health Research Board TMRN (Trials Methodology Research Network)'s START campaign. They START (Schools Teaching Awareness of Randomised Trials) campaign aims to help young students *"become the scientists of tomorrow and the critical thinkers of today"*(320).

5.2.4 Summarising the threads; my reflections on the patient role in research

Patients and members of the public can fulfil many different roles in health research, including contributing to the prioritisation of health outcomes. This PhD provided the opportunity to collect data and discuss patient and public input in health research across a variety of areas. By reflecting on the various issues and challenges raised we, as researchers, can work towards finding appropriate training, support and methods for facilitating meaningful *involvement* and *participation* in various types of health research. It is important that this training and support not only considers patients and members of the public, but also researchers, particularly those who are early in their careers. Furthermore, when considering patient participation in health research is it important to consider the distinction between various types of health research. In clinical studies where patient participants are receiving treatment, they may feel more familiar and engaged in the process. COS development studies are somewhat removed from direct treatment but these studies are still related to the patients' health condition. Patient participants may feel even more removed from wider methodological research, such as that undertaken by the MiRoR group. Thus, inviting them to participate in this type of research is likely to present unique challenges and require different types of support and training to facilitate. However, given the importance of patient and public input in all types of health research and the unique value such can bring, it is imperative that we work toward facilitating their input as meaningfully as possible.

5.3 Dissemination of this thesis

I have taken steps to ensure that the findings from the various studies undertaken during my PhD are disseminated widely and appropriately since the inception of this project. The COS work has been disseminated via poster and oral presentations at international conferences including COMET Initiative conferences(114, 321) and the ICTMC (International Clinical Trials Methodology Conference)(322, 323), journal articles, blog posts and in-house presentations to the COMET Initiative team. Two of the main supervisors of this project are associated with the COMET Initiative team, thus, the results can be actively communicated to future COS developers who seek methodological advice from COMET. Future efforts at promoting these specific

findings include further conference presentations and plain language blog posts, specifically via the MiRoR network.

The work in relation to NICE clinical guideline development was undertaken with NICE's support and approval. They have been kept updated and informed of the findings and have expressed interest in using them to inform future practice. The findings have been shared via in-house reports and presentations at NICE and also via an oral presentation at the G-I-N (Guidelines International Network, (https://g-i-n.net/document-store/g-i-n-conferences/manchester-2018/gin-abstracts-book-2018/view) conference. The findings described in Chapter 4 have been written up as a manuscript for submission to a relevant peer-reviewed journal.

All participants in my study will be provided via email with a copy of the published manuscripts and a plain language summary, unless they opted out of future contact at the time of consent.

5.4 Implications of this thesis

Patient and public input in health research is rapidly gaining recognition as a way of ensuring research is patient relevant and as a result, less wasteful. Furthermore, health research is often funded through the taxes members of the public pay, thus it can be argued that patient and public input is a democratic right. As previously discussed in this thesis, patients and members of the public are the ultimate beneficiaries of health research, thus their input is important from a moral and ethical standpoint. Improving health outcomes is likely to be the single most significant aspect of a patient's health, as health outcome are how we measure change in a patient's health status. Thus, as researchers we need to consider the most relevant health outcomes to patients from as early a stage as possible. By doing so we can ensure that our research output is relevant to patients, their needs and expectations. Including patients in health research that considers the selection and prioritisation of outcomes is a logical way of doing this as they are the ones living with the impact of the illness, which we as researchers are striving to alleviate. This thesis makes recommendations on how best to support and guide patient participation in COS development and clinical guideline development. COS can inform and guide the health outcomes measured in trials of potential treatments

while guidelines use health outcomes to inform how everyday healthcare should be delivered to patients. Thus, given the importance and influence of both these settings patient input in ensuring the resulting COS and guidelines are relevant and credible is critical.

5.5 Future work arising from this thesis

Suggestions for future research are based on both the results and limitations of the current research. Future research based on the findings and insights from this thesis should include the input of patients and members of the public whenever possible. Patient and public input can be achieved via PPI, patient participation or co-production. PPI and participation have been discussed in depth elsewhere in this thesis. Co-production allows the various stakeholders who are most affected by an issue to come together and find a shared solution to a problem (228, 324, 325). It also provides a sense of ownership and equality, as all stakeholders work collaboratively on finding solutions, as opposed to consultations in which stakeholders usually offer an opinion or insight for use by the research team. Thus, the concept of co-production appears to be the next logical step in many of the avenues of research that could stem from this PhD. Co-production in the creation of guidance for enhancing and supporting patients in health research is just one example of where it could be beneficial; specifically co-production could be applied to both COS development and clinical guideline development. The findings detailed in Chapters 3 and 4 provide insights and pointers from which meaningful guidance can be co-produced, applied and validated. Another example of where co-production should be considered is when exploring alternative methods of incorporating patient perspectives in COS development and clinical guideline development. In both these examples, patients as co-producers can offer different insight and expertise to researchers, which can be incorporated from the very beginning. Furthermore, by co-producing with patients we can ensure the result is patient centred and thus relevant to patients.

One particular avenue of research which I believe should be considered in future is more in-depth exploration of how patient participants react and respond to the Delphi survey for COS development via cognitive interviewing methods or think-

aloud studies. These types of studies would be a natural follow-up to the findings in Chapter 3 and provide real-time insight and perspective. Furthermore, such a study could provide exposure to a wide range of participants and their experiences rather than simply those who self-select for retrospective research studies.

As reflected upon in section in 5.2 there is much debate and complexity surrounding the question of "who is a patient?" and "what is their role in research design?" These are wide-ranging questions throughout health research and not unique to outcome selection. It is important that we as researchers have conversations to address these questions given the rapid expansion in recent years of the patient role in research and the ever-increasing move toward ensuring patient-centred research. As section 5.2 illustrates, it is important for researchers at every career stage to think about this and to receive training on how to facilitate patient input in their studies, if relevant. Such conversations should occur on an international platform, as science is becoming ever more globalised, as is health research and health care. As section 5.2 also illustrates, countries differ in how PPI and patient participation is viewed and facilitated. There is a need to collaborate across borders as we move toward defining the patient role in COS research and other health related methodological research and how we facilitate patient input.

The active uptake of the future research recommendation described in what follows will help ensure that the findings of this PhD serve their purpose in providing a useful benchmark to inform future guidance and research.

5.5.1 Generating outcomes for Delphi surveys through alternative methods

The following suggestions for future research stem from the finding that the Delphi survey including patient participants is a frequent component of COS development. Traditionally, the Delphi survey long-lists of health outcomes are populated via systematic reviews of the existing literature and national audit surveys. Other methods, although less frequently used, are reviews of published qualitative work, interviews with a sample of patients or focus groups, or any combination of all the aforementioned. This raises the question of whether all relevant health outcomes are captured, as systematic reviews and national audits are often researcher centred and do not capture the patient voice. On the other hand, interviews and focus groups

are patient centred, but have large resource implications and are often limited to mainly high-income countries. Furthermore, the success of qualitative research can be largely dependent on the skills of the interviewer or facilitator. Thus, it is possible that not all health outcomes important to patients are generated from these processes.

One idea is to "give every patient a voice" through the development of a mobile applications or "apps" co-produced with patients. These would collect patient relevant health outcomes directly from patients via prompts, over a pre-specified period of time. Furthermore, such apps would collect data from patients in their own voice, either through text or voice recording. This added feature would have potential uses in ensuring that researchers can learn from patients how they word their own experiences and outcomes. By following patients' own terminology and language we can then word the Delphi survey appropriately at a later stage.

5.5.2 Educational tools to communicate the purpose of Delphi surveys

My findings from interviews with patients suggest that not all the interviewees represented in Chapter 3 thought their participation in COS development was meaningful, as the purpose and process of the study was communicated in ways that were not accessible for them. Theory surrounding health literacy advocates for information to be made accessible to all patients in appropriate formats (232-235). Thus, finding the most appropriate language and context to communicate the purpose and process of the study, including concept and methods is of vital importance. Ensuring we use different media to communicate with patients and members of the public has the potential to enhance our engagement with a wider range of participants and help ensure a more meaningful experience for all, resulting in a useful and relevant COS. The language and context of the message communicated and the medium through which it is delivered is unlikely to fit into a one-size-fits-all approach, instead COS developers should be prepared to offer multiple types of support and guidance to their COS Delphi participants.

It is reported in COS development that demonstration videos of the Delphi survey enhanced participant retention to the study (198). Development of such a video is another example of successful co-production in health research. For example the

COMET Initiative's "What are Core Outcome Sets?" video was co-produced between a panel of researchers and patients. The video has received positive feedback from various sources including the expert individuals I consulted with at ECRIN (as discussed in section 5.2 above). Thus, these interactions piqued my interest in co-producing with patients a video detailing the purpose of the Delphi survey, how to approach it and what to expect as an alternative method of communication. I discussed the potential to develop such a video as an educational tool with my PPI contributor and my supervisory team. Based on findings from the EPITOME study described in Chapter 3 and the reflections from the European consultations described in section 5.2, such a video should consider including the following content:

1. What are health outcomes, how they are used?
2. What is a COS? Why they are important and how they are used.
3. Examples of when COS have been used.
4. Why is patient input important (i.e. the patient is also an expert and it is ok to differ in opinion from the health professionals)?
5. How to approach the Delphi survey and how to consider the following:
    - Purpose and objective
    - Scoring system value
    - Stakeholder feedback

The COMET video "What are Core Outcome Sets?" covers points 1-4 as outlined above. None of the interviewees from the EPITOME study had seen this video as it only became available after the interviews. Thus, it is important that future COS Delphi participants view this video to develop an understanding of the concepts and rationale behind COS studies. Subsequently, the follow up video that I am suggesting for future development should mention points 1-4 briefly and focus predominantly on point 5.

As I mentioned above such a video should be a co-production between a panel of researchers, COS developers, patients and members of the public, with a mixture of COS Delphi experience from none to some. Such a panel could collaborate over a series of meetings, conducted face-to-face, online or via telephone to decide and

agree upon the format and content of the video. This includes the script, characters, explanations and language amongst other relevant points which may be identified during the process. To ensure the video can be used by international audiences it should be produced in multiple languages or be developed to allow translated subtitles. While it is important that the findings of the studies presented in this thesis contribute to the development of such a video, it is equally important that new ideas and thoughts from all co-producers, including patients and members of the public, are also discussed and considered.

