Mapping the uncertainties in internet-based clinical trials: a systematic review and qualitative study

Anne Brice

A thesis submitted for the degree of

Doctor of Philosophy in Evidence-Based Health Care

Kellogg College, Department of Continuing Education
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Trinity 2017

ABSTRACT

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This thesis maps the growth of the use of internet technologies in randomised controlled trials in health care and public health, and explores the methodological and ethical issues that arise from their use from the perspective of researchers and participants. Online clinical trials are growing in number, and claim to offer benefits for researchers and participants, providing solutions to some of the inherent problems associated with traditional trials. However, little is known about how many internet-based trials have been conducted, what methodological research has been undertaken, or what impact the new technologies might have on researcher or participant experience.

The thesis followed a step-by-step approach, using information science, research synthesis, and qualitative methods. The creation of a database of internet-based clinical trials established that they have grown rapidly in number, use internet technologies primarily to deliver an intervention, predominantly in

behavioural, mental health, or life-style public health settings. A two-stage systematic review, comprising a descriptive map and a qualitative synthesis, established what is known about the methods, conduct or participant experience in internet-based trials. A qualitative primary study was then carried out, based on the findings of the review, to further explore the views, attitudes and experiences of researchers, participants and the public, into the motivations, benefits or barriers to taking part in internet-based clinical trials.

Themes emerging from the research suggest complex interactions between design and technology, particularly in the area of participant characteristics and choice; convenience versus intrusion; impact of time and place; the pace of change and impact of societal changes in the use of technology. A range of ethical considerations emerged, including the nature of informed consent, ethical approval, and the need for a systematic approach to patient and public involvement. Recommendations are made to help inform and improve research practice in the digital age.

ACKNOWLEDGEMENTS

Professor Sue Ziebland and Professor Amanda Burls provided academic supervision for this thesis. Their respective expertise, and the guidance, support and constructive challenge they have provided throughout the course of my research has been both critical, and rewarding.

I acknowledge the support provided by the Department of Continuing Education, and Department of Primary Health Care Sciences, University of Oxford for making this part-time DPhil programme possible, and for their continued efforts to widen access to learning across the health care system. Warm thanks are also extended to the staff and students of Kellogg College, who have provided facilities, grants, stimulation, and food, but also a place to meet and share experiences, and to feel welcomed and supported. Professor Sandy Oliver (The Institute for Education, University of London), a champion of patient and public involvement, gave me help and guidance at the crucial first stage of this thesis, and the encouragement to continue.

Thanks are extended to my professional colleagues, including Nia Roberts (University of Oxford), Nicola Pearce-Smith (Public Health England) who provided advice on information science. Special thanks to Caroline De Brun (Public Health England), who acted as a second researcher during quality appraisal and thematic analysis in the systematic review. I am indebted to my Spanish colleagues, Marimar Ubeda and Eukene Ansuategi, for help with searching in Spanish, and to Jose Emperanza for his support and hospitality during my Santander Award placement in San Sebastian. Very special thanks are given to Amy Price, who has sustained me with shared experience, counselling and encouragement for the last 5 years. I would also like to acknowledge the researchers and members of the public for taking part in my primary research.

In April 2016 I was awarded a research residency at The Brocher Foundation in Geneva, whose mission is to encourage research on the ethical, legal and social implications of new medical technologies, and who host visiting researchers and students. This Award provided a unique and timely opportunity to work in depth on my thesis, and I am very grateful to the Foundation for their help and support.

I would not have taken this road without the inspiration and guidance of two of the founders of evidence-based health care, who I have been lucky enough to work with, and who helped me gain the confidence and motivation to undertake this thesis, Sir Muir Gray, and Sir Iain Chalmers. Their steadfastness, enthusiasm, respective beliefs and encouragement have underpinned all of my work. I also acknowledge the funding provided by the NHS National Knowledge Service, and Ann Southwell for help in facilitating and administering the grant.

Finally, I am grateful and inspired by the support of my family and friends who have accompanied me through this doctorate with patience, unconditional support, and valiant attempts to understand the rationale and need for me to undertake it, at this stage in my life. Thank you to my children Ruth, Rebecca and Thomas, and to my husband Graham, for everything.

STATEMENT OF CONTRIBUTIONS

This doctoral thesis is independent and original work of which I am the sole author. Supervisors Professor Sue Ziebland and Professor Amanda Burls provided academic guidance on the research strategy and methodologies, analyses, preparation and presentation of results. Other individuals have made contributions in the following ways:

Nia Roberts: Information Specialist, University of Oxford assisted in peer reviewing the search strategy for the database creation in Chapter 3.

Nicola Pearce-Smith: Senior Information Scientist, Public Health England assisted in peer reviewing the search strategies for the descriptive map in Chapter 4.

Caroline De Brun: Knowledge & Evidence Specialist, Public Health England provided feedback on the data extraction process; acted as a second reviewer for the quality assessment; and as a second reviewer in the coding themes for quality assurance purposes in Chapter 5.

Rebecca Brice: Clinical Trial Co-ordinator, Primary Care Health Sciences, University of Oxford assisted in data extraction of study characteristics in Chapter 5.

Amy Price: DPhil student, Primary Care Health Sciences, University of Oxford assisted in the screening for the ORCHID database; screening for the descriptive map; and thematic analysis for the qualitative synthesis. She facilitated ethical approval for the primary study. She also reviewed all Chapters for the thesis, and provided feedback, comments and help with locating relevant citations and experts.

Jeff Brunton: EPPI-Centre, Institute of Education, University of London provided technical and functional support for the use of the EPPI-Reviewer software.

Alison McPherson: Premier Typing Services provided transcription services for the primary study interviews and focus groups.

TABLE OF CONTENTS

List of Tables

List of Figures

1 Introduction

1.1 Overview of thesis

This thesis maps the growth of the use of internet technologies in randomised controlled trials in health care and public health, and explores the methodological and ethical issues that arise from their use from the perspective of researchers and participants. Following an analysis of the background to the topic, the first phase of the research created a database of reports of randomised controlled clinical trials that have used internet technologies, and indexed their core characteristics including country; condition under investigation; and interventions being tested. The second phase produced a two-stage systematic review to identify factors influencing the effective use of internet-based technologies in clinical trials, including the impact on trial management; recruitment and retention; ethics; and public, patient and researcher attitudes, preferences and experiences. The first stage of the review developed a descriptive map of the landscape and coverage of published studies and established the relevant themes and the size of the literature. For the second stage of the review an in-depth qualitative synthesis of the findings of a sub-set of the studies was undertaken. This explored the views, experiences and expectations of participants and researchers about taking part in internet-based clinical trials, and how these might impact on trial design and conduct. The third phase of the thesis comprised a primary qualitative study to further explore the attitudes and experiences of people involved in internet-based clinical trials, including patients and the public, study participants, and researchers. The final section of the thesis includes a critique of the research undertaken, combines the findings of the

various stages, and provides guidance to support researchers and the public improve the planning and design of internet-based clinical trials. A timeline for the thesis is provided in Appendix 1A.

1.2 Aim of thesis

This thesis maps the factors determining the effectiveness of internet-based clinical trials in health care and public health, and explores the views, attitudes and experiences of researchers and participants in order to improve their conduct and implementation.

1.3 Research methodologies

The research strategy for this thesis used methods combining information science and information management; systematic review methodologies, including two-stage review using descriptive mapping and qualitative synthesis; and qualitative research using semi-structured interviews and focus groups, and thematic analysis based on modified grounded theory.

1.4 Research objectives

The research objectives of this thesis were to:

1) Explore the background and context of internet-based randomised controlled clinical trials.
2) Establish the extent and nature of internet-based clinical trials by creating a database of reports to establish:
    a) How many randomised controlled trials in health and well-being research have used internet-based technologies as part of the trial process.
    b) At what stages of the trial process have internet-based technologies been used and how might these be characterised.

c) How the use of internet-based technologies in randomised controlled trials has developed over time.

3) Identify and explore the methodological, ethical, technological or experience-based issues relating to internet-based randomised controlled clinical trials, by:
   a) Producing a descriptive map of the landscape and coverage of identified studies, to establish the size of the knowledge base, and relevant themes.
   b) Identifying findings for further synthesis and to determine an appropriate methodology for reviewing these systematically.
   c) Producing a synthesis of the evidence base on the views, experiences and expectations of participants and researchers about taking part in internet-based clinical trials, and determine how might these impact on trial design and conduct.
4) Conduct a primary research study, determined by the findings of the systematic review, to explore the attitudes and experiences of people involved in internet-based clinical trials, including patients and the public, study participants, and researchers, to help improve the design, recruitment, conduct and relevance of internet-based health research.
5) Create a summary of findings to inform a framework for shared learning and guidance for researchers, patient and public representatives and the wider research community.

1.5 Structure of thesis

1.5.1 Chapter 2. Internet-based clinical trials and the research environment

Chapter 2 outlines the background to the development of internet-based clinical trials in the context of the technical, methodological and social changes that technology has had on health care and information generally, and for health research. The potential benefits, but also technical and methodological issues and challenges that surround it are discussed, along with perspectives from the movement to improve patient and public involvement in research. The chapter considers the results of an exercise to harvest uncertainties in the field of internet-based trials, and sets out the rationale for the research.

1.5.2 Chapter 3: Creating a database of internet-based clinical trials: a descriptive analysis

Chapter 3 describes the creation of a database which set out to determine the characteristics of randomised controlled clinical trials using the internet as a primary tool. The process aimed to establish the relevant concepts and size of the literature base through an analysis of the reports of published trials in a broad sample of bibliographic databases. In addition to gaining a better understanding of where the internet has been used in trials, this forms a baseline from which to begin to identify existing methodological and qualitative research in this area.

1.5.3 Chapter 4. Internet-based randomized controlled trials: a systematic descriptive map of methodological issues and perspectives.

Chapter 4 reports on the first stage of a two-stage systematic review, which created a descriptive map to establish the size and nature of the published evidence base about internet-based clinical trials, from a methodological or qualitative research perspective. The results of the mapping exercise provide the basis for refining the topic and scope for the second stage of the review.

1.5.4 Chapter 5. Factors influencing patient and public experience in internet-based randomised controlled trials: a qualitative evidence synthesis

Chapter 5 reports on the second part of the two-stage systematic review on the methods and conduct of internet-based trials, using qualitative methods to explore and analyse the views, attitudes and experiences of participants and the public in relation to taking part in internet-based clinical trials.

1.5.5 Chapter 6. Understanding participant experience in internet-based trials.

Chapter 6 reports on the results of a primary qualitative study to explore the views, attitudes and experiences of people involved with internet-based clinical trials, including patients and the public, study participants, and researchers. The study used a modified grounded theory approach, including thematic analysis with constant comparison, to help inform future research practice.

1.5.6 Chapter 7. Discussion and conclusion

Chapter 7 summarises the thesis findings, and discusses methodological strengths and weaknesses. A critique of the research is undertaken, and findings combined to inform a framework for shared learning for researchers, and guidance to inform those involved in the development of internet-based clinical trials in the future.