To evaluate the impact of such a video as an educational tool, I suggest using a "SWAT" (Study Within a Trial)(326), SWATs are a useful way of closing methodological research gaps within trials research. To assess a video for its impact on COS Delphi participation, researchers could embed a SWAT to evaluate the video in multiple ongoing COS studies. To do this a relevant protocol detailing the aims, objectives and methods should be registered here: https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/SWATSWARInformation/Repositories/SWATStore/. In table 5.2 below I suggest a potential protocol, based on conversation with my PPI contributor and research team, for assessing the influence of an educational video for COS Delphi participants. However, any future SWAT or other evaluation of such an education tool should be devised, designed and analysed with appropriate PPI contribution at all relevant stages of assessment.

Objective	To assess the effects of an educational video on participants' understanding and experience of a COS Delphi. Study area: Core outcome sets (COS) Sample type: Participants of COS Trial team: COS methodologists and developers Estimated funding level needed: None (assuming the video is already available free of charge via the internet)
Background	A key challenge in inviting patients and members of the public to participate in COS development via the Delphi survey is how to best communicate the purpose and process of the study in a meaningful manner. Empowering patients and members of the public to participate fully in COS Delphi studies relies on ensuring they understand and engage with the process as fully as possible. Recent findings suggest that new forms and mediums of guidance and support are needed to facilitate this. Furthermore, the findings point to specific aspects of the process which should be communicated to patients and members of the public to allow them to engage ad maintain their interest. A potential solution to these challenges is an educational video co-produced with patients which describes the purpose and process of COS Delphi.
Interventions and comparators	Embedded across multiple COS Delphi studies. Intervention 1: Invitation to view the educational video in advance of COS Delphi participation. Intervention 2: Invitation through standard study information (email or leaflets) in advance of COS Delphi participation. Index type: Method of invitation.
Methods for allocating to intervention or comparator	Randomisation.
Outcome measures	Primary outcomes: Participant understanding of the COS Delphi. Secondary outcomes: Participant satisfaction with their experience of the COS Delphi. Participant completion of the Delphi.
Analysis plan	The primary analysis will compare results from an exit survey of all participants probing their experience and understanding of the COS Delphi.
Possible problems in implementing this SWAT	It may be difficult to truly ascertain a participant's experience and understanding via a survey only and additional methods of exploration such as follow up interviews or think aloud studies might be required.
Researcher details	Person to show as the source of this idea: Alice Biggane Contact email address: abiggane@liverpool.ac.uk Date of idea: 20th July 2019.

Table 5.2: Sample protocol of a SWAT to assess the impact of an educational video for COS Delphi participants

5.6 Conclusion

In summary, the body of work in this PhD has shown that there has been an increase in patient and public participation in COS development, but a lack of parallel increased focus on how to optimise such patient and public input, internationally and across other health related methodological research. These reflections and issues highlight the need for researchers and patient groups to provide more robust training and support, for both patients and researchers, particularly early stage researchers, looking to collaborate in health research projects. The importance of including patients in COS development (106, 123) and in guideline development is increasingly recognised, as it is in wider health research (227-229). There is also growing appreciation of the importance of supporting patient involvement and participation in ways that are meaningful, thus avoiding tokenism and enhancing the credibility and validity of the resulting research or products (230, 231). My research suggests that not all patients experience meaningful involvement or participation in relation to health outcome selection and prioritisation. This was largely because the purpose and process of both COS development and clinical guideline development were communicated in ways that were not accessible for them. The findings of my research provide clear evidence that COS developers and guideline developers need to pay more attention to this communication if they are to ensure meaningful patient input in future.

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Appendices

A1 Publications

The following section notes the first author publications arising from this thesis

Chapter 2

Survey indicated that core outcome set development is increasingly including patients, being conducted internationally and using Delphi surveys.
Biggane AM, Brading L, Ravaud P, et al. *Trials*.2018; 19: 113. doi:10.1186/s13063-018-2493-y

Chapter 3

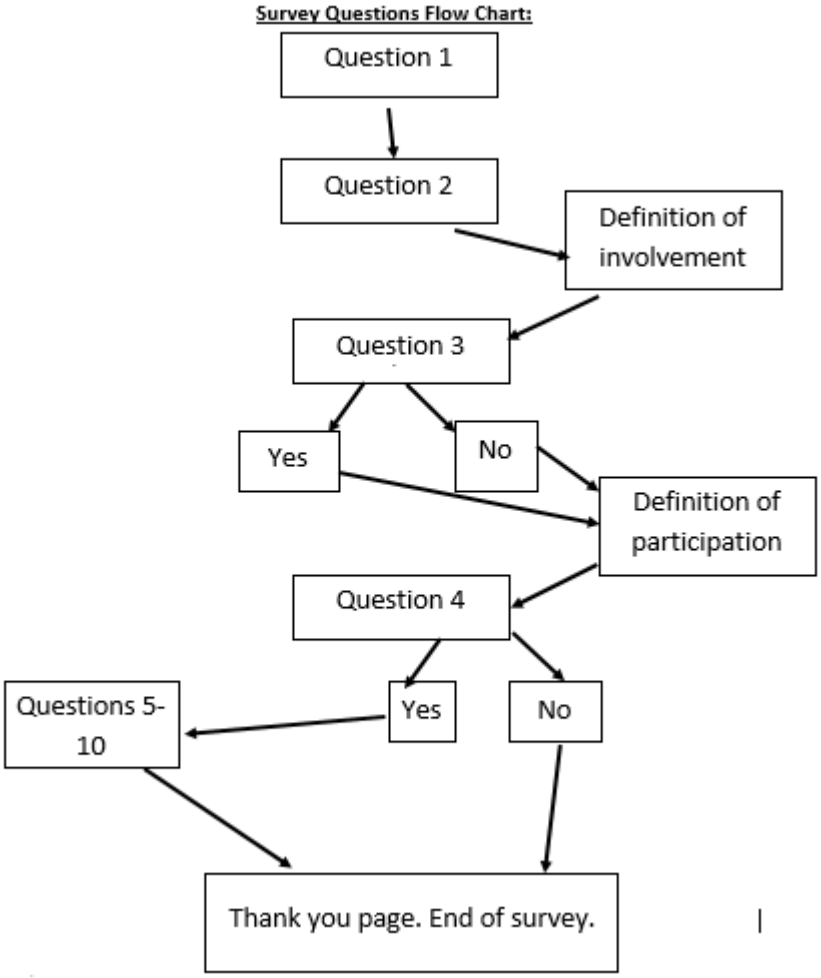
Participating in core outcome set development via Delphi surveys: Qualitative interviews provide pointers to inform guidance.
Biggane AM, Williamson PR, Ravaud P, Young B. *BMJ Open* [Published November 2019]

Chapter 5

PPI in research: a reflection from Early Stage Researchers.

Biggane AM, Olsen M, Williamson PR. *Research Involvement and Engagement* [Published November 2019]

A2.1 Survey- Flow Chart and Questions



Survey Questions:

Exploring patient input in core outcome set (COS) development.

Please answer the following questions in relation to the most recent COS study in which you have been involved.

1) Name:

2) What is the current status of your core outcome set (COS) study?

- Published
- Completed- COS is being currently written up, under review or in press
- Ongoing- data collection has started and is currently in process or under analysis
- Planning stages - data collection has not yet started

Involvement: is where patients and the public are involved as research partners, co-investigators, advisors, or team members of a COS study. In this role, typically they will help in the design and conduct of your COS study (e.g. sitting on the study management or steering group, advising on the participant recruitment strategy or commenting on patient information leaflets and survey materials).

3) Have you/ do you plan to involve the public or patients (as a research partner, co-investigator, advisor, or research team member) in your COS study?

- ○ Yes
- ○ No

Participation: is where patients or the public take part in the development of a core outcome set by giving data on their opinions regarding what outcomes are important (e.g. by completing a Delphi survey or taking part in interviews). We refer to people in this role as 'patient participants'.

4) Have you included/do you plan to include patient participants (i.e. completing your Delphi survey or taking part in qualitative interviews, attending consensus meetings) in your core outcome set study?

- ○ Yes
- ○ No

Questions 5-11 as follows relate to patient participation only.

5) Please indicate which of the following groups you included/plan to include as patient participants in the development of this COS (Please select all that apply.)

- ☐ Patients
- ☐ Public
- ☐ Patient support group/ patient charity representative
- ☐ Other (Please specify): _____

6) From what countries are your patient participants from?

- ☐ United Kingdom (UK)
- ☐ United States of America (USA)

- ☐ Australia
- ☐ Belgium
- ☐ Canada
- ☐ China
- ☐ France
- ☐ Germany
- ☐ Ireland
- ☐ Italy
- ☐ Japan
- ☐ Netherlands
- ☐ Singapore
- ☐ Spain
- ☐ Other (Please specify):

7) Please indicate which methods you used or intend to use to facilitate patient participation in your COS study. (Please select all that apply.)

- ☐ Delphi survey (a structured technique to reach consensus)
- ☐ Questionnaire
- ☐ Focus group
- ☐ Qualitative Interview
- ☐ Consensus Meeting
- ☐ Other: _____

8) How did you decide on the above methods (as indicated in Q.3) for facilitating patient participation in your COS study? (Please select all that apply.)

- ☐ Based on the literature

- [ ] Own previous experience with same methods for COS development
- [ ] Problems with other methods
- [ ] Suited our situation and circumstances
- [ ] Based on the resources available
- [ ] Based on expert advice
- [ ] Other (please specify):

9) From where did you/do you intend to recruit the patient participants for your study? (Please select all that apply.)

- [ ] Health institutions/ centres e.g. National Health Service (NHS). Health Service Executive (HSE) etc.
- [ ] Patient support/advocacy groups/ social media
- [ ] Patient organisations/ charities
- [ ] Word of mouth
- [ ] Patient research partner (access to patients)
- [ ] Other (please specify):

10) How did you decide on the recruitment methods to use above in Q.5? (Please select all that apply.)

- [ ] Based on the literature
- [ ] Own previous experience with same methods for COS development
- [ ] Problems with other methods
- [ ] Suited our situation and circumstances
- [ ] Based on the resources available
- [ ] Based on expert advice
- [ ] Other (please specify):

A2.2 Survey- Personalised Email for Developers

From: [Alice Biggane]

Cc: [Lucy Brading]

To: [COS Developer]

Subject: Re your study: [Study Title]

Dear [COS developer],

We are two PhD students working with Professor Paula Williamson and Professor Bridget Young at the University of Liverpool, UK and Professor Philippe Ravaud at the Universitè Paris Descartes, France.

We are conducting studies into how the public and patients are involved and participate in the development of core outcome sets (COS). These studies have been approved by the COMET Initiative, with the aim of informing ways to will facilitate improved engagement with patients in future COS studies.

As the COS developer of [study title], we would like to invite you to participate in a short online survey about your study. Your insights about including the public and patients in your COS will be invaluable to us.

We would be very grateful if you would take the time to complete our survey. Data from the survey will be aggregated using basic descriptive analysis, and your responses will remain confidential. All data will remain anonymous and will be destroyed after 10 years.

The survey should take around 5 minutes to complete and can be found at [- LINK] We would appreciate it if you could complete the survey in the next two weeks.

Thank you very much for reading this email. Please feel free to contact us by telephone [number] or email if you have any queries.

Best Wishes,

Alice Biggane and Lucy Brading

A2.3 Survey- Ethical Approval

UNIVERSITY OF LIVERPOOL

Health and Life Sciences Committee on Research Ethics (Human participants, tissues and databases)

16 February 2017

Dear Professor Williamson,

I am pleased to inform you that your application for research ethics approval has been approved. Details and conditions of the approval can be found below:

Reference:	1339
Project Title:	Exploring patient input in core outcome set development
Principal Investigator/Supervisor:	Professor Paula Williamson
Co-Investigator(s):	Miss Alice Biggane, Professor Bridget Young
Lead Student Investigator:	-
Department:	Biostatistics
Reviewers:	Miss Helen Orton, Dr Anna Daroszewska
Approval Date:	16/02/2017
Approval Expiry Date:	Five years from the approval date listed above

The application was **APPROVED** subject to the following conditions:

Conditions

- All serious adverse events must be reported via the Research Integrity and Ethics Team (ethics@liverpool.ac.uk) within 24 hours of their occurrence.
- If you wish to extend the duration of the study beyond the research ethics approval expiry date listed above, a new application should be submitted.
- If you wish to make an amendment to the research, please create and submit an amendment form using the research ethics system.
- If the named Principal Investigator or Supervisor leaves the employment of the University during the course of this approval, the approval will lapse. Therefore it will be necessary to create and submit an amendment form using the research ethics system.
- It is the responsibility of the Principal Investigator/Supervisor to inform all the investigators of the terms of the approval.

Kind regards,

Health and Life Sciences Committee on Research Ethics (Human participants, tissues and databases)

edreseth@liverpool.ac.uk

0151 795 4358

Page 1 of 1

A2.4 Survey- Full Method Combinations

Methods used	Total n (%)	Published n (%)	Completed n (%)	Ongoing n (%)
Number of COS studies included	**140**	37	38	65
Qualitative interviews, Delphi survey and consensus meeting	**22** (16)	2 (5)	4 (10)	16 (24)
Delphi survey	**21** (15)	12 (33)	7 (18)	2 (3)
Focus group, questionnaire, Delphi survey and consensus meeting	**16** (11)	2 (5)	8 (20)	6 (8)
Delphi survey and consensus meeting	**15** (11)	1 (3)	7 (18)	7 (11)
Focus group**,** qualitative interviews, Delphi survey and consensus meeting	**10** (7)	0	1 (3)	9 (14)
Focus group, Delphi survey and consensus meeting	**7** (5)	1 (3)	0	6 (8)
Questionnaire, Delphi survey and consensus meeting	**6** (4)	2 (5)	1 (3)	3 (5)
Questionnaire, qualitative interviews, focus group, Delphi survey and consensus meeting	**6** (4)	1 (3)	0	5 (6)
Qualitative interviews and Delphi survey	**5** (4)	2 (5)	2 (5)	1 (2)
Delphi survey and focus group	**3** (2)	0	2 (5)	1 (2)
Questionnaire	**3** (2)	2 (5)	0	1 (2)
Qualitative interviews	**2** (1)	0	0	2 (3)
Consensus meeting	**2** (1)	2 (5)	0	0
Focus group, qualitative interviews and Delphi survey	**2** (1)	0	1 (3)	1 (2)
Qualitative interviews and consensus meeting	**2** (1)	1 (3)	0	1 (2)
Focus group, qualitative interviews and consensus meeting	**2** (1)	2 (5)	0	0
Focus group and consensus meeting	**2** (1)	1 (3)	0	1 (2)

Questionnaire, qualitative interviews, Delphi survey and consensus meeting	**2** (1)	2 (5)	0	0
Questionnaire, focus group and qualitative Interviews	**1** (1)	0	0	1 (2)
Questionnaire, focus group**,** qualitative interviews and consensus meeting	**1** (1)	0	1 (3)	0
Questionnaire and Delphi survey	**1** (1)	1 (3)	0	0
Questionnaire, focus group and Delphi survey	**1** (1)	1 (3)	0	0
Focus group	**1** (1)	0	1 (3)	0
Questionnaire, qualitative interviews and Delphi survey	**1** (1)	0	0	1 (2)
Questionnaire and qualitative interviews	**1** (1)	0	1 (3)	0
Focus group and questionnaire	**1** (1)	0	1 (3)	0
Focus group**,** qualitative interviews, Consensus meeting and other (nominal group technique)	**1** (1)	0	1 (3)	0
Other (nominal group technique)	**1** (1)	0	0	1 (2)
Other (nominal group technique) and consensus meeting	**1** (1)	1 (3)	0	0
Focus group and other (group concept mapping) and consensus meeting	**1** (1)	1 (3)	0	0

Table 2.4- Full Version shows the methods used to facilitate patient participation. The methods were used either singularly or in combination.

A3.1 EPITOME- Recruitment Advert

HAVE YOUR VOICE HEARD BY THE EPITOME STUDY

WHAT IS EPITOME?

EPITOME stands for "**E**xploring **P**articipant **I**nput in Core **O**utcome Set Develop**ME**nt".

At the University of Liverpool, the COMET Initiative are keen to learn about people's experience to help us develop the best methods for future COS studies.

COMET INITIATIVE

WHY IS EPITOME IMPORTANT?

Stakeholder input into core outcome set (COS) projects has been increasing. But the perspectives of people who have taken part in such studies haven't yet been explored.

Calling all patients, member of the public and health professionals, who have taken part in a study to develop a core outcome set (COS)*:
WE NEED YOU!

*COS: an agreed minimum set of outcome measures that should be measured and reported in all trials in a specific area. Outcomes are things like pain, fatigue, quality of life etc.

CAN I HELP?

YES! Your insights are very valuable to us!
We are inviting you to take part in a telephone interview about your experiences of taking part in a study to develop a COS. The interview will be at a time that's convenient for you and last about 45 minutes.
We have already spoken to the developers of your COS and they are happy to facilitate our research

WHO IS WORKING ON EPITOME?

The lead researcher is Alice Biggane. Alice is a Research Fellow at the University of Liverpool and will be doing the interviews.
She'd love to hear from anyone who's interested in being interviewed for EPITOME. She's also happy to answer any questions that you may have.
Email: abiggane@Liverpool.ac.uk
Tel: +44 (0)151 794 9744

MiRoR Methods in Research on Research

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 676207.

A3.2 EPITOME- Topic Guide

The idea of this topic guide is that the interviewer will be able to employ cognitive interviewing techniques as much as possible. By asking open and general questions it is hoped that the interviewee will retrospectively recall most of the events without interference from the interviewer, only to clarify certain aspects. However this will not always be the case and as such more detailed questions and prompts are also included. For the "engagement phase" topic of this guide, it should be noted that it may be repeated, depending on how many methods the interviewee was involved in.

Tick list:

Item	**Done**
Consent Form	
Expected duration of interview	
Introduction/ Explanation of process	

Topic guide (chronological)

Topic	**Prompts**
Background *Aims: to get interviewee talking and to find out contextual information about how his/her experience of the COS development began.*	Talk me through how you became involved in the study? How did you become aware of the study? –*Prompts: recruitment advert, methods* What were initial thoughts on it? *Prompts: Relevance, worthiness, was it explained adequately etc.* How did you make the decision to participate? How would you describe your feelings surrounding your decision?
Preparation *Aims: to understand how the interviewee prepared for the COS development. From their perspective and also how the study developers informed them.*	Talk me through what happened once you decided to participate? *Prompts: what were the various stages?* What contact with the COS developers did you have before meeting them? *Prompts: post, phone calls, emails* Was this contact useful? Were you supplied with a patient information sheet? Did you look at it? *Prompts: Was it satisfactory? Did you feel like it was explained in terms you could understand?* How were outcomes described to you?

	Prompts: Priorities, effect of research/ effects of treatment on life, lived experience, what is important to the patient/ what matters to them? Did you have a clear idea about what was happening? *Prompts: Length of time, process* Was there support available to you should you need it? Did you use the support? Was it helpful to you?
Engagement phase *Aims: to elicit information regarding the process itself.*	Talk me through what happened at the meeting/interview/ focus group/ Delphi etc.? What methods were used by the developers to elicit your thoughts and perspectives? What did you think of these methods? Were you able to express your thoughts and feelings? Do you feel they that your opinions were clearly respected/ represented? Dis you have any questions about the process? Was there support/someone to help with these? Did you access this support? Did it help? In what capacity? For how long did your involvement in the study run? Or was it a once off? Were you comfortable with that length of time? *Prompts: too long, too short, gaps in between contact* Is there anything you would have liked to change?

Present Day *Aims: to encourage the interviewee to retrospectively analyse their experience; the emotions, the process, whether the process worked or not, suggestions and messages to others.*	Looking back on the experience what you are your thoughts about it? Anything surprised or puzzled you? Any suggestions for change- would you do it again? would you recommend it to others? Face to face meetings with health professionals: experiences, concerns, thoughts Did you receive a copy of the final results *(if the results have been published- interviewer discretion*)? Do you have messages that you would like others to know or hear? Other participants, academics, developers, health professionals
Other	Anything else that wasn't covered that you think is important?

A3.3 EPITOME- NHS Ethics Query

NHS Ethics Query:

ENQUIRY TO QUERIES LINE

Dear Alice,

Thank you for your enquiry.