2 Internet-based clinical trials and the wider research environment

Features of this chapter are published in the following peer-reviewed journal: Brice A, Price A, Burls A. Creating a database of internet-based clinical trials to support a public-led research programme: A descriptive analysis. Digital Health. 2015;1.

2.1 Background

The social, technological and environmental changes that have taken place in the last few decades have implications for the way health care research is conducted. An increase in the use of internet and mobile technologies as a channel for health-related information and advice has led to the development of computer-supported decision aids [1-3] and other self-management initiatives [4, 5], in tandem with the informal explosion of social media applications [6]; through forums and discussion groups [7], and communication activities designed to promote behaviour change [8]. Measures to improve the health of citizens by enabling them to make better informed decisions about their health and well-being have been supported by national public health initiatives, media campaigns, the development of patient education resources, and tools to support shared decision making. Pew Internet research in 2012 showed that 59% of adults searched online to find health information [9], and in the UK government policies to tackle issues such as smoking cessation and obesity, self-management of long-term conditions, and improvements in mental health have been implemented through national digital initiatives such as Change4Life [10] and NHS Choices [11].

2.2 The rise of internet technologies in health

Internet technologies may provide an efficient and cost-effective mechanism for the delivery of good quality health information, public health focused interventions, and health and social care transactions. The rapid rise in the use of smart phones, tablets and an increase in the accessibility of mobile internet technologies has led to the promotion of a UK Digital Strategy, and a “digital first public health” strategy in England [12, 13], which has the stated aim of making all public facing transactions in health and social care digital by default. However, there are concerns about a lack of research into the impact of digital technologies in terms of harms [14, 15]; on issues relating to digital skills [16]; self-diagnosis [17]; and on health inequalities [18-20]. Mobile technologies may provide an opportunity to support community engagement [21] but, although systematic reviews report that community engagement initiatives can impact positively on policy and practice, there is a lack of strong evidence on whether there is a beneficial effect on health inequalities, comparative effectiveness between models, or on cost-effectiveness [22]. More high-quality syntheses or studies are needed to inform policy and practice about whether the increasing use of internet-based technologies has the potential to improve health equity.

The ability to disseminate and collect information using Web 2.0 and mobile technologies has impacted on the relationship between health care providers and consumers, most notably in information provision, but the impact of the use of these technologies in the relationship between health researchers and research participants is less well established. These changes are also global, and challenge the traditional environment of research systems, particularly in relation to data collection and accuracy.

2.3 Randomised Controlled Trials (RCTs)

Randomised controlled trials (RCTs) are the methodology of choice for testing the effects of interventions because they minimise bias, confounding, and the play of chance. Despite being the accepted methodology, there are known limitations and problems associated with their conduct, including failure to recruit sufficient sample sizes, the costs associated with running large trials, problems in follow-up, and the failure to address health inequalities [23-26]. For example, in traditional clinical trials, where recruitment and assessment is mediated by clinicians, certain questions have been difficult to investigate because the sample sizes required are unfeasibly large [27], and clinicians often overestimate the speed of recruitment. Moreover, researchers may have tended to be conservative in their estimates of the sample sizes required in their studies, in order to reduce the cost and burden of running a trial, and to increase their chances of obtaining funding [24]. This has led to many trials producing inconclusive results, and can be particularly problematic in terms of inherent problems in generating good quality evidence in public health, where very large studies are required, and that also tend to involve complex interventions. Representativeness can be difficult to achieve, with trial participants often recruited through their clinicians because they are already attending or receiving care in some way.

Follow-up of participants using professionally-mediated methods is expensive and time consuming, tending to lead to limited follow-up periods, which in turn lead to the measurement of intermediate and surrogate outcomes, with the potential for misleading results. All of these factors may impact on the

ability to provide answers to the most important questions for patients, the public and clinicians.

Another problem with current research is the lack of transparency, particularly around research undertaken by commercial organisations [28]. Protocols are often not disclosed and results selectively reported. This lack of transparency undermines the confidence placed in reported findings [29-32] as well as creating a potential barrier to the improved public understanding of science, and damaging efforts to involve patients and the public in trial design and conduct [33]. There is empirical evidence of bias resulting from the selective publication of results and the suppression of information about adverse events and harms [34], and this lack of transparency therefore undermines the confidence placed in reported findings [29, 35, 36]. These concerns have led to a number of initiatives to improve the quality of research evidence through synthesis in systematic reviews, better reporting standards [37-39] and a commitment to make patients aware of research, including the inclusion of a commitment in the NHS Constitution in England, which states that,

> *'the NHS will do all it can to ensure that patients, from every part of England, are made aware of research that is of particular relevance to them'.[40]*

However, the failure to register and report all clinical trials remains a matter of serious concern, [41] and has led to initiatives such as the AllTrials Campaign [42]. Even where investigation of the current challenges of the RCT as a method are heavily scrutinised, the conclusion is that rather than being obsolete, they require constant development of the research 'ecosystem' in the light of technological developments such as machine learning and big data [43].

2.4 The potential of the internet-based RCT

Online trials offer a potential solution to some of the issues raised above, and could provide increased benefits to researchers, patients and society, such as: reducing the cost of studies; reducing the marginal cost of recruiting additional participants, enabling larger sample sizes and reducing random error; improving the representativeness of trials by enabling the involvement of participants who tend to be neglected by current research methods; improving recruitment to trials; improving stakeholder involvement in trials; testing cheaper treatments; permitting easier long-term follow up of participants; allowing novel questions to be addressed that would not have been logistically possible to test in traditional trials; and, improved dissemination of results. Benefits could include:

2.4.1 Enabling large, pragmatic trials

It has been suggested that using internet based technologies within the research process would particularly enable more large, pragmatic clinical trials to be undertaken, [44] for example focusing on patient self-reported health outcomes. These could also allow indefinite long-term follow up, which could in turn address a wider range of health and lifestyle topics.

2.4.2 Self-selection by participants.

The initial set-up costs for an internet trial could be more expensive than traditional trials because the instruments and interface will need to be developed and piloted extensively beforehand. However, because fewer researchers or health professionals are involved in recruitment or measuring outcomes, the marginal cost of recruiting additional patients may be minimal in internet trials thereby permitting very large trials to be run and recruitment to carry on indefinitely until sufficient strength is achieved.

2.4.3 Increased involvement

Harnessing internet technologies, particularly mass, personalised communication tools could help increase, and improve patient and public involvement, at all stages of the research process. The International Network for Knowledge on Well-being (ThinkWell) aims to promote the use of new technologies in researching health issues that affect the day-to-day decisions of individuals, and to take engagement one step further to focus on 'involving the public in the prioritisation, design and conduct of research'. ThinkWell suggests that 'engaging directly with the public when conducting research' should become the norm, with researchers exploiting technology to do this, in the way it has been used in health information provision. Internet technologies could be used to engage and involve patients and the public in the prioritisation, design and conduct of research, as well as in peer review [45]. In addition to helping ensure that research questions become more relevant to a substantial proportion of the population, there may be benefits in terms of ensuring a larger pool of eligible trial participants.

2.4.4 Openness, transparency and inclusivity

Informal discussions the author held with health researchers suggested that using internet technologies could increase the potential for more open and transparent processes in both the conduct of research, in reporting and dissemination, and that using the internet and mass media methods to access participants could result in a reduction of the geographical and service provision limitations to recruitment. This could help address issues of equity, an important issue in health research as well as practice, and reaching wider, more diverse

populations has been suggested as a benefit of internet-based research, for example in using Twitter for recruitment [46]

In summary, the large number of potential participants now using internet technologies, the potential for more widespread awareness of, and access to, information about trials, self-selection for participation, and lower marginal costs for each additional patient recruited are seen as ways of improving trial success, either by reducing the need to limit sample sizes or length of follow up, and increasing relevance of clinical outcomes that could be assessed.

2.5 Current practice in internet-based RCTs

While a growing interest in the use of internet technologies within clinical trials has been identified from an early stage in the development of the medium [47, 48] there is variety in the aspect and degree to which these tools are employed, and at which stage of the trial process. Scoping searches revealed that the most common use in reports of clinical trials was in the delivery of the intervention or comparison, such as in studies investigating substance misuse [49, 50]; smoking cessation [51]; weight loss [52]; and in the use of cognitive-behavioural therapies [53]. The growth of this type of trial is reflected through an increasing number of published systematic reviews of these types of studies [54-57], and also in the appearance of national guidance for clinicians [58].

Online trials may be relatively easy to set up but bring potential concerns such as poor quality assurance; ease of recruitment leading to large attrition rates and uninterpretable results; contamination between arms of the trial due to social media or communication between participants; the technological challenges of doing research online leading to failed trials; and, exposure to hacking and potential breaches of participant confidentiality. Early in the

development of the online trial Murray [59] suggested that they share similar problems with traditional trials, such as in recruitment and retention, randomisation, data quality and fidelity, but also have an additional set of challenges related to their technological characteristics, including ‘spamming’ and ‘cybersquatting’.

As the adoption of internet-based technologies in clinical trials has increased, this has led to inconsistent approaches to reporting and indexing, which in turn have caused problems in the retrieval of relevant studies, and in the assessment of quality and reliability. There are currently no agreed standards for the description or indexing of these concepts in individual studies, or in systematic reviews. In a rapidly changing technical environment, the problems associated with the ability to replicate interventions in reports of clinical trials [39] may be an even greater challenge [60]. It is important, therefore, that this new technology is robustly evaluated to identify the advantages and disadvantages of online clinical trials in practice and to learn what factors can help maximise benefits and minimise risks.

2.6 Patient and Public Involvement

In addition to the increased awareness of the need to promote better informed and shared decision making, there has also been an acknowledgement of the need for a corresponding increase in patient and public involvement (PPI) in policy making, planning and service delivery [61-63], health and social care guidance [64], patient safety [65], and importantly, in the research process itself [66]. Lack of meaningful stakeholder involvement has the potential to add to the waste identified in the research process by Chalmers and Glasziou [37], and

represents a lost opportunity to harness new technologies for socially-led research [67].

Without full involvement at all stages of the research process, Chalmers and others hold that much of the research that is conducted does not answer the questions that are most important to patients and the public [68-70] and that a more participative research process could lead to better quality and more relevant research results. A range of policies and programmes have been implemented with the aim of improving PPI in health-related research, although there are concerns that this has been largely driven by a researcher, or research funder-led agenda [70]. Evans et al suggest that a significant amount health-related research is commissioned by policy makers and designed primarily by researchers, and often only involves patients and future participants after its initiation [71], although some national agencies such as the National Institute for Health Research (NIHR) in England are aiming to address this problem. Failure to involve potential participants in the prioritisation and design of research may partially explain why trials fail to recruit sufficient numbers or encounter a lack of co-operation from those who enrol patients at the point of care. The use of social networking sites to increase public involvement in health research and practice has been increasing, and guidance has been published to aid researchers [72], however further exploration of the full potential is required.

Although a wide body of knowledge has been published concerning patient and public involvement initiatives and methods, little comparative research on particular methods is available, and there are concerns that some approaches are ‘tokenistic’ [73], underestimate costs [74], or were a low priority in outline planning [75]. Some mechanisms are perceived as being successful, such as

early involvement in the research planning process [76], but it is not clear whether this is transferable to research that uses internet-based technologies. Despite considerable interest from enthusiastic individuals, and action from bodies such as INVOLVE working with NIHR, the level of awareness and understanding within the research community, information community and other public bodies concerning the characteristics of patient-led research, and in particular the opportunities presented by internet applications in this area, could be improved. Important research undertaken to explore participant experience in taking part in clinical research, such as that provided by Healthtalk [77] may need to be further developed to address the new technological environment [78, 79].

2.7 Initiatives in internet-based trial development

Interest in the wider impact of internet technologies within clinical trials is growing, and a number of specific initiatives have been launched to focus attention on the issues and the future development of using technologies in this way. The ThinkWell programme suggests that conducting pragmatic randomised controlled trials via the internet would allow researchers to address research questions outside the narrower focus on diseases and conditions, and their diagnosis and management, and look at more complex interventions that affect health and life expectancy which operate outside the health care system. It is suggested that many of these topics, particularly where patients can address a specific health behaviour, e.g. exercise, smoking, diet, would translate very effectively to an internet-based research environment. The focus on interventions that people can choose to do for themselves, without the involvement of a health care professional (such as exclusion diets, online psychological therapies, lifestyle choices, dietary supplements etc.) may also support this aim.

2.8 ThinkWell uncertainties project

ThinkWell members decided to take a systematic approach to identifying what questions people in the network had about conducting internet-based RCTs, based on the methods developed by the UK DUETs programme [80]. UK DUETs was established in 2007 in order to identify, collate and publish uncertainties about the effects of treatments. This involves identifying important gaps in knowledge about, and subsequent prioritisation of research according to:

- the self-identified concerns and values of the public
- the potential for health gain
- the feasibility of the required research design
- the probability of the research being able to clarify uncertainty.

A project to adapt the UK DUETs methodology to investigate the most important questions in relation to the use of internet-based technologies in clinical trials was piloted, and initial analysis of the results provided a number of important uncertainties [81]. These included methodological topics such as data security; data collection; self-report issues; and technological solutions, but also raised questions concerning wider ethical issues, and questions concerning the views, attitudes and experiences of researchers and participants *(*Table 2.1*).*

Secondary analysis of the data from the ThinkWell uncertainties project was undertaken to identify key areas for further investigation for this thesis. As previously mentioned, internet-based trials are likely to share a range of methodological and ethical issues with those carried out using more traditional clinical trial methods, but may also engender a new set of concerns and challenges.

Raw question	Key concepts	Formulated question
"validity and quality assurance of the data collection (via the internet) that would need to be addressed"	validity; quality assurance; data collection; internet;	What methods can be used to assure the validity of research data collected via the internet?
"the patient base for the internet trials will be 'geeks only' and that the selection will be biased towards 'net users' only"	research participants; selection; recruitment;	Are patients recruited to internet trials representative of the general population? What methods can be used to improve recruitment to internet based clinical trials?
"ensuring confidentiality in data storage and communication"	data storage; confidentiality; internet; clinical trials	What methods can be used to assure confidentiality of communication and data storage in internet based clinical trials?
"dealing with selection bias - working with social strata and young people (who see health very differently"	selection bias; social status; young people; sampling; internet based clinical trials	How can selection bias be reduced in internet based clinical trials?
"need to develop methods for priority setting and voting"	priority setting; voting; research questions; public involvement in research	Are there validated methods for priority setting and voting as a means to improve public-led research?
"perceptions of what constitutes a research question"	research questions; perceptions; attitudes	How do people perceive the concept of the 'research question'?
"validity issues; self-declaration, selection bias"	validity; quality assurance; internet; self-declaration; selection bias	What do we know about validity issues in internet based research, in particular self-declaration and selection bias?
"cultural/organisational differences between countries e.g. trial regulations; language issues"	clinical trials; cultural issues; language; flagging; trial regulations	What cultural issues may impact on internet based clinical trials?
"Human Tissue Act and data/tissue storage - who has responsibility"	Human Tissue Act; data storage; tissue storage	What issues are there for the storage of data and tissue in internet based clinical trials?
"loss to follow up - when does follow up become harassment"	follow up; loss to follow up; acceptability	How acceptable is follow up to research participants, and what issues might this have for internet based clinical trials?
"incentives to take part - are these bribes?"	research participants; selection; recruitment; incentives	What are the ethical issues concerning incentives to take part in clinical trials?
"what can be measured easily (i.e. by patient)"	self-measurement; self-measurement tools; data collection	How effective are self-measurement tools in internet based clinical trials? How easy to use/acceptable are self-measurement tools for participants in internet-based clinical trials?

Table 2.1 ThinkWell uncertainties and questions

The analysis identified a need to explore the ethical and experience-based factors relating to internet trials with researchers and participants in order to determine how this may impact on future conduct of good quality research, improve patient experience, and patient and public involvement, and support parallel initiatives to promote public-led research, such as the Cambridge Patient Led Research Hub [82]. In keeping with the ethos of UK Duets, a key element of this thesis is to identify existing methodological research, to explore participant experiences to ensure these are better understood, and to enable researcher and participant knowledge to be shared. This ensures that existing knowledge informs the generation of new knowledge, and that these are combined to inform practice.

2.9 Rationale for the research

There are a number of important methodological and ethical issues that arise from the use of mass media and the internet as fundamental research tools, including the need to explore researcher and participant experiences of these new methods.

Results from the ThinkWell uncertainties project showed that it was unclear how many clinical trials had used internet-based technologies, and to what extent this involved use at specific stages or elements of the trial. There was also uncertainty as to which trial methods are most effective, or how this may impact on participant experience. It was hypothesised that problems in identifying and learning from existing methodological research could be the result of a number of factors, including difficulties in identifying and retrieving relevant studies, lack of

specific methods to assess their quality, and the need to search through an increasing range of knowledge sources to determine what is already known. Following presentation and discussion of the results of the uncertainties project, four key questions emerged which were:

- How many randomized controlled trials have used internet-based technologies as part of their trial processes?
- In what stages of the trial process have internet-based technologies been used and how might these be characterised?
- How has the use of internet-based technologies in randomized controlled trials developed?
- What is known about the methods and conduct of internet-based randomized controlled trials, and how this might impact on participant experiences

This thesis approached the research question from an information science and qualitative research perspective, using systematic methods to identify, map and synthesise what is known. The rationale for the thesis was formulated to address the key questions, but also to focus the qualitative synthesis and exploration of the impact of trial technologies on participants, with a view to helping researchers better understand these factors, and to help them plan and conduct better trials. The first phase of the research identified reports of trials that had used internet technologies, and mapped these across a number of key facets, including the stage of the trial, location, study topic and intervention, and date of conduct, to form a baseline understanding of the nature of the internet-based clinical trial environment.

2.10 Chapter Summary

- The use of internet technologies has increased exponentially over the last two decades, particularly in relation to internet-enabled mobile devices.
- The internet is increasingly used as the main channel for providing health information, with an increasing focus on health improvement applications.
- Use of the internet in research has also increased, and it has been suggested that using the internet in clinical trials could solve some of the latent problems in trial design and conduct, including better recruitment and the delivery of interventions at lower cost.
- There is little evidence of increased public-led research or involvement of patients and the public in the planning and design of trials, although work to harvest important questions from patients and carers has been undertaken.
- It is not clear what the potential impact of internet-based trials might be for patient and public involvement, or how patient and participant experiences might be affected.
- The development of internet-based clinical trials has increased but it is unclear how many have taken place, what has been learned about the impact on trial planning and conduct, or whether the expectations of researchers or participants are being met.
- A project to harvest and analyse researcher uncertainties about internet-based clinical trials identified a number of important questions, which would benefit from further investigation, including exploring the methodological issues and experiences of all involved.

3 Creating a database of internet-based clinical trials: a descriptive analysis

Features of this chapter are published in the following peer-reviewed journal:

Brice A, Price A, Burls A. Creating a database of internet-based clinical trials to support a public-led research programme: A descriptive analysis. Digital Health. 2015;1.

3.1 Overview of Chapter

This chapter describes the creation of a database of internet-based RCTs. The process aimed to identify reports of published internet-based RCTs in a broad sample of bibliographic databases, and to analyse and descriptively code the results. In addition to gaining a better understanding of the internet research landscape, this provides a sampling frame from which to identify potential themes and priorities for further methodological research in this area.

3.2 Background

Much of the potential benefit and impact of using new technologies in clinical research has yet to be fully understood. Methodological, ethical and qualitative research undertaken to explore the conduct of traditional trials may be relevant to internet-based trials, but this requires further exploration. The key questions or uncertainties identified in the ThinkWell project [81] included issues such as data security, data collection, self-reporting, and technological development, but also raised broader questions concerning ethical issues and the experiences of those conducting, or taking part in, this type of study. For example, the benefits or barriers perceived by trial participants identified by Locock [83], which are complex and multi-factorial, may be similarly experienced in internet-based trials,

however, there may be specific or additional factors that it would be helpful for researchers and the public to be aware of, or to consider.

Scoping searches conducted in 2010 found no current standardised ontology or taxonomy which could be used to index reports of internet-based trials for easier retrieval, nor an existing analytical framework describing the current application of technologies in this context.

3.3 Aims

The aim of developing the Online Randomised Controlled trials of Health Interventions Database (ORCHID) as part of this thesis was to identify, classify, and analyse published reports of internet-based trials in health and well-being topics. The database would provide a baseline understanding of the internet-based clinical trial environment, including trial topics and types of interventions, and identify emerging trends. The study aimed to address the following questions:

- How many randomised controlled trials in health and well-being research have used internet-based technologies as part of the trial process?
- In what stages of the trial process have internet-based technologies been used and how might these be characterised?
- How has the use of internet-based technologies in randomised controlled trials developed over time?

3.4 Definitions and scope

One of the major impediments in identifying internet-based clinical trials is the lack of an established vocabulary to describe them. This has led to the use of a wide range of terms for trial reporting, and to poor quality indexing in

bibliographical databases. For the purposes of this study, the following definitions were used for the key concepts:

3.4.1 Internet-based

The “internet” concept is defined in the Oxford English Dictionary as “a global computer network providing a variety of information and communication facilities, consisting of interconnected networks using standardized communication protocols”. The term ‘internet-based’ was therefore used predominantly to refer to applications which use the world-wide web as a primary means of communication or data entry, including the use of mobile technologies where these are used in combination with the internet. Throughout this thesis ‘online’ is also used as a synonym for ‘internet-based’.