Your query was reviewed by our Queries Line Advisers.

RE: Participant Interviews: Interviews with patients and health professionals included as participants in COS development to investigate whether the current methods of inclusion are fit for purpose and acceptable to participants

Thank you for your email seeking additional clarity on whether your project should be classified as research and whether it requires ethical review by a NHS Research Ethics Committee (REC).

You provided the following information:

- An summary outlining your proposal
- A PDF /screenshot of the results page of the decision tool(s)
- An explanation of which questions you have difficulty in answering and why and/or
- An explanation of why you disagree with the outcome of the decision tool(s)

Based on the information you have provided, our decision is that the project is **considered to be research but does not require review by an NHS Research Ethics Committee.**

In giving this decision our advisors noted that participants were recruited from outside the NHS, either as Clinical Trial Participants or as Developers (from a public database). They are not being recruited as or because they are NHS patients. The advisers concluded that this study does not involve the NHS and no NHS REC review is expected.

This decision is in line with:

- The harmonised UK-wide edition of the Governance Arrangements for Research Ethics Committees (GAfREC), (updated April 2012);
- Research Governance Framework for Health and Social Care (Second edition, 2005)
- The National Research Ethics Service (NRES) guidance "*Defining Research*" and "*Does my project require review by a Research Ethics Committee?*".

This decision should not be interpreted as giving a form of ethical approval or endorsement to your project on behalf the HRA. However, it may be provided to a journal or other body as evidence if required.

You should also be aware that:

- This response only covers whether your project is classified as research and whether it requires review by an NHS REC. You are strongly advised to consider other approvals that may be required for your project.
- All types of study involving human participants should be conducted in accordance with basic ethical principles, such as informed consent and respect for the confidentiality of participants. Also, in processing identifiable data there are legal

requirements under the Data Protection Act 1998. When undertaking an audit or service/therapy evaluation, the investigator and his/her team are responsible for considering the ethics of their project with advice from within their organisation.

Regards

HRA Queries Line

Ref. 88/86/81

The HRA Queries Line is an email based service that provides advice from HRA senior management, including operations managers based in our regional offices throughout England. Providing your query in an email helps us to quickly direct your enquiry to the most appropriate member of our team who can provide you with an accurate written response. It also enables us to monitor the quality and timeliness of the advice given by HRA to ensure we can give you the best service possible, as well as use queries to continue to improve and to develop our processes.

Please note:

- If you have been asked to follow a particular course of action by a REC as part of a provisional or favourable opinion with conditions, then the REC requirements are mandatory to the opinion, unless specifically revised by that REC.
- Should you wish to query the REC requirements, this should either be through contacting the REC direct or, alternatively, the relevant local operational manager (details available from the HRA website http://www.hra.nhs.uk/contact-us/).

Health Research Authority
Ground Floor, Skipton House

80 London Road

London SE1 6LH
E: hra.queries@nhs.net | www.hra.nhs.uk

IMPORTANT – **Click here** for the latest details of the roll-out of HRA Approval in England

The HRA is keen to know your views on the service you received – our short feedback form is available **here**

A3.4 EPITOME- Ethical Approval

Health and Life Sciences Committee on Research Ethics (Human participants, tissues and databases)

22 June 2017

Dear Prof Williamson,

I am pleased to inform you that your application for research ethics approval has been approved. Details and conditions of the approval can be found below:

Reference:	1969
Project Title:	The EPITOME Study: Exploring Participant InpuT in Core Outcome Set DevelopMEnt
Principal Investigator/Supervisor:	Prof Paula Williamson
Co-Investigator(s):	Ms Alice Biggane, Prof Bridget Young
Lead Student Investigator:	-
Department:	Biostatistics
Approval Date:	22/06/2017
Approval Expiry Date:	Five years from the approval date listed above

The application was **APPROVED** subject to the following conditions:

Conditions

- All serious adverse events must be reported via the Research Integrity and Ethics Team (ethics@liverpool.ac.uk) within 24 hours of their occurrence.
- If you wish to extend the duration of the study beyond the research ethics approval expiry date listed above, a new application should be submitted.
- If you wish to make an amendment to the research, please create and submit an amendment form using the research ethics system.
- If the named Principal Investigator or Supervisor leaves the employment of the University during the course of this approval, the approval will lapse. Therefore it will be necessary to create and submit an amendment form using the research ethics system.
- It is the responsibility of the Principal Investigator/Supervisor to inform all the investigators of the terms of the approval.

Kind regards,

Health and Life Sciences Committee on Research Ethics (Human participants, tissues and databases) edreseth@liverpool.ac.uk

A3.5 EPITOME- Participant Information Sheet

PARTICIPANT INFORMATION SHEET

Exploring methods of participant inclusion in the development of core outcome sets (COS).

We would like to invite you to take part in our research study. Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and feel free to ask if you would like more information or if there is anything that you do not understand. Please also feel free to discuss this with your friends, relatives and anyone else you wish.

What is the purpose of the study?

There has been an increase in studies selecting **core outcome sets** (COS). A COS is an agreed standardised set of outcomes, which represent the minimum that should be measured and reported in all clinical trials of a specific condition.

Many of these studies have included patients and members of the public and health professional as **participants**. These participants take part in the development of a core outcome set by giving data on their opinions regarding what outcomes are important (e.g. by completing a Delphi survey or taking part in interviews).

However in the field of COS studies there is little now about how best to include these groups of participants.

This study will explore what it is like to **participate** in COS development. We hope the findings will help us to improve engagement with patients in future COS development.

Why have I been chosen to take part?

You have been asked to take part because you are participating or have participated in the development of a COS. Your insight and experience of participation in COS development is invaluable to us.

Do I have to take part?

It is completely up to you whether or not you agree to take part. If you do decide to take part, you will be asked to sign a consent form. If you decide to take part but then change your mind, you are free to do so at any time without giving a reason.

What will happen if I take part?

You will be asked to take part in an interview with a researcher, Alice Biggane, about your experience and your views of having participated in a COS project. The interviews will last approximately 45-60 minutes, or as long as you would like to talk about your experience. With your permission, the interview will be audio recorded. You can stop the interview at any time, and you do not have to answer a particular question if you don't want to.

Where will the interview take place?

The interview will be carried out over the telephone at a date and time convenient to you.

Are there any risks in taking part?

We do not expect there to be any risks or discomfort associated in this research study. However, if you feel uncomfortable then you can stop the interview at any time, without giving a reason.

Are there any benefits in taking part?

You will be helping develop our understanding of participation in selecting which outcomes to measure in clinical trials and facilitate improved engagement with participants in the development of future COS.

Will my participation be kept confidential?

All the information that you give us will be kept strictly confidential. The procedures for handling, processing,

storing and destroying the data will comply with the Data Protection Act of 1998.

This means that only the researchers will see what you have said. The audio-recording of your interview will be identified by a code number only. These audio-recordings will be transcribed, and identifying details such as place names and people's names removed from the transcripts. We will use quotes from the interviews in the write-up of the study but will ensure no one can be identified from these.

At the end of the study the research data, including consent forms, anonymised interview transcripts, field notes and your contact details, will be kept (in locked filling cabinets and/ or password protected university computers) for up to ten years.

What will happen to the results of the study?

After the study has finished, the results will be written up as part of Alice Biggane's postgraduate research thesis and submitted for examination. The results will also be submitted for publication in an academic journal and presented at conferences.

If you would like to receive a copy of the findings please let us know and we will happily provide you with one.

What will happen if I want to stop taking part?

If you decide at any point that you no longer wish to be part of the study, then you can withdraw without giving a reason. You can also ask for your data to be removed from the study and destroyed.

What if I am unhappy or if there is a problem?

If you are unhappy, or if there is a problem, please feel free to let us know by contacting the lead researcher, Alice Biggane at the University of Liverpool on 0151 794 9744 (abiggane@liverpool.ac.uk) who will try to help or put you in touch with someone who can.

If you remain unhappy or have a complaint which you feel you cannot come to us with then you should contact the Research Governance Officer at University of Liverpool on 0151 794 wilwill90 (ethics@liv.ac.uk). When contacting the Research Governance Officer, please provide details of the name or description of the study (so that it can be

identified), the researcher(s) involved, and the details of the complaint you wish to make.

Who is funding the research?

This research is funded by the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 676207. If you would like to find out more about the funding body please see here https://ec.europa.eu/programmes/horizon2020/

Who is doing this research?

The research and interviews will be conducted by Alice Biggane, a Marie Curie Research Fellow at the University of Liverpool, UK.

How can I find out more?

Just get in touch with Alice Biggane, who will be happy to answer any questions you might have:

Department of Biostatistics,

Institute of Translational Medicine

Block F/Waterhouse Building,

University of Liverpool,

Liverpool,

L69 3BX

Telephone no.: +44 (0)151 794 9744

Email address: abiggane@liverpool.ac.uk

Thank you for taking the time to reading this

This information sheet is for you to keep

A3.6 EPITOME- Informed Consent Script

Hello again, I'm Alice Biggane from the University of Liverpool and I wanted to talk to you about the project I gave you an information sheet about before. To recap, the broad aims of my project are to understand more about the perspective and opinions of participants who have taken part in core outcome set development.

Are you still interested in taking part in the project? *[Await confirmation].* Now I'd like to confirm some of the details of the project to make sure you are clear about what's involved for you:

- It's a project about exploring the role of participants such as yourself in the development of core outcome sets and it's being used for my postgraduate project.
- If you take part, I'll need you to take part in an interview where we will discuss your experiences and opinions of taking part in a core outcome set development. It will last=approximately 45 minutes.
- We do not expect there to be any risks or discomfort associated in this research study. However, if you feel uncomfortable then you can stop the interview at any time, without giving a reason.
- You don't have to say yes to taking part; you can ask me any questions you want before or throughout; you can also withdraw at any stage without giving a reason and without any negative consequences.
- You do not have to answer any questions that you do not wish to.
- You are aware that a University of Liverpool Research Ethics committee has approved this research project and how to contact me (in the first instance) or the committee in case of any concerns or complaints. I have given you the project's ethics reference number and relevant contact details.
- I won't keep any of your details for longer than necessary.
- I may use brief quotes of what you say during the interview in the write up of this study, but they will remain anonymous.
- I will safely store your data electronically on encrypted, secure filestores. All identifiable data will be destroyed at the end of the study.
- I will audio record you unless you say that I can't.
- You're aware that my written work will be published online and this project will may also be published in an academic journal/ book / website.
- Are you happy for me to collect detail sensitive personal data?
- Are you still willing to take part? Do you give your permission for me to re-contact you to clarify information?