3.4.2 Randomised Controlled Trials

To be considered for inclusion, reports of studies needed to include reference to a randomisation process in the abstract; to be indexed with a relevant publication type; or to have ‘randomised controlled trial’ included in a declarative title. No assessment of trial quality was undertaken.

3.4.3 Health and Wellbeing

The concept of ‘health’ is subject to a range of different interpretations and definitions, therefore the potential range and scope of the topic was extremely large. Inclusion was therefore limited to reports of trials of interventions in diagnosable illnesses or disorders, including non-communicable diseases and conditions, as contained in the Medical Subject Headings (MeSH) used in the MEDLINE database. ICD10 categories were used to provide additional guidance for the inclusion or exclusion of borderline topics, for example in the area of addiction. There is even less consensus concerning how the term ‘well-being’

should be defined, particularly in the relationship between this concept and that of 'mental health'. The recent government strategy for mental health "No health without mental health; a cross–government mental health outcomes strategy for people of all ages, 2011" [84] provided the following definition,

> *'Well-being is a positive state of mind and body, feeling safe and able to cope, with a sense of connection with people, communities and the wider environment'*

In order to help manage the scope, studies concerned with 'well-being', as well as those dealing with social determining factors such as housing, transport and planning; environmental health; issues around ageing; domestic violence; or accidental injury were excluded unless they were being managed in a commissioned health care, or public health, setting.

3.4.4 Trial participants

Trials were included if the participants were patients or members of the public. Trials dealing exclusively with health care professionals or students were not included in the scope.

3.5 Methods

3.5.1 Identifying studies

A broad and comprehensive search strategy was developed, and a wide range of sources used to retrieve reports of internet-based RCTs. Given the range of databases searched, and their different functionalities and tools, the search strategy was adapted for each source. For health-related databases the 'internet' concepts were combined with a validated methodological filter for RCTs. For non-health related databases, the 'internet' concepts were combined with health or well-being terms, as well as any relevant RCT concepts or methodological

filters if available. The search sources and strategies are provided in Appendix 3A.

3.5.2 Selecting search terms

Search terms were derived from MeSH, EMBASE, and other relevant taxonomies; from core articles identified from scoping searches, using text word analysis; and through consulting experts in the field. The potential thesaurus and free-text terms were tested using a variety of combinations (see Appendix 3B). The terms used to describe the use of technologies, such as 'internet', 'web' or 'online', are fuzzy and widely used concepts. As the use of technology in trials has increased, the terms have become almost ubiquitously included in study reports, for example, in statements such as "we searched the web for xx". During testing of potential terms some searches retrieved very large numbers of irrelevant results, for example, using "e-" as a prefix to terms such as "e-research" retrieves examples such as "Vitamin E". Where possible controlled vocabularies were preferred, such as the MeSH term "internet" which was created in 1999, with the previous indexing term of "computer communication networks" becoming a broader term. Subheadings of controlled terms were included to increase sensitivity.

3.5.3 Search filters

Given the nature of the search, which aimed to identify all RCTs that had used internet technologies, search filters were used where appropriate to increase sensitivity. Methodological search filters are pre-tested literature search strategies that provide a more effective way of refining a search to find evidence appropriate to the type of question under investigation. They help to retrieve records of research that have used a specific study design, such as systematic

reviews or RCTs. Search filters may be designed to maximise sensitivity (or recall) or to maximise precision (and reduce the number of irrelevant records that need to be assessed for relevance). Relevant search filters for RCTs were identified through the InterTASC Information Specialists' Sub-Group Search Filter Resource [85]. This is a collaborative enterprise which helps identify, assess and test methodological search filters designed to retrieve research by study design. The site provides access to published and unpublished search filters, information and guidance on how to appraise filters, and notifications of study design filters in development. An analysis of the available, validated filters for use in MEDLINE, EMBASE, PsycINFO and CINAHL was undertaken, along with test searches to estimate likely outcomes [86-88].

Due to the very broad nature of the other search concepts, test searches using the most sensitive filters indicated the potential retrieval of a very large number of results. Therefore, although the preference was to use a highly sensitive search strategy, a pragmatic approach was taken to achieve an optimal balance between sensitivity and precision. In the smaller databases, single term or less sensitive searches were undertaken due to the lack of validated filters. The Literatura Latino Americana em Ciencias de Saude (LILACS) database was searched in order to avoid a bias towards research reported in English-language sources. This proved problematic, with difficulties experienced in establishing key terms and relevant filters due to language and interpretation problems. Colleagues from the Spanish CASP network (CASPe) were consulted to advise on systematic retrieval from this source. This work led to a collaboration in 2011 on a text-mining validation study, where the ORCHID searches were used as a reference standard to compare with text-mining software [89]. The use of text-

mining approaches has since gained popularity as a tool for information retrieval and systematic reviews [90].

3.5.4 Search Limits

Date limits were difficult to establish as it was not clear when internet tools were first available for use in clinical trials. The search was therefore conducted with no date limits. RCTs in health research are international in scope, and therefore no language limits were applied. However, research reports in languages other than English were only included if an English abstract was available.

3.5.5 Selection of studies

Search results were downloaded to the EndNote bibliographical reference management software, and then transferred to the SENTE software package for screening and indexing. SENTE includes functionality for developing colour-coded 'hot words' to aid screening, and for creating coding frameworks and tagging schemes (see Appendix 3C). Study abstracts were screened against inclusion and exclusion criteria. A second round of screening was carried out, at which stage full reports of trials were retrieved where possible for those trials where a decision could not be made from the abstract alone. Inclusion and exclusion criteria are presented in Table 3.1.

One of the intentions of the database was to identify how the number of trials had increased over time, and also at which stage of the trial process internet technologies have been used. Potential uses were hypothesised as gaining informed consent; self-enrolment; the delivery of the intervention; data collection and analysis. Given that the use of internet tools for trial registration, randomisation, publicity and promotion, or dissemination had become standard

practice in most clinical trials, reports of studies where the only reference to the use of the internet is related to these trial stages were excluded.

All studies that met the following criteria were included: • RCTs using internet-based technologies in the trial process • Studies using mobile devices in which internet-based technologies are used • Studies investigating health or public health research topics • Studies including clinical, educational or behavioural interventions of health and well-being topics • Studies involving patients or members of the public The following studies were excluded: • Studies using mobile telecommunications technologies exclusively, with no internet-based content • Studies investigating interventions in social care or educational settings, where the main topic of investigation was not health related, or where clinical interventions are not included in ICD10 • Studies where participants were health professionals or students

Table 3.1 Database inclusion and exclusion criteria

3.5.6 Iterative classification and labelling

The retrieved studies were indexed to record their core characteristics, including the conditions being investigated; the interventions being tested; and the country in which the trial was conducted. Source databases use a range of different controlled vocabularies, and given the additional lack of indexing consistency within databases, a pragmatic, hybrid system of coding was developed. This involved a two-stage process, where the condition and intervention indexing terms were extracted from the relevant field in each study report, using the classification label provided by the source database, such as MeSH. This was then mapped against the existing set of codes, and if a relevant code was

already in the list, this was applied. If no relevant code was available, a new code was created using the terminology from the study abstract in question. When the indexing of all the included studies was completed, the results were scanned for consistency and re-labelling where required.

3.6 Results

The initial database searches were run in January 2011, with update searches completed in September 2013, and January 2015. The combined searches identified 21,813 results. Following first and second screening, 2024 studies were included. Each study report was analysed and coded to the following domains.

3.6.1 Date of publication

The number of reports of internet-based RCTs retrieved and added to the database by year of publication increased as expected over time, with the majority published between 2007 and 2015 (Figure 3.1).

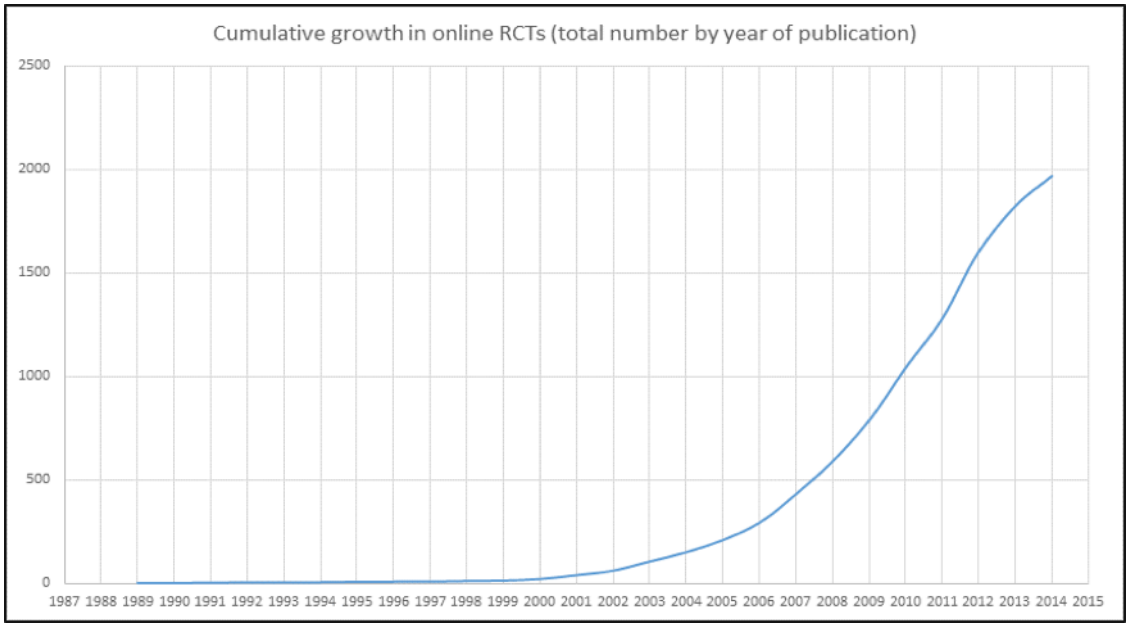

Figure 3.1 Date of publication

3.6.2 Geography

The largest number of trials reported as using internet technologies were conducted in the USA (944/46.6%), followed by The Netherlands (202/10%), Australia (196/9.7%), the United Kingdom (122/6%), Sweden (118/5.8%), Canada (80/4%), and Germany (76/3.8%). South Korea (27/1.3%) has the highest number of reported trials for other continents. The top 20 countries by number of trials is shown in Figure 3.2, and full results are provided in Appendix 3D. Between 2013 and 2015 the rate of increase in the number of reported trials dropped off. The relative percentage of trials conducted in the top twenty countries remained fairly stable and is shown in Figure 3.3.

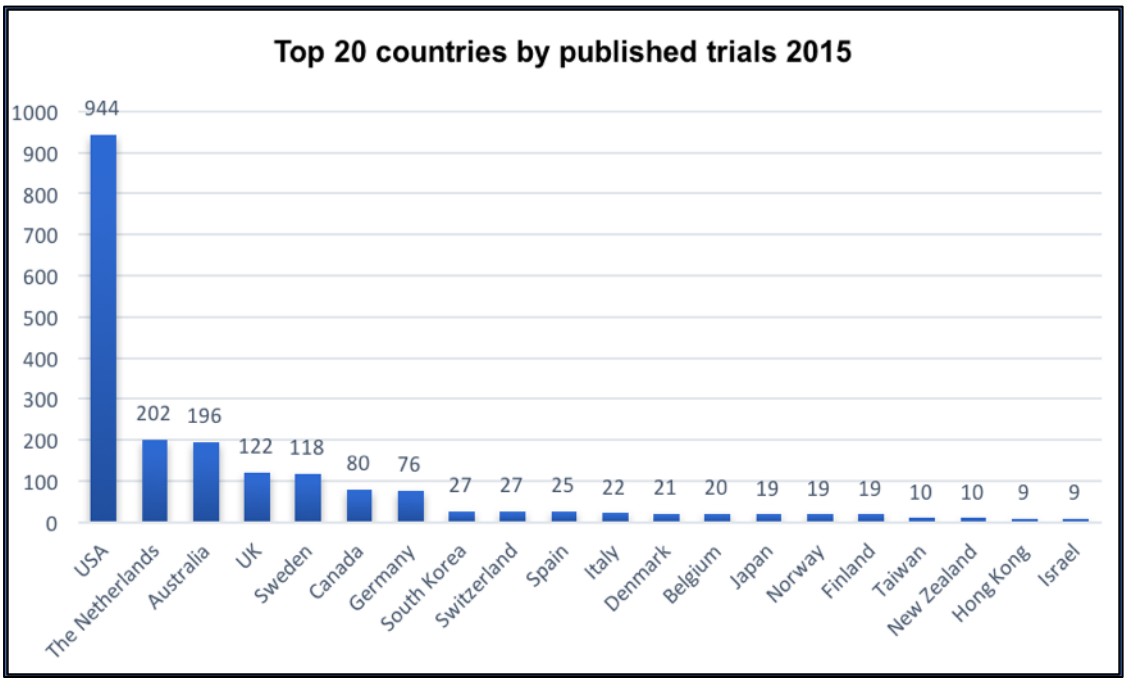

Figure 3.2 Top 20 countries by published trials

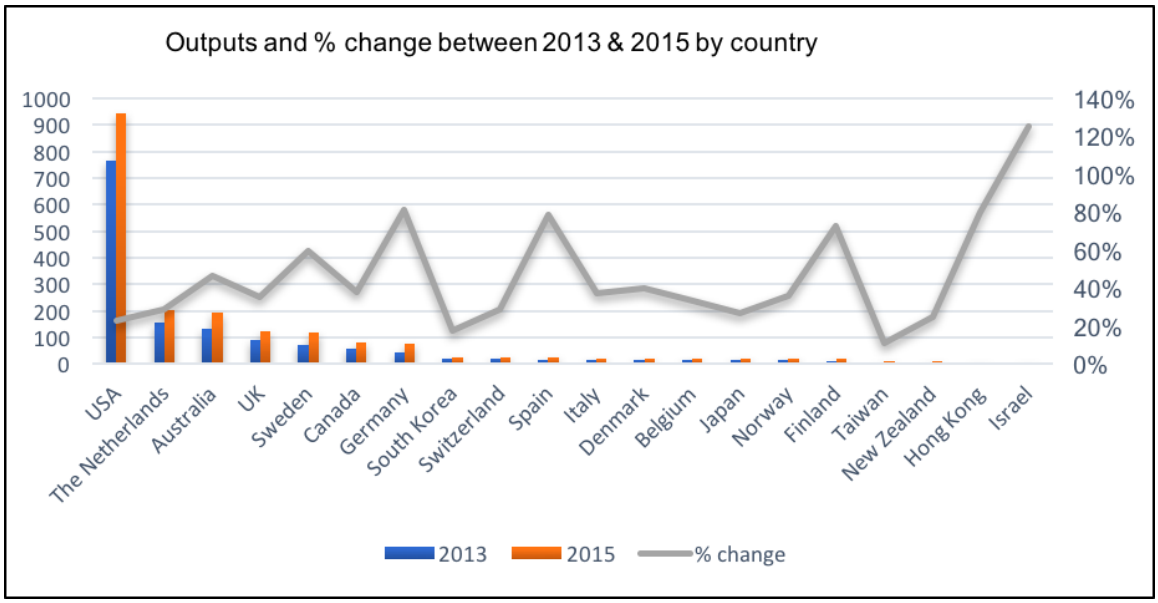

Figure 3.3 Change in Top 20 trials by country between 2013 - 2015

3.6.3 Topic

The topics most often reported were those involving interventions for non-communicable conditions such as obesity, smoking and substance abuse, depression, anxiety and phobias. The second largest group were for conditions where self-management is already a major feature of clinical care, for example in diabetes and cardiovascular conditions. Details of the highest ranked topics by major MeSH categories can be seen in Figure 3.4, and by specific condition in Figure 3.5. The full data set mapping of MeSH categories and conditions is in Appendix 3E.

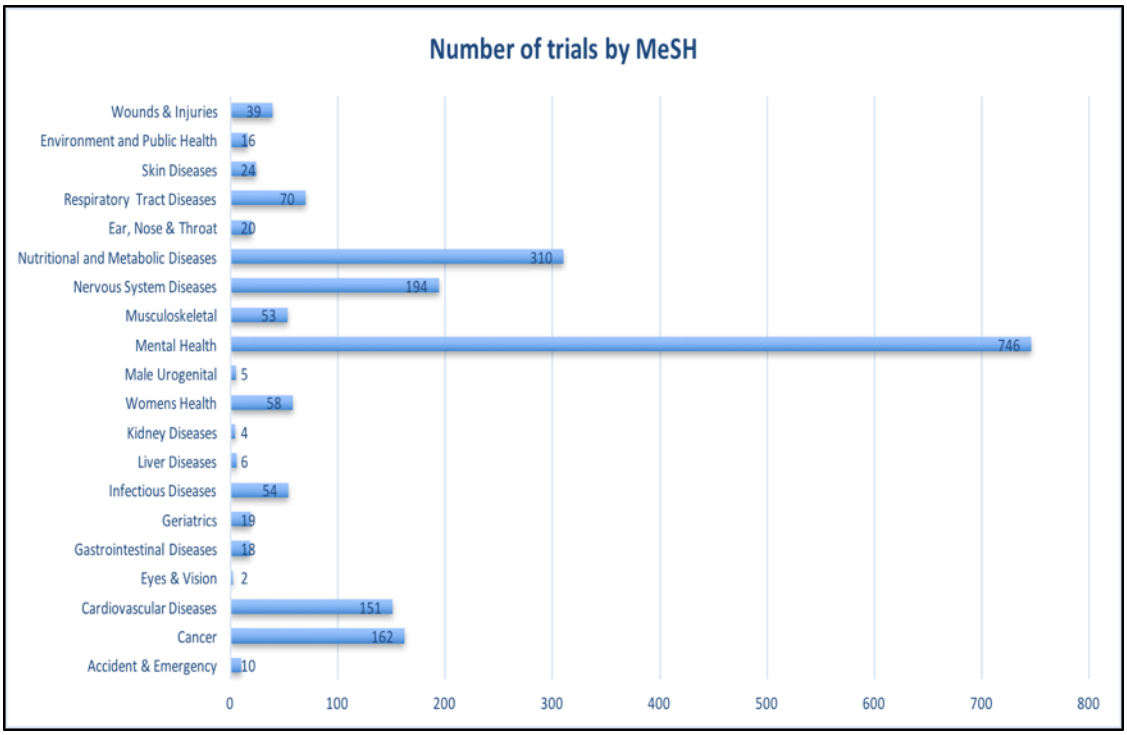

Figure 3.4 Highest ranked MeSH categories

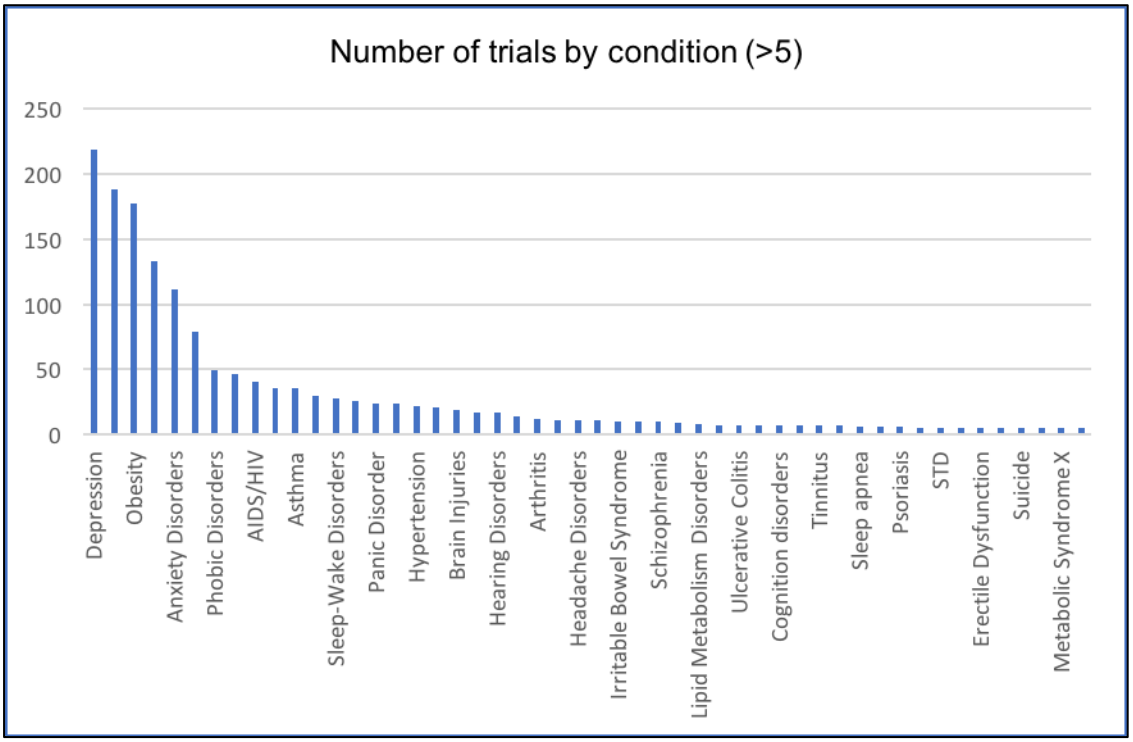

Figure 3.5 Number of trials by condition (>5)

3.6.4 Type of intervention

The highest numbers of concepts indexed for study interventions related closely to the nature of the conditions, for example, behaviour change therapies, such as Cognitive Behaviour Therapy for anxiety and depression; smoking cessation interventions, and interventions to increase physical activity. The ranked concepts are based on the most specific terms indexed by the source database. Full details of the types of intervention used can be found in Appendix 3F.