[*Await confirmation]* So if you're happy with all of that, and have no more questions, let's start.

A4.1 INVoLVED- Guideline Developer Request

Dear X,

My name is Alice Biggane and I'm a MiRoR project PhD student at The University of Liverpool. I'm undertaking a secondment with NICE as part of studies, under the guidance of my NICE mentor Dr (Removed).

I'm interested in observing clinical guideline committee meetings at NICE, with the hope of understanding and characterising the influence of the opinions and perspectives of lay-members chosen clinical guideline outcomes. I'm also interested in exploring how lay members navigate the process. Therefore, I'm writing to you as I'm hoping to observe two upcoming clinical guideline developments that you are the guideline commissioning manager of:

- Guideline name removed
- Guideline name removed

(NICE mentor name removed) informed me of these developments and their start dates. They fit well my project aim and I would really like to observe the committee meetings from the start to as near possible the final meeting, if that is agreeable to you and the committee?

I'm currently writing an ethics application for The University of Liverpool Research Ethics Committee, I hope to submit it shortly. Of course that is if you are happy for me to observe the above guideline developments?

If you are, and I receive ethical approval I'll be able to supply all the appropriate documentation such as information sheets, consent forms etc.

I look forward to hearing from you.

Many thanks for your time.

Kind regards,

Alice

A4.2 INVoLVED- Observations Participant Information Sheet

The INVoLVED Study: Investigating Lay-members' Views in Clinical Guideline Development

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

Please ask us if there is anything that is not clear or if you would like more information.

1. What is this project about?

This project aims to explore how lay members influence which outcomes are chosen within clinical guideline development.

2. Why am I being asked to take part?

You have been chosen because you are on our have been part of a committee developing a clinical guideline for NICE. This clinical guideline is one of three that has been selected for observation by the research team.

3. Do I have to take part?

No – it is entirely your decision. If you do decide to take part, you will be asked to give verbal consent. You can withdraw from this project at any time without giving a reason.

4. What would taking part involve?

Alice Biggane the researcher will spend time at each committee meeting observing the process. She may also chat with you about your experiences at the time of the meetings. Alice will take notes about these observations and chats, these notes will document interactions, take quotes of what has been said, have a schema of the room and set-up, take note of the documents being distributed etc.

If you would rather not be observed and recorded in any notes, that is ok, Alice will not include any observations or recordings relating to you.

It is possible that Alice will ask some committee members to take part in an in-depth interview. This part of her project is explained in a separate participant information sheet. Please ask Alice if you would like to find out more about the interviews.

5. What are the possible risks and benefits of taking part?

We do not expect there to be any risks. If you feel uncomfortable, then you can stop taking part in the project at any time, without giving a reason.

Your participation in this project is very valuable to us. We hope the findings will enhance support for lay-members in future clinical guideline development.

6. What will happen if I want to stop taking part?

If you decide at any point that you no longer wish to be part of the project, then you can withdraw without giving a reason. You can also ask for data specific to you to be removed from the project and destroyed.

7. More information about taking part

Will my participation be kept confidential?

Information collected during this project will be kept confidential. The procedures for handling, processing, storing and destroying the data will comply with the Data Protection Act of 1998.

This means that only the researchers will know what you have said. The field notes will be written up and pseudo-anonymised, with identifying details such as place names and people's names changed or removed. We may use brief quotes from the observations in our reports but we will always make sure that no one can be identified from these.

Any identifying information that you give us will be stored securely and kept confidential and destroyed at the end of the study. At the end of the project, with your consent, the anonymised research data will be kept in secure folder for potential re-use by other ethically approved projects which is line with research integrity and preservation standards.

What if I am unhappy or if there is a problem?

If you are unhappy, or if there is a problem, please feel free to let us know by contacting the lead researcher, Alice (see '**How to contact us**') who will try to help or put you in touch with someone who can.

If you remain unhappy or have a complaint which you feel you cannot come to us with then, you should contact the Research Governance Officer at the University of Liverpool on 0151 794 8290 (ethics@liv.ac.uk). When contacting the Research Governance Officer, please provide details of the name or description of the project (so that it can be identified), the researcher(s) involved, and the details of the complaint you wish to make.

What will happen to the results of the study?

After the project has finished, the results will be written up as part of Alice Biggane's doctoral thesis and submitted for examination. The results will also be submitted for publication in an academic journal and presented at conferences.

We can send you a summary of the findings at the end of the project if you would like us to. Alice will ask you about this while seeking your consent.

8. How to contact us

If you have any questions, please get in touch with Alice Biggane, who is the researcher on this project:

Telephone no.: +44 (0)151 794 9744

Email address: abiggane@liverpool.ac.uk

Postal address: Department of Biostatistics, Institute of Translational Medicine, University of Liverpool, Waterhouse Building – Block F, Liverpool, L69 3BX

You may prefer to contact, Professor Bridget Young, who is supervising this project:

Telephone no.: +44 (0)151 794 5525

Email address: Bridget.young@liverpool.ac.uk

Postal address: Institute of Psychology, Health and Society , University of Liverpool, Whelan Building Liverpool, L69 3GB

Thank you for taking the time to read this. This information sheet is for you to keep

A4.3 INVoLVED- Observations Informed Consent

Committee on Research Ethics

PARTICIPANT CONSENT FORM

Title of Research Project:	Exploring via observation the influence of lay members' views on the outcomes chosen in the National Institute for Health and Care Excellence (NICE) clinical guidelines.
Researcher(s):	Alice Biggane

	Please initial box
1. I confirm that I have read and have understood the information sheet dated [DATE] for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation and that of the committee is voluntary and that I am free to withdraw at any time without giving any reason as is any committee member, without my rights being affected.	☐
3. I understand that, under the Data Protection Act, I can at any time ask for access to the information I provide and I can also request the destruction of that information if I wish.	☐
4. I agree to take part in the above study.	☐

Participant Name	Date	Signature

Researcher	Date	Signature

Principal Investigator:

Professor Bridget Young

Institute of Psychology, Health and Society,

University of Liverpool, L69 3GB

Bridget.Young@liverpool.ac.uk

+44 (0)151 794 5525

Student Researcher:

Miss Alice Biggane

Department of Biostatistics,

University of Liverpool, L69 3BX

abiggane@liverpool.ac.uk

+44 (0)1517949964

[V1.0 10/08/2017]

Statements

- The information you have submitted will be published as a report; please indicate whether you would like to receive a copy.

- I understand that every effort will be taken to ensure confidentiality and anonymity, however, I understand that the guideline will be named in the write-up of the report

- I agree for the anonymised data collected from me or the committee to be used in future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee.

- I understand and agree that the committee's interaction and processes will be recorded as fieldnotes via observation. I am aware of and consent to your use of these recordings for the purpose of further analysis

- I agree for the data collected from me and the committee to be used in relevant future research.

- I understand that my responses and those of the committee members will be kept strictly confidential. I give permission for members of the research team to have access to the anonymised fieldnotes. I understand that my name or those of the committee members will not be linked with the research materials, and I or the committee members will not be identified or identifiable in the report or reports that result from the research.

- I understand and agree that once I submit my data it will become anonymised and I will therefore no longer be able to withdraw my data.

A4.4 INVoLVED- Interviews Patient Information Sheet

The INVoLVED Study: Investigating Lay-members' Views in Clinical Guideline Development

You are being invited to take part in a research project. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

Please ask us if there is anything that is not clear or if you would like more information.

3. What is this project about?

This project aims to explore how lay members influence which outcomes are chosen within clinical guideline development.

2. Why am I being asked to take part?

You have been chosen because you are or have been part of a committee developing a clinical guideline for NICE. Your experiences of the clinical guideline development process are really important to us.

3. Do I have to take part?

No – it is entirely your decision. If you do decide to take part, you will be asked to give consent. You can withdraw from this project at any time without giving a reason.

4. What would taking part involve?

Taking take part will involve being interviewed by a researcher, Alice Biggane. If you are happy to be interviewed, Alice will ask about your experiences of developing a clinical guideline. The interviews will usually last about 45 minutes, but can be shorter or longer depending on how much there is to talk about.

The interviews can be done in person (at a place of your choice), or over the phone – whichever you prefer. With your permission, Alice will audio-record the interview. You can stop the interview at any time, and you do not have to answer a particular question if you don't want to.

5. What are the possible risks and benefits of taking part?

We do not expect there to be any risks. If you feel uncomfortable, then you can stop taking part in the project at any time, without giving a reason.

Your participation in this project is very valuable to us. We hope the findings will enhance support for lay-members in future clinical guideline development.

6. What will happen if I want to stop taking part?

If you decide at any point that you no longer wish to be part of the project, then you can withdraw without giving a reason. You can also ask for data specific to you to be removed from the project and destroyed.

7. More information about taking part

Will my participation be kept confidential?

Information collected during this project will be kept confidential. Handling, processing and storing the data will comply with the Data Protection Act of 1998.

This means that only the researchers will know what you have said. The audio-recording of your interviews will be identified by a code number only. The audio-recordings will be transcribed by a professional transcription agency and pseudo-anonymised, with identifying details such as place names and people's names changed or removed. We may use brief quotes from the interviews in our reports but we will always make sure that no one can be identified from these.

Any identifying information that you give us will be stored securely and kept confidential and destroyed at the end of the study. At the end of the project, with your consent, the pseudo-anonymised research data will be kept for in a secure folder for potential use by future ethically approved projects. You do not have to consent to making your pseudo-anonymised data available for re-use and can still be interviewed.

What if I am unhappy or if there is a problem?

If you are unhappy, or if there is a problem, please let us know by contacting the lead researcher, Alice (see '**How to contact us**') who will try to help or put you in touch with someone who can.

If you remain unhappy or have a complaint which you feel you cannot come to us with, you should contact the Research Governance Officer at the University of Liverpool on 0151 794 8290 (ethics@liv.ac.uk). When contacting the Research Governance Officer, please provide details of the name or description of the project (so that it can be identified), the researcher(s) involved, and the details of the complaint you wish to make.

What will happen to the results of the study?