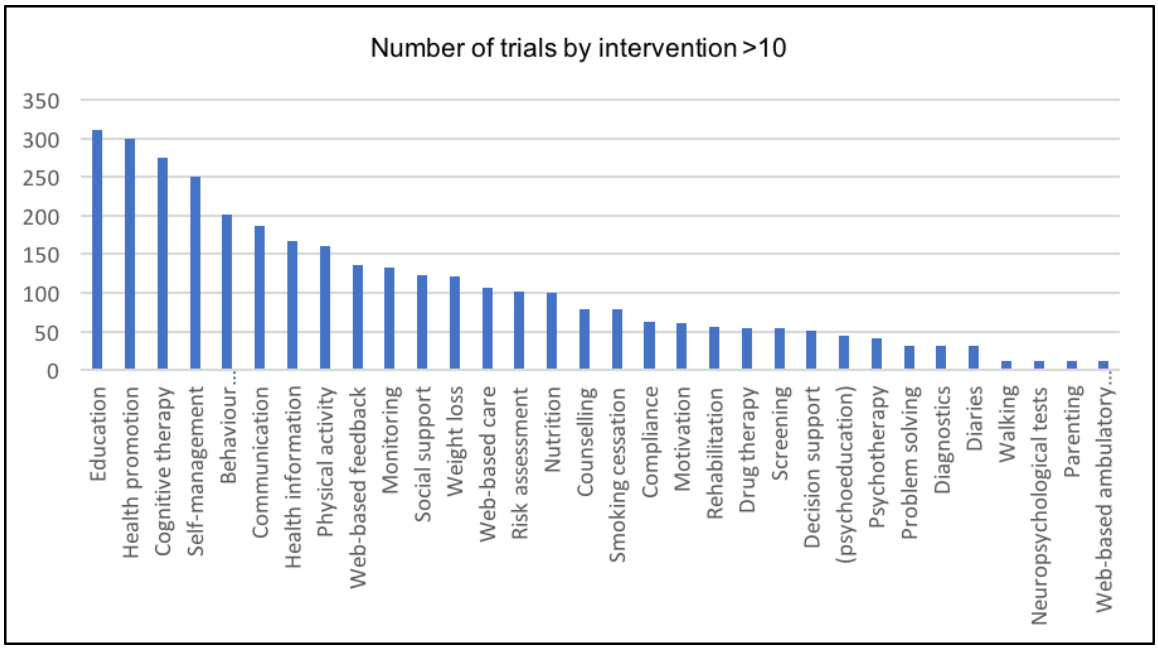

Figure 3.6 Type of intervention >10

3.7 Discussion

A number of key themes emerged from the analysis of the study reports included in ORCHID. These themes reflect the rapid growth of the use of internet technologies in clinical trials research, and raise issues which require further investigation.

3.7.1 Terminology

A number of different approaches to the description of terms were identified, including the development of taxonomies on behaviour change [91] regular updates of MeSH [92], the work of individual review groups or researchers, and organisations such as WHO [93], and the National Institute of Health and Care Excellence (NICE). Work is underway to improve the reporting of interventions [39] and this research on the identification of internet-based trials could feed into better co-ordination of approaches to taxonomies and labelling. Standardisation in indexing methodology could complement transparency in research and lead to more effective searching and reporting of internet-based clinical trials research.

3.7.2 Location of trials

It is clear from the analysis of the trial location mapping that a high percentage of internet-based trials were conducted in a small number of countries. This may reflect publication bias in the scientific literature, and in the selection of journals indexed in bibliographic databases. This was previously found in studies of country and language of publication, such as in MEDLINE where in a 60 year period the USA (22.2%) and United Kingdom (12.5%) produced most publications reporting randomised controlled trials [72]. Of 468,191 journal articles added to MEDLINE in 2000, 67.9% were initiated in the “Anglo” countries [94]. This is confirmed in some respects from the ORCHID data, although a trend was also observed where a small number of centres of excellence with expertise in specific types of internet-based clinical trials have developed, within specific countries. This may reflect the interest and publications of one research group or researcher, who publish multiple studies on either the same set of trials or

sequences of trials on similar interventions, and may skew the position of that country in the overall table.

Expertise in the conduct and evaluation of internet-based clinical trials has therefore developed in small pockets, and this learning could be usefully shared to benefit others. Improvements in the ability to recruit and retain trial participants for example could help improve clinical trials in a number of environments, including large-scale public health trials, and also potentially in the availability and conduct of research in low income countries. Currently research using these technologies tends to favour the diseases and conditions of higher income countries.

The issue of resource constraints must be considered as lower income countries may experience bandwidth limitations, limited access to the technology required for online trial development, or reduced access to the internet-enabled devices. Other considerations such as research capacity, governance, online and data security, and technological capacity also need to be in place to fully exploit internet-based trial potential. There is no evidence in the findings so far of partnerships or collaboration between researchers in high and low-income countries to promote knowledge transfer.

3.7.3 Type of topic and intervention

There is clearly a predominance of results in two main areas. The first of these relates to modifiable risk factors for preventable causes of death and illness that impact on public health priorities, such as tobacco; obesity and lack of physical activity; and alcohol and substance abuse. The second area relates to mental health conditions such as depressive disorders, anxiety and phobias. It is not surprising therefore, that the most common interventions in ORCHID relate to

treatment options for these conditions. This may be because these interventions transfer more easily to an internet-based mode of delivery, such as those for weight loss and smoking cessation programmes, talking therapies and physical activity interventions. What is not known is how much the nature of the technology may pre-dispose researchers to a particular choice of intervention, whether that is the prevalence of the technology, or their own preferences or interest. It was not possible to tell from these data whether the relevance or acceptability of specific interventions being tested through online environments was informed by patients and the public. As previously noted in Chapter 2, ensuring that research is based on known uncertainties and the most important questions for patients, carers and practitioners could help increase relevance and decrease waste. Whether this could help ensure that the technological options under consideration are driven by research need rather than by researcher preference is not clear.

3.7.4 Stage of trial

The majority of internet applications represented in ORCHID are in the delivery of the intervention. Six hundred and sixty-nine studies were using the internet for data collection, with 387 coded as self-reporting, and most of these were reported in behavioural trials. Sixty-four studies were indexed as reporting use of the internet for data analysis or follow-up. Very few of the studies identified use internet technologies in other stages of the trial process. One hundred and seventy-six studies were retrieved that reported methodological issues related to internet-based trials. These were not entered into the database, but were used to inform the systematic review reported in the next stage of the thesis. Further

work has been undertaken by ThinkWell researchers to mine the database for specific investigations into methods and trial conduct [95].

3.8 Limitations

The large number of results from the United States, United Kingdom and Australia, and therefore the predominance of English speaking, high-income countries may be due to publication bias in terms of reported studies, journal indexing and the choice of databases searched.

The development and piloting of search terms and phrases, with their potential number of combinations, proved to be a major challenge in balancing sensitivity with precision. Indexing in some non-medical databases is uncontrolled, with inadequate reporting of studies and unstructured abstracts leading to retrieval problems, and the need for excessive amounts of filtering and screening. Although comprehensive search strategies and filters were used, the changing nature of the terminology, in line with the pace of socio-technological change, required an exponential list of free-text search terms, in the absence of recognised controlled vocabularies and ontologies, which had to be pragmatically curtailed.

Given the need to retrieve as many relevant studies as possible, the search strategy needed to be highly sensitive, but when combined with the poorly controlled terms for the ‘internet’ concept, this led to extremely large numbers of results with very poor precision. Because of this, the range and scope of databases used was restricted, and made it difficult to determine the impact of not using validated filters.

Health and well-being is a very broad concept, and ICD10 categories were used as a pragmatic way of limiting the scope. This may have resulted in missed

trials. Similar limitations were experienced in the terms used for coding and indexing included studies. A literature search found a number of potential alternative systems for the coding of studies, particularly in the area of behaviour change interventions. Grimshaw [96] draws attention to four Cochrane Reviews that cover interactive health communication applications; interventions to enhance medication adherence; patient-practitioner contracts; and new methods of communication. Within the original cited reviews, specific elements of existing controlled terms, consistent with MeSH and other major taxonomies, are used in different combinations, including social support, decision support, and behaviour change support. Haynes et al [97] identify a range of interventions used within trials for medication adherence, including instruction, counselling, family interventions, and mentoring. Coding was based on the terms used by authors to report their studies, and on the indexing terms chosen by the host database. This approach, although providing consistency with the original decisions made by authors and database indexers, does not reflect consistency across all the included studies. Therefore, the results tables may include intervention headings and classifications that are not comparable, and contain multiple facets. No quality appraisal of individual studies was made, other than that of determining whether the study was an RCT by looking for reports of randomisation.

Location was categorized using the country where the trial intervention was carried out, based on the information contained in the bibliographical record abstract. For trials where the interventions were reported as operating in more than one country, both countries were indexed. If no location was reported in the abstract the affiliation of the first named author was used. Although a full examination of the full text of all reports would have provided a more reliable

analysis, this was not undertaken due to time constraints and was not considered to warrant the additional time and cost.

3.9 Conclusion

ORCHID has the potential to be a useful resource for researchers to mine data from the included studies, determine trends in this rapidly developing area, and to support the development of a knowledge base which any researcher or member of the public could use. Key learning points for the research community were noted if potentially of use, and the database has helped to identify practitioners and experts in the field. The study findings helped answer questions regarding the number, type, and location of a large number of the internet-based clinical trials that have been undertaken, but have also generated further questions relating to the wider questions relating to ethics, methodology, expectations and experience-based perspectives. The creation of ORCHID therefore provided a basis on which to inform the next stage of the research. This explored what is known about how trials are conducted through a methodological and qualitative systematic review, as the next stage in starting to learn from, and share this knowledge.

3.10 Chapter Summary

- ORCHID provides a baseline understanding of the online trial environment, determining how many trials have used internet-based technologies; how they have been used; and how use has developed over time.
- Online trials have grown rapidly in number, with 1992 internet-based trials included in the database to March 2015.
- Identifying internet-based RCTs is time consuming and complex due to poor reporting and indexing, and requires comprehensive searches with poor precision.
- The largest number of trials were conducted in the USA (46.6%), followed by The Netherlands (10%); Australia (9.7%); the United Kingdom (6%); Sweden (5.8%); Canada (4%); and Germany (3.8%). South Korea (1.3%) has the highest number of reported trials for other continents.
- There is a predominance of interventions addressing public health challenges including obesity (8.6%); smoking cessation (5.9%); alcohol abuse (7.7%); and physical activity (10.2%); in mental health issues such as depression (10.9%) and anxiety (5.6%); and in conditions where self-management (16.6%) or monitoring (8.1%) is a major feature of care.
- The internet is most commonly used in the intervention stage of an RCT.
- ORCHID provides a resource and sampling frame for other researchers, to mine, or add, data.
- The creation of ORCHID has provided a basis on which to explore further what is known about how trials are conducted through a methodological and qualitative systematic review, as a key stage in starting to learn from, and share this knowledge.

4 Internet-based RCTs: a systematic descriptive map of methodological and qualitative studies.

4.1 Overview of Chapter

This chapter reports the first stage of a two-stage systematic review, which created a descriptive map of published studies about the methodological, ethical and experience-based issues relating to the conduct of, or participation in, internet-based RCTs. The process builds on the set of methodological studies retrieved during the development of the ORCHID database described in the previous chapter, supplemented by additional searches, and uses thematic analysis to present the findings by topics and themes. The results of the mapping exercise provide the basis for refining the topic and scope for the second stage of the review.

4.2 Background

Following the identification of study reports of internet-based RCTs, it was clear that a large amount of research funding and time is being used to conduct these trials, but it was less clear whether any methodological knowledge gained by researchers was being shared. ORCHID showed that the number of clinical trials using internet technologies increased dramatically in the last ten years [98] and highlighted the need to understand more about the impact of technology on trial conduct, and on the relationship between researcher and participant in the context of these emerging methods. It was not clear whether adapting existing trial methods to an online setting was effective, how this might affect both researcher and participant experience, or influence patient and public involvement.

ORCHID confirmed that the use of internet technologies in RCTs varies in aspect and degree, and in the stage of the trial process, including:

- use of internet technologies in the delivery of the intervention and/or comparison
- use of internet technologies within a specific stage of the trial process
- use of the technology in the overall conduct of a trial, even if the intervention or comparison is delivered in another medium

The search strategy and screening process for the development of the ORCHID database focused on identifying reports of results from individual internet-based RCTs. However, the search also identified a number of methodological papers addressing the impact of internet technologies on trial conduct, and studies exploring the views and experiences of researchers and participants. In addition to understanding the methodological challenges and issues, it is also important to ensure that the views, attitudes and experiences of participants are understood, as well as those of researchers and their funders [79, 83]. As impact of the relatively recent increase and use of the online clinical trial environment is not well established, it could be hypothesised that there is a tendency to abstract the findings from the traditional trial environment and apply these to the online environment, based on assumptions and without clear evidence.

The purpose of the mapping review was to build an understanding of the methodological, ethical, technical or experience-based research that has been conducted about internet-based trials, using categorisation and thematic analysis to inform practice and provide focus for further synthesis.

4.3 Rationale

The need to bring together different types of knowledge to inform practice, and to adopt a more holistic approach to knowledge translation, has led to the development of new techniques for evidence synthesis [99, 100]. These have

enabled reviewers to address a broader range of questions than those concerned with effectiveness carried out through quantitative systematic reviews or meta-analyses. In particular, the need to tailor systematic reviews to support decision making in policy and practice has been raised by both researchers and practitioners interested in knowledge translation [101-106]. Methodological challenges remain, for example, in the area of integrating data from experimental studies with data from other study types, conducting qualitative syntheses, and for allowing the rapid review of evidence for policy and practice, when constraints require a trade-off between speed and rigour [106-109]. These concerns have led to the development of new methodologies, pioneered by organisations such as the EPPI-Centre [110], Cochrane Collaboration [111], and the Joanna Briggs Institute [112], to increase the potential for the synthesis of evidence from a range of types of data, which will in turn answer different types of questions, and to address important issues such as how equity is defined and reported within reviews [113].

Methodological guidance developed at the EPPI-Centre [114] uses the term "descriptive mapping" [115] to define a series of methods which help reviewers determine the current evidence base and activity in a specific research topic. The benefits of a two-stage design include help in managing the scope of a review question; identifying known uncertainties as a primer for further primary research; and helping to manage the resource costs involved with systematic reviewing [115]. This type of review is particularly relevant in a policy and practice context, and has been used in education [116]; for clinical topics such as dementia [117] and abortion [118]; microfinance in low-income countries [119]; and community engagement [120]. However, as well as being an essential part of a full

systematic review, they can also be a useful resource in themselves, fulfilling the purpose of a traditional bibliography or literature review, but with a more systematic, comprehensive and transparent methodology. The methodology is closely related to the emerging trend for the production of evidence 'gap maps', which also aim to provide an easy to assimilate textual or visual representation of the body of knowledge available for any given topic. They can provide essential tools for research funding and prioritisation decisions, as well as aiming to reduce duplication and waste relating to scientific effort [37, 121-123].

4.4 Aim and objectives

The study aimed to identify factors influencing the effective use of internet-based technologies in RCTs, including the impact on trial management, recruitment and retention, ethics, and the role of public, participant and researcher attitudes, preferences and experiences. The objectives were to:

- Identify studies that report on methodological, ethical, technological or experiential issues relating to internet-based RCTs
- Develop a map of the landscape and coverage of these studies, and to establish the relevant concepts and the size of the literature.
- Identify findings which might require further synthesis and to determine the appropriate methods for reviewing these systematically.

4.5 Scope

The mapping stage of the review was informed by the scope, definitions and results derived from the development of ORCHID, as described in the previous chapter, but refined to include:

4.5.1 Condition or domain

Studies reporting outcomes relating to trial design, conduct or management, or the experiences and perspectives of the public, participants, or researchers, in the context of internet-based randomised controlled trials investigating interventions in health treatments and conditions.

4.5.2 Participants/population

Studies which have collected data from patients and the public, trial participants, and researchers were included, where they relate to the domains outlined above.

4.5.3 Geography and Language

Studies from all countries were included. No restrictions for language were applied in the search.

4.5.4 Types of information

For the descriptive map, study types included systematic reviews; RCTs; process and outcome evaluations; qualitative studies; practice-based information including case studies, which reported one of more of the outcomes listed in Table 4.1. Editorials and opinion pieces were excluded.

4.5.5 Stage of trial

All core stages of the trial process were included, however studies describing the use of the internet solely for dissemination of results, or for providing access to health information for the public, were excluded.

Outcomes of interest:
• Acceptability, feasibility and satisfaction relating to internet-based trial conduct and management; barriers and facilitators to recruitment, engagement, adherence and retention; understanding or knowledge of internet-based trials • Participant or researcher attitudes and experience relating to core trial principles such as informed consent, bias, risks and benefits. • Participant or researcher attitudes, views and experiences of involvement in the design, planning and conduct of internet-based trials • Impact on trial performance and results of management, strategies and experiences related to trial design and conduct, recruitment, data collection, engagement, adherence, retention and attrition.

Table 4.1 Descriptive map: outcomes of interest

4.6 Methods

4.6.1 Identifying studies

The topic of the review encompasses a broad range of perspectives and potential studies, and required the use of a wide range of search techniques and sources. As with the previous ORCHID search strategies, problems resulted from the need to retrieve relevant studies in a wide range of primary and secondary sources in multiple disciplines. Papaioannou [124] noted for example, that reports of studies in the social sciences are spread across very large number of multi-disciplinary databases. Potential studies may not have been reliably indexed due to the lack of consistently applied controlled vocabularies, or publication types in some databases, therefore a range of techniques to optimise sensitivity were applied [124].

In order to improve retrieval in complex topics, information specialists have tested different techniques, including citation searching, reference list checking, contact with experts, and pearl growing, and found that these can increase retrieval of relevant studies. It was found that using pearl growing was less successful for this search, and that the 'pearls' were so diffused across many databases, with no one database indexing more than a few, therefore this technique was not used. Search strategies were peer-reviewed, using the Peer Review of Electronic Search Strategies (PRESS) tool [125], and term testing and piloting used where possible. Search terms were adapted for use in relevant subject or methodological bibliographic databases, with database-specific methodological search filters used where available. No language or date restrictions were applied.

4.6.1.1 Qualitative studies

It has traditionally been more difficult to identify qualitative research in the literature, partly due to the lack of agreed and consistently applied controlled terms in bibliographic databases, but also to the range of theoretical and conceptual frameworks around the description of qualitative enquiry and methods. Attempts have been made to evaluate specific strategies to help identify qualitative research across different bibliographic databases for recall and precision. Shaw et al [126] tested three search strategies across six electronic databases. Their findings confirmed that optimising search results requires a wide range of terms, and leads to a large number of false positives, adding to the time needed to both conduct the searches and to filter and screen results. Booth [127] provides an analysis of methods for searching for qualitative studies in systematic reviews.

It was anticipated that relevant qualitative papers would be located across a very wide range of multi-disciplinary databases, which could lead to extensive searching time for a small number of relevant records, and also increase the time needed to screen large numbers of results [127]. The InterTASC ISSG Search Filters Resource was consulted in order to identify and assess relevant filters for identifying qualitative research in MEDLINE, CINAHL, EMBASE and PsycINFO [128].

4.6.1.2 "Hard to find"' evidence

Another aspect identified as requiring an alternative approach relates to the concept of "hard-to-detect" evidence, as outlined by O'Mara [129]. When looking for evidence where the key concepts to be identified relate to complex interventions, and are not the primary outcome of the study, the authors found that finding relevant studies in the published literature across multiple disciplines required new search techniques, including the use of text mining to support term generation, the use of a wide range of sources, and multiple screening stages and processes. These techniques were incorporated in the design of the searching and screening stages of the mapping review.

4.6.2 Search strategy

The ORCHID database was used to extract an initial set of relevant studies. These included coded studies about internet-based RCT methods, conduct or management, and qualitative studies associated with internet-based trials. Additional search strategies were developed to supplement the ORCHID import to incorporate the additional concepts needed for this stage of the review, and included the following elements:

4.6.2.1 Subject search

The search strategy developed for ORCHID was re-run, using the original core concepts, but with an additional strategy to identify qualitative studies, and a systematic review filter.

4.6.2.2 Citation searching

Web of Science was used for citation searching of key articles. In addition, the 'Related articles' option on PubMed was used where appropriate, or the web site citation links for individual journal articles.

4.6.2.3 Reference list checking

Checking of reference lists from primary studies and systematic reviews was used to supplement database searches.

4.6.2.4 Contact with experts

Active research groups and experts were identified via ORCHID or key papers, and ThinkWell [130] group members were used to identify additional unpublished sources and publication types. Searches were downloaded into EndNote for de-duplication, and then into EPPI-Reviewer 4 software. Once all results were imported into EPPI-Reviewer, they were checked again for duplicates using manual and automatic coding, to identify linked studies, and ensure that no corrections to published studies, or sibling studies were missed. Search strategies are provided in Appendix 4A.

All studies that met the following criteria were included:

- Methodological and qualitative studies concerning the use of internet technologies in RCTs, including:
    - Trial planning and design
    - Recruitment, enrolment and screening
    - Adherence, engagement, compliance, retention and attrition
    - Ethical issues
    - Acceptability, feasibility and satisfaction
    - Attitudes, views or experiences
    - Barriers and facilitators for participation
    - Factors relating to technologies and web-based platforms
    - Studies investigating health research, public health and clinical research topics and settings.
    - Studies involving patients, members of the public, or researchers.