After the project has finished, the results will be written up as part of Alice Biggane's doctoral thesis and submitted for examination. The results will also be submitted for publication in an academic journal and presented at conferences.

We can send you a summary of the findings at the end of the project if you would like us to. Alice will ask you about this while seeking your consent.

8. How to contact us

If you have any questions, please get in touch with Alice Biggane, who is the researcher on this project:

Telephone no.: +44 (0)151 794 9744

Email address: abiggane@liverpool.ac.uk

Postal address: Department of Biostatistics, Institute of Translational Medicine, University of Liverpool, Waterhouse Building – Block F, Liverpool, L69 3BX

You may prefer to contact, Professor Bridget Young, who is supervising this project:

Telephone no.: +44 (0)151 794 5525

Email address: Bridget.young@liverpool.ac.uk

Postal address: Institute of Psychology, Health and Society , University of Liverpool, Whelan Building Liverpool, L69 3GB

Thank you for taking the time to read this. This information sheet is for you to keep

A4.5 INVoLVED- Interviews Informed Consent (Written)

Committee on Research Ethics

PARTICIPANT CONSENT FORM

Title of Research Project:

Researcher(s):

		Please initial box
5.	I confirm that I have read and have understood the information sheet dated [DATE] for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
6.	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my rights being affected. In addition, should I not wish to answer any particular question or questions, I am free to decline.	☐
7.	I understand that, under the Data Protection Act, I can at any time ask for access to the information I provide and I can also request the destruction of that information if I wish.	☐
8.	I agree to take part in the above study.	☐

Participant Name	Date	Signature
Researcher	Date	Signature

Principal Investigator:

Professor Bridget Young

Institute of Psychology, Health and Society,

Student Researcher:

Miss Alice Biggane

Department of Biostatistics,

University of Liverpool, L69 3GB

Bridget.Young@liverpool.ac.uk

+44 (0)151 794 5525

University of Liverpool, L69 3BX

abiggane@liverpool.ac.uk

+44 (0)1517949964

[V1.0 10/08/2017]

Statements

- The information you have submitted will be published as a report; please indicate whether you would like to receive a copy. ☐
- I understand that confidentiality and anonymity will be maintained and it will not be possible to identify me in any publications ☐
- I agree for the data collected from me to be used in relevant future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. ☐
- I agree for the data collected from me to be used in this research project exclusively and do not agree for it to be used in relevant future research. ☐
- I understand and agree that my participation will be audio recorded and I am aware of and consent to your use of these recordings for the following purposes transcription and analysis ☐
- I understand that my responses will be kept strictly confidential. I give permission for members of the research team to have access to my pseudo-anonymised responses. I understand that my name will not be linked with the research materials, and I will not be identified or identifiable in the report or reports that result from the research. ☐
- I understand and agree that once I submit my data it will become anonymised and I will therefore no longer be able to withdraw my data. ☐

A4.6 INVoLVED- Interviews Informed Consent (Oral)

Hello again, I'm Alice Biggane from the University of Liverpool and I wanted to talk to you about the project I gave you an information sheet about before. To recap, the broad aims of my project are to understand more about the perspective and opinions of committee members who have taken part in a clinical guideline development.

Are you still interested in taking part in the project? *[Await confirmation].* Now I'd like to confirm some of the details of the project to make sure you are clear about what's involved for you:

- It's a project about exploring the role of participants such as yourself in the development of clinical guidelines and it's being used for my postgraduate project.
- If you take part, I'll need you to take part in an interview where we will discuss your experiences and opinions of taking part in a clinical guideline development. It will last approximately 45 minutes.
- We do not expect there to be any risks or discomfort associated in this research study. However, if you feel uncomfortable then you can stop the interview at any time, without giving a reason.
- You don't have to say yes to taking part; you can ask me any questions you want before or throughout; you can also withdraw at any stage without giving a reason and without any negative consequences.
- You do not have to answer any questions that you do not wish to.
- You are aware that a University of Liverpool Research Ethics committee has approved this research project and how to contact me (in the first instance) or the committee in case of any concerns or complaints. I have given you the project's ethics reference number and relevant contact details.
- I won't keep any of your details for longer than necessary.
- I may use brief quotes of what you say during the interview in the write up of this study, but they will remain anonymous.
- I will safely store your data electronically on encrypted, secure filestores. All identifiable data will be destroyed at the end of the study.
- I will audio record you unless you say that I can't.
- You're aware that the findings of this study will be published online as my doctoral thesis and this project may also be published in an academic journal/ book / website.
- Are you still willing to take part? Do you give your permission for me to re-contact you to clarify information?

[*Await confirmation]* So if that sounds ok and you've no more questions, let's start.

A4.7 INVoLVED- Topic Guide

1. **Q.** Could you talk me through how you became involved in the clinical guideline development?

Prompts: *How did you become aware of the study? –recruitment advert, methods*

2. **Q.** Can you tell me about how you prepared for the guideline development meetings? (both before and throughout the meetings)

Prompts: *Can you tell me about any support provided for the first meeting?*

What was included in this?

For lay-members: What were your experiences of the lay member training sessions

3. **Q.** Can you tell me about your experiences of being involved in the guideline development meetings?

Prompts: *Thinking back to the very start, what did you expect being involved in this guideline development would be like?*

How has the reality compared with your expectation?

How do you think your involvement affected the guideline development? (If so, in what way? (Can you tell me a little bit more about that?))

How was your relationship with the rest of the committee? (Were there any challenges? If so, how were these challenges resolved?)

Is there anything that stands out about the meetings?

What's your understanding of what was expected of you in relation to your participation in the guideline development meetings?

For lay members: *How did you experience having other lay members on the committee with you?*

What was it like being a part of a committee with health professionals?

For healthcare professionals: *What was your experience of having lay members on the committee with you?*

4. **Final Questions:**

Q. Do you have any suggestions for improving the process?

Q. Is there something else that is important to you that we haven't talked about today?

A4.8 INVoLVED- Ethical Approval

Health and Life Sciences Research Ethics Committee (Psychology, Health and Society)

18 October 2017

Dear Prof Young,

I am pleased to inform you that your application for research ethics approval has been approved. Details and conditions of the approval can be found below:

Reference:	2025
Project Title:	The INVoLVED Study: Investigating Lay-members' Views in Clinical Guideline Development
Principal Investigator/Supervisor:	Prof Bridget Young
Co-Investigator(s):	Ms Alice Biggane, Prof Paula Williamson
Lead Student Investigator:	-
Department:	Psychological Sciences
Approval Date:	18/10/2017
Approval Expiry Date:	Five years from the approval date listed above

The application was **APPROVED** subject to the following conditions:

Conditions

- All serious adverse events must be reported via the Research Integrity and Ethics Team (ethics@liverpool.ac.uk) within 24 hours of their occurrence.
- If you wish to extend the duration of the study beyond the research ethics approval expiry date listed above, a new application should be submitted.
- If you wish to make an amendment to the research, please create and submit an amendment form using the research ethics system.
- If the named Principal Investigator or Supervisor leaves the employment of the University during the course of this approval, the approval will lapse. Therefore it will be necessary to create and submit an amendment form using the research ethics system.
- It is the responsibility of the Principal Investigator/Supervisor to inform all the investigators of the terms of the approval.

Kind regards,

Health and Life Sciences Research Ethics Committee (Psychology, Health and Society)
iphsrec@liverpool.ac.uk 0151 795 5420

A5.1 ECRIN- Consultant Email Request

R&D ENGAGEMENT OPPORTUNITY:
A researcher looking for participants from different countries (with a good cultural / societal understanding of their country), for a short consultation / telephone interview.

Please write to the researcher (Alice.Biggane@liverpool.ac.uk) if you're keen.

==========

"We are looking to consult with interested individuals to better understand potential societal and cultural issues in their country regarding patient participation in research. Ideally, we are looking for someone who has experience of patient participation in research and can speak from a more representative perspective of the country. Thus, this person does not necessarily need to be a patient themselves.

We are specifically interested in applying this knowledge to improving methods for patient participation in core outcome set (COS) development via the Delphi survey. BUT The individual(s) we are looking to speak to does not need to be familiar with COS and Delphi, as I can explain to them via teleconference.

We would like to propose to any interested individuals that we set up a teleconference at a time and date of their choosing. The meeting should last approximately one hour, or however long they wish to speak with us. Unfortunately, we are not in a position to offer any payment or reimbursement for this consultation. However, we will ensure that you and/or your organisation in acknowledged in any publication."
==========

A5.2 ECRIN- Topic Guide

Questions re COS video/ patient participation in research (after viewing it- either in advance or with me, their choice)

1. What were your thoughts on the video I sent to you?
2. Having watched the video do you think patients would understand the purpose of a COS from watching it?
3. Do you have any comments or suggestions about the content of the video? *Ask about subtitling and dubbing over of content.*
4. The video shows patients working together with other stakeholders like health professionals – what do you think the benefits and challenges might be with this kind of working in your country / health area?

Questions regarding the Delphi (after presentation of how it works)

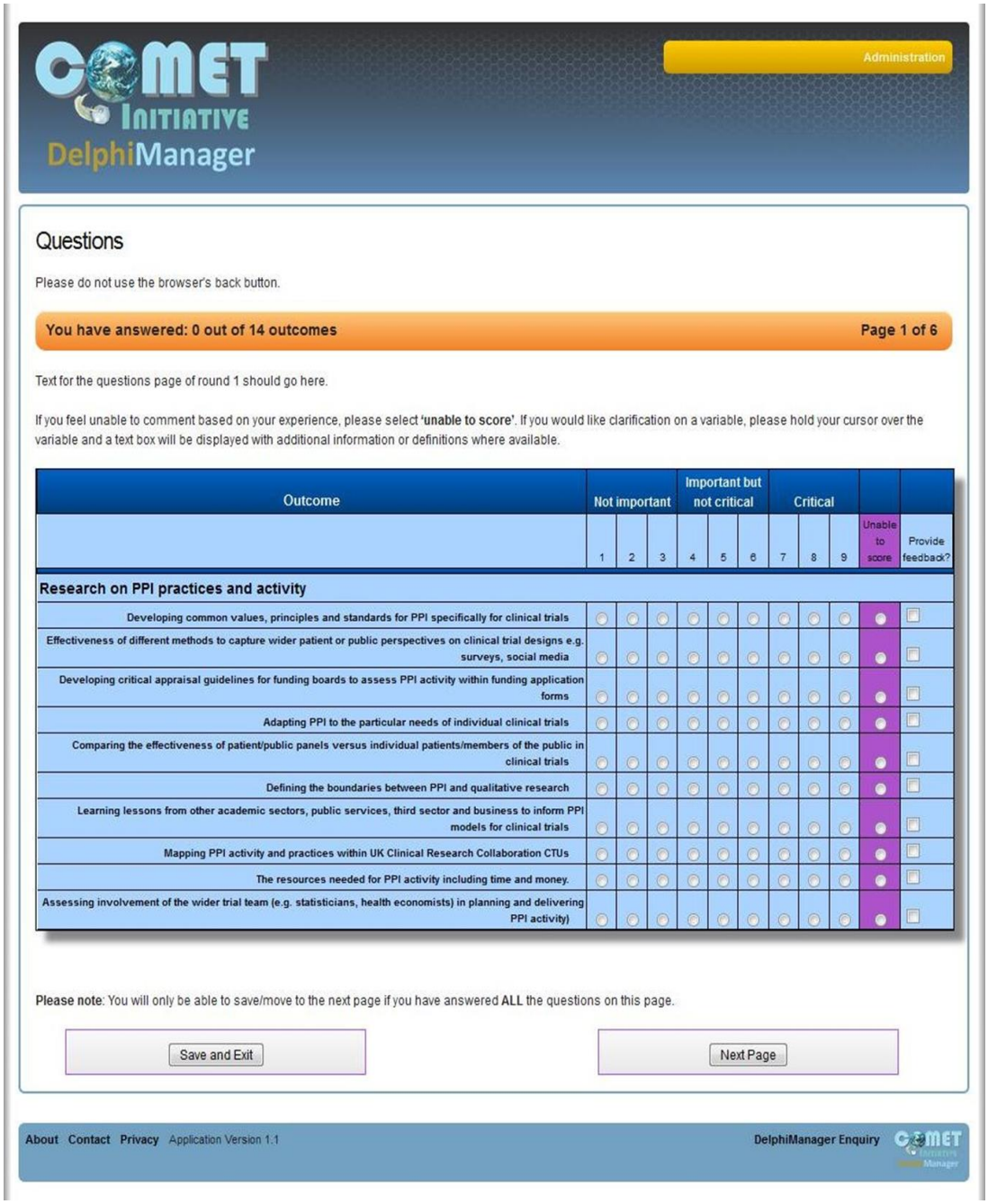
1. Do you have any questions about the process I just described *(feel free to ask me any questions at any point as we continue*)?
2. What do you think of it as a process of participation? How do you think patients and members of the public in your country would react to this type of participation?
3. What do you think of it as a consensus method?
4. I have described and shown you an image of how the participants receive feedback from previous rounds. Do you think it is clear how participants would be expected to use that information to respond in the second round?
5. In the countries you represent, do you think patients can voice their opinions if they are different to that of their health provider? Patients can do this anonymously in the Delphi
6. How do you think patients in your country and health condition will react to being asked to take part in this process? *Is it usual to have patients involved in health service design, what sort of voice do people have in decision making*
7. In your opinion how do you think we can prepare patients to participate in a Delphi?
8. Thinking of your own country and/ or health area are there any particular issues that we should consider when asking patients to participate? *Societal/ cultural Relate it to their own work- suggestions*
9. From what I have explained to you today, are there any issues/ points that you think we should include in the video to explain the Delphi process as clearly as possible? *Feedback, scoring system, recruitment into the study, future rounds of the study*

General

1. Is there anything else you would like to add?

A5.3 ECRIN- DelphiManager Screenshots

1. Outcomes as displayed in Round 1



COMET Initiative DelphiManager

Administration

Questions

Please do not use the browser's back button.

You have answered: 0 out of 14 outcomes — **Page 1 of 6**

Text for the questions page of round 1 should go here.

If you feel unable to comment based on your experience, please select **'unable to score'**. If you would like clarification on a variable, please hold your cursor over the variable and a text box will be displayed with additional information or definitions where available.

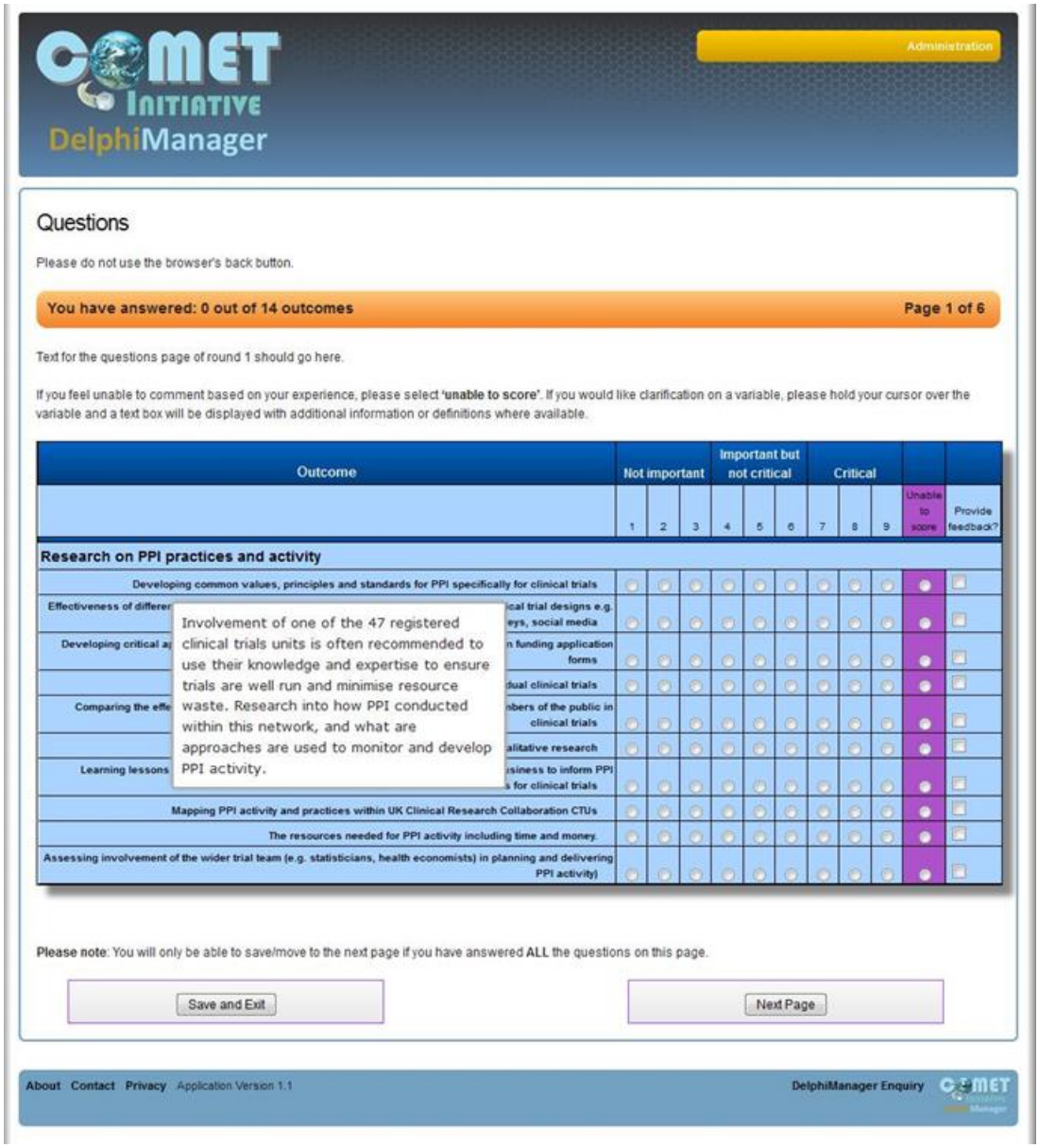
Outcome	Not important			Important but not critical			Critical				
	1	2	3	4	5	6	7	8	9	Unable to score	Provide feedback?
Research on PPI practices and activity											
Developing common values, principles and standards for PPI specifically for clinical trials	○	○	○	○	○	○	○	○	○	●	☐
Effectiveness of different methods to capture wider patient or public perspectives on clinical trial designs e.g. surveys, social media	○	○	○	○	○	○	○	○	○	●	☐
Developing critical appraisal guidelines for funding boards to assess PPI activity within funding application forms	○	○	○	○	○	○	○	○	○	●	☐
Adapting PPI to the particular needs of individual clinical trials	○	○	○	○	○	○	○	○	○	●	☐
Comparing the effectiveness of patient/public panels versus individual patients/members of the public in clinical trials	○	○	○	○	○	○	○	○	○	●	☐
Defining the boundaries between PPI and qualitative research	○	○	○	○	○	○	○	○	○	●	☐
Learning lessons from other academic sectors, public services, third sector and business to inform PPI models for clinical trials	○	○	○	○	○	○	○	○	○	●	☐
Mapping PPI activity and practices within UK Clinical Research Collaboration CTUs	○	○	○	○	○	○	○	○	○	●	☐
The resources needed for PPI activity including time and money.	○	○	○	○	○	○	○	○	○	●	☐
Assessing involvement of the wider trial team (e.g. statisticians, health economists) in planning and delivering PPI activity)	○	○	○	○	○	○	○	○	○	●	☐

Please note: You will only be able to save/move to the next page if you have answered **ALL** the questions on this page.

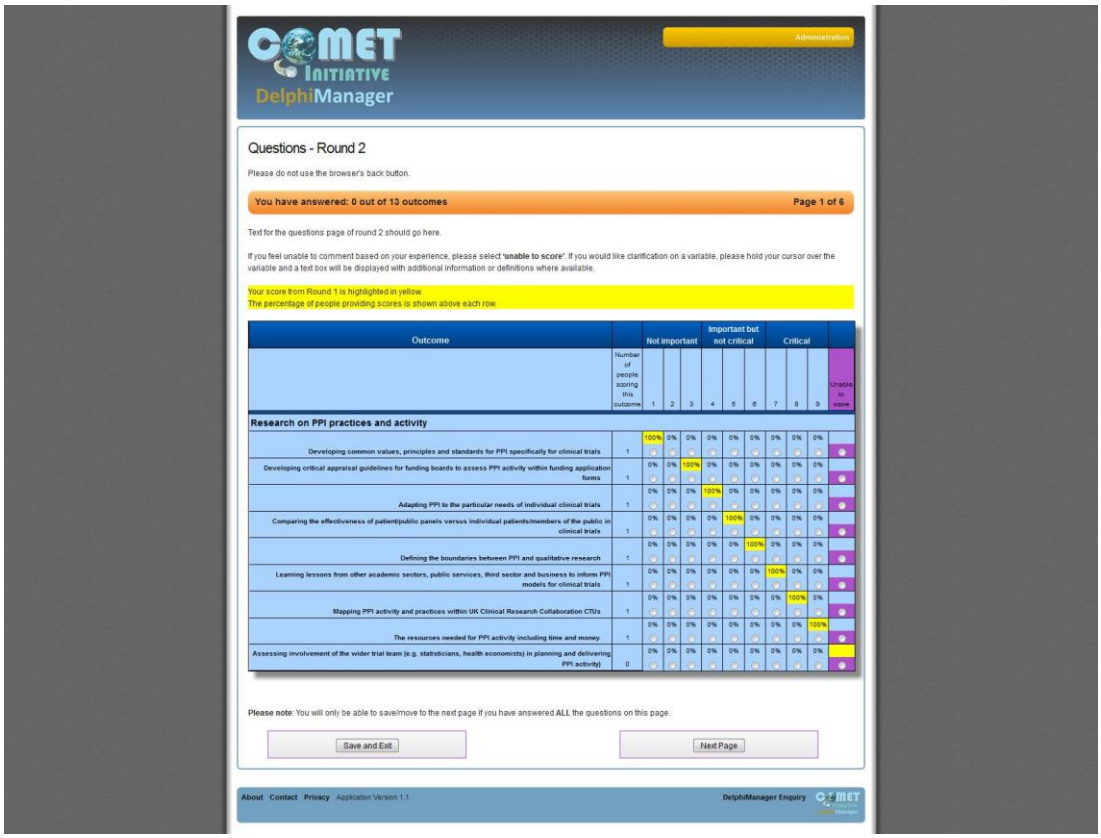
Save and Exit — Next Page

About Contact Privacy Application Version 1.1 — DelphiManager Enquiry

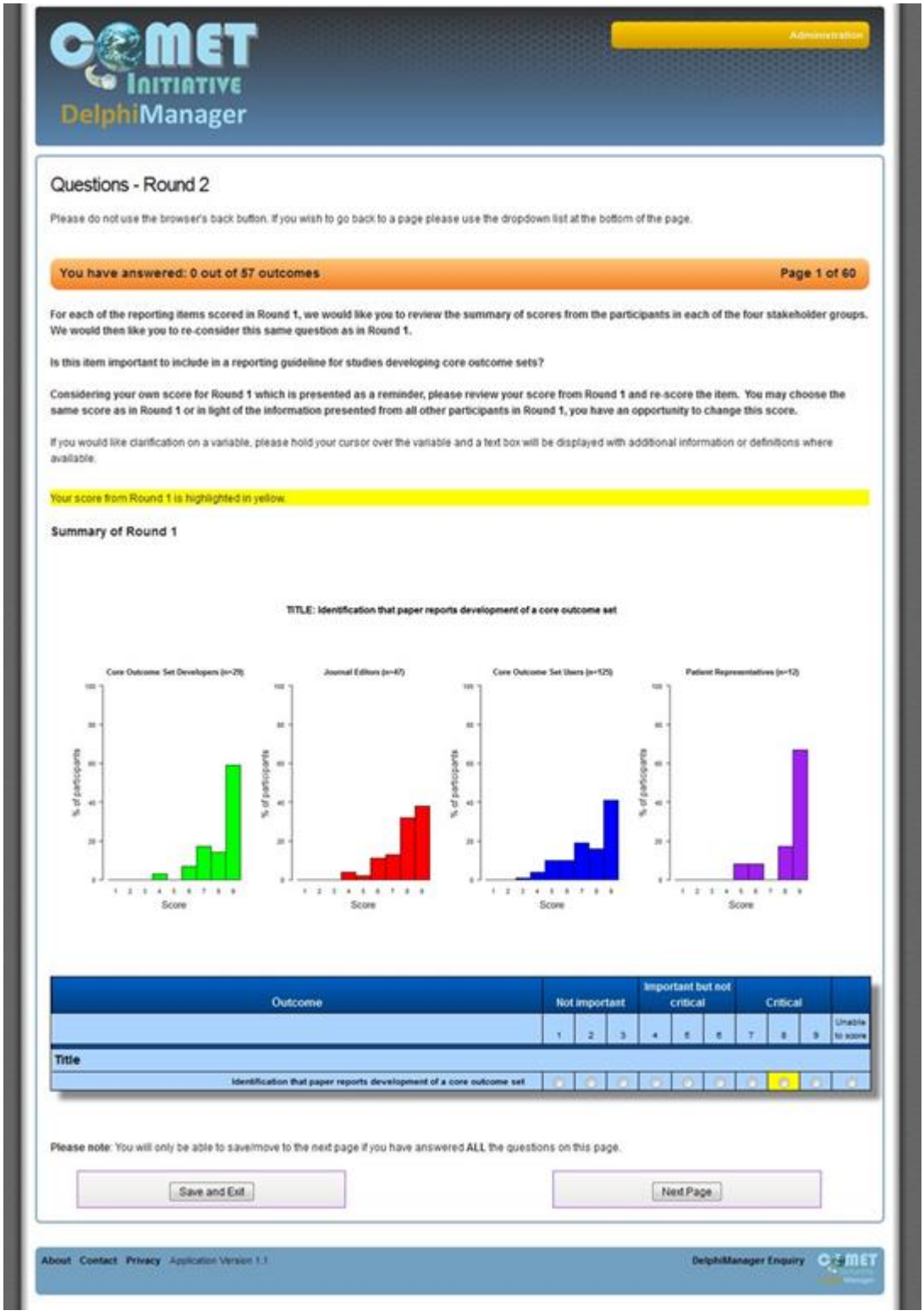
2. Explanation of outcomes



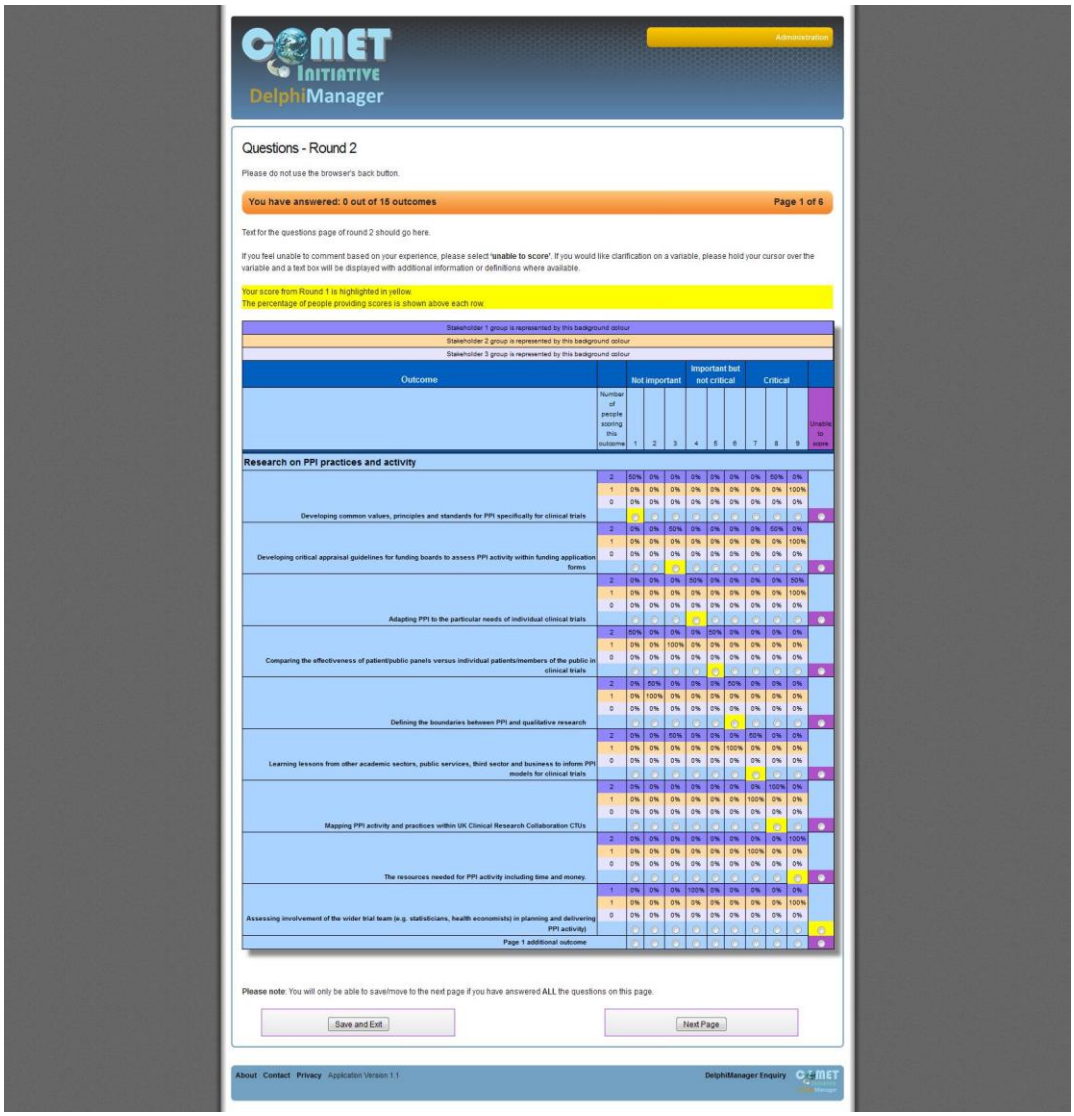
3. Outcomes as displayed in Round 2



4. Round 2- Stakeholder feedback via graphs



5. Round 2- Stakeholder feedback via % points



A6 Relevant qualitative training

1. Introduction to Qualitative Interviewing course; completed 2017 (University of Oxford)
2. Analysing Qualitative Interviews course; completed 2017 (University of Oxford)
3. MiRoR Qualitative training; completed 2017 (University of Liverpool)
4. Ethnographic Studies of Science and Technology; completed 2017 (University of Liverpool)