The following studies were excluded:

- Primary studies reporting the clinical outcomes of a health or wellbeing intervention.
- Studies using mobile telecommunications technologies, with no internet-based content.
- Methodological or qualitative studies not investigating a health, wellbeing or clinical condition topic.
- Qualitative primary studies which did not report on the views, attitudes or experiences of the public, participants, or researchers in relation to internet-based randomised controlled trials.
- Studies where trial participants were exclusively health professionals, health care personnel, or health care students in training or education.

Table 4.2 Descriptive map: inclusion and exclusion criteria

4.6.3 Selection of studies

Titles and abstracts of potentially relevant citations were screened using EPPI-Reviewer. For quality assurance purposes a sample of 10% of studies were independently screened by two reviewers against the pre-defined inclusion and exclusion criteria (Table 4.2). A full list of inclusion and exclusion criteria for each

stage of screening process can be found in Appendix 4B. A flow chart is provided in Figure 4.1.

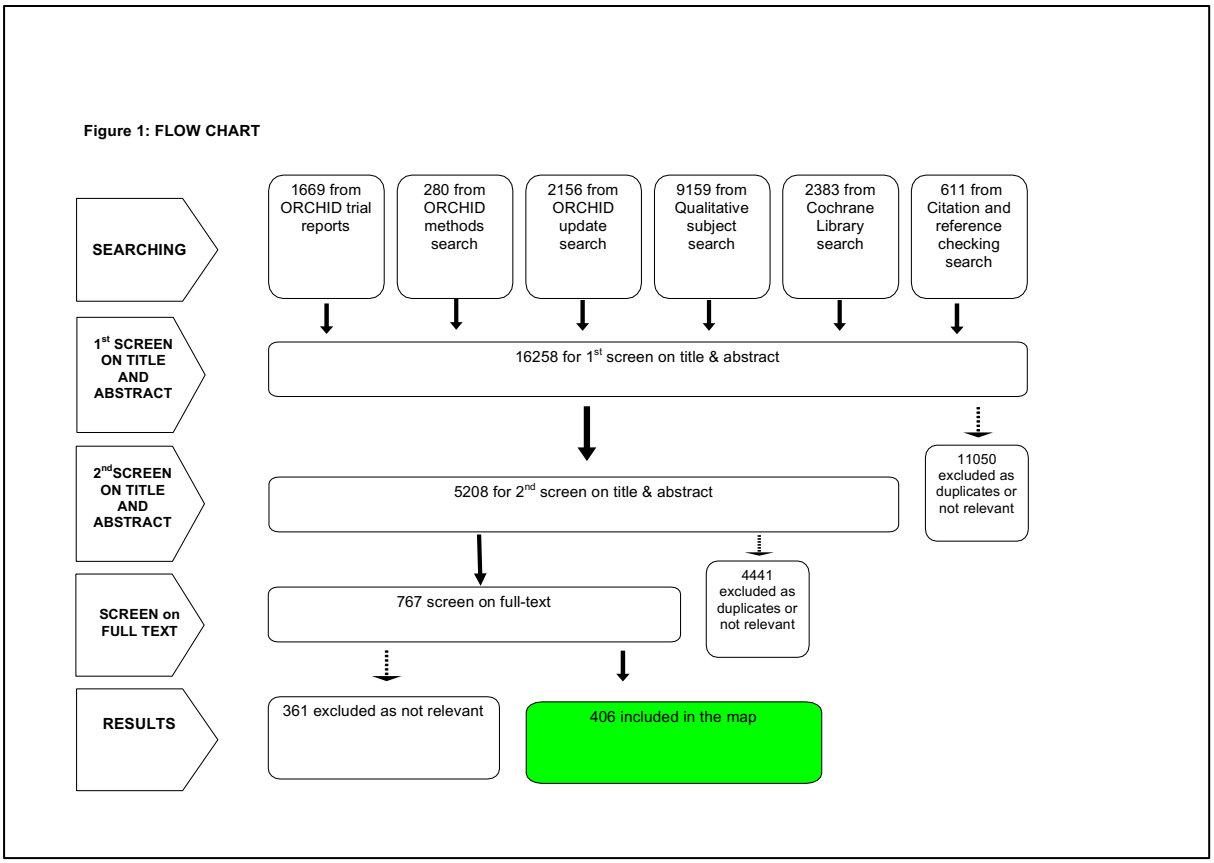

Figure 4.1 Flow chart of included studies

4.6.4 Coding of studies

Included studies were descriptively coded following screening on full-text where possible. An initial coding system based on the ORCHID results, informed by the issues relating to internet-based clinical trials identified by Murray [59], was used as the formative thematic structure for the mapping with new codes developed using an iterative thematic approach. For an initial sample, two reviewers coded a sample of 50 included studies independently, and then compared notes to reach consensus. A third reviewer was available if consensus could not be

reached, but this was not necessary. The coding structure was refined to remove any ambiguities, and subsequent coding completed by the author. Following completion of screening, each code set was reviewed. Amendments and adjustments were made to reflect the nature of the evidence base, and to iterate key themes. The descriptive map was developed from the results of the selection and coding.

4.7 Results

Two hundred and eighty results were downloaded from ORCHID. Following the update of the ORCHID search, additional subject searches, and citation searches a total set of 16,258 results were retrieved and downloaded to Endnote. 2178 duplicate records were identified, leading to a total set of 14,080 records. Study reports ranged in publication date from 1997 – 2016. Results were screened using the pre-specified inclusion and exclusion criteria. A total of 13,674 results were excluded resulting in a final set of 406 studies.

4.7.1 Dates of studies

Some papers, particularly those dealing with specific software developments, web site development or technical infrastructure were of interest only in a historical context, and not relevant in terms of providing shared knowledge for future trials. These studies are therefore not included in the thematic description. A set of key papers were identified which contained a range of detailed methodological or substantive issues.

4.7.2 Coding

Each study was described in terms of the stage of the trial that internet technologies were used; the type of methodological, technical or ethical issues discussed; the topic under consideration; the perspective of the qualitative

enquiry; the geographical base of the lead researcher; and specific setting or key issues. The initial and final coding structures can be seen in Appendix 4C.

4.7.3 Country of study

Papers were coded for country of the lead researcher, except where the paper was described as an international co-operation, and results are presented in Figure 4.2. The largest number of studies originated from the USA (178), followed by the UK (57), Australia (43), The Netherlands (29), Germany (20), and Canada (18).

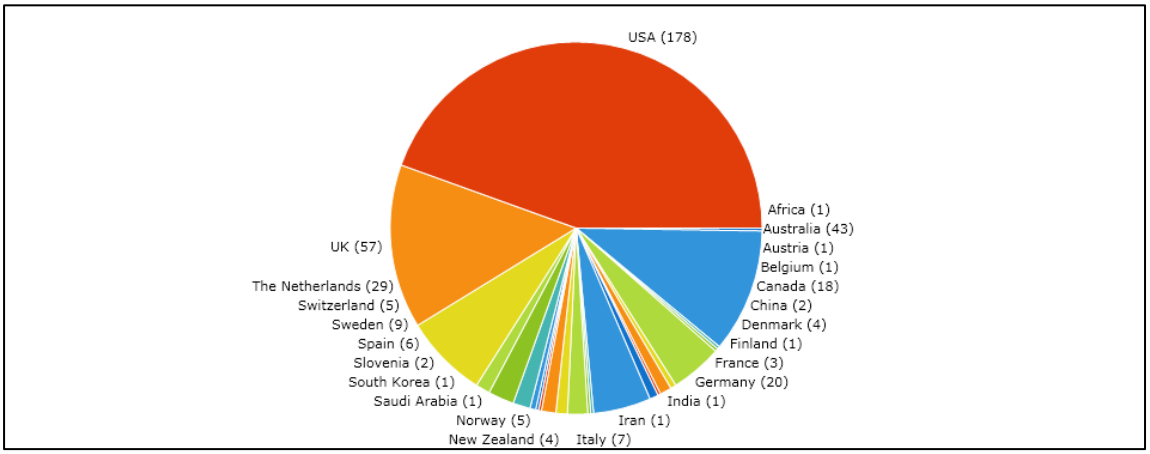

Figure 4.2 Map: Country of study

4.7.4 Condition, topic and subjects covered

Figure 4.3 lists studies coded to core subject topics of the trials where stated. The largest number of studies were coded as relating Psychological and Behavioural treatments (83), Mental Health conditions (61), Smoking cessation (31), Obesity (30) and HIV/Sexual Health (14), Alcohol (12), Cardiovascular diseases (12), Neurological diseases (12), Child Health (10), Physical Activity (10).

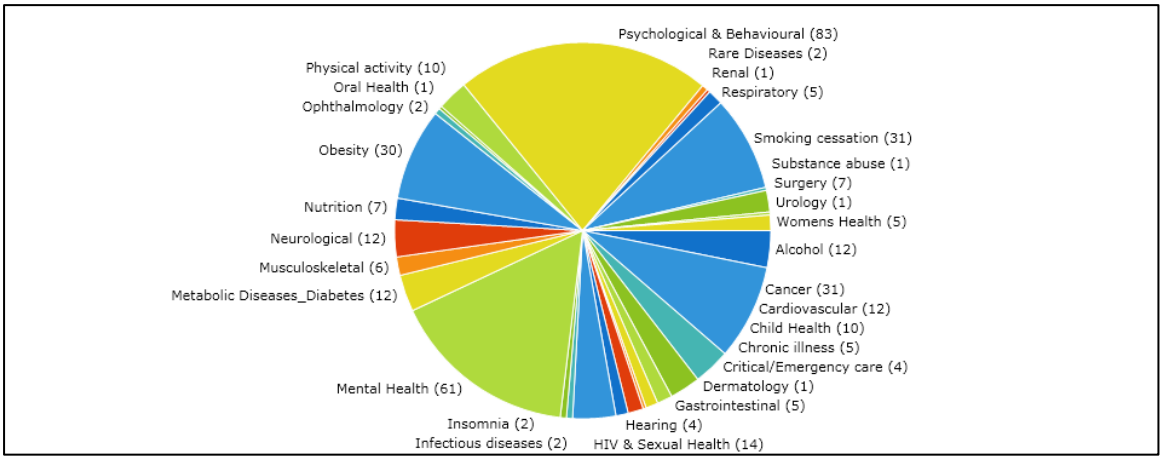

Figure 4.3 Map: Conditions and topics

4.7.5 Type of information

The 'Types of Information' schema developed by the National Institute of Health and Care Excellence (NICE) and Public Health England (PHE) [131] was initially used to code study types. However, as the study types included in review did not require this full range the code set was restricted to include the following major types: systematic reviews; primary research studies; use studies; qualitative studies; and practice-based reports.

4.8 Describing the literature

Summary results from the thematic coding of the included studies are shown in Figure 4.4, and a more detailed analysis by theme is provided below. Qualitative studies are reported in a specific mapping section as they were of primary interest. Qualitative studies were included in the mind maps for each methodological theme, but not in the textual mapping in order to avoid repetition. To aid presentation of the themes, each section will be started on a new page.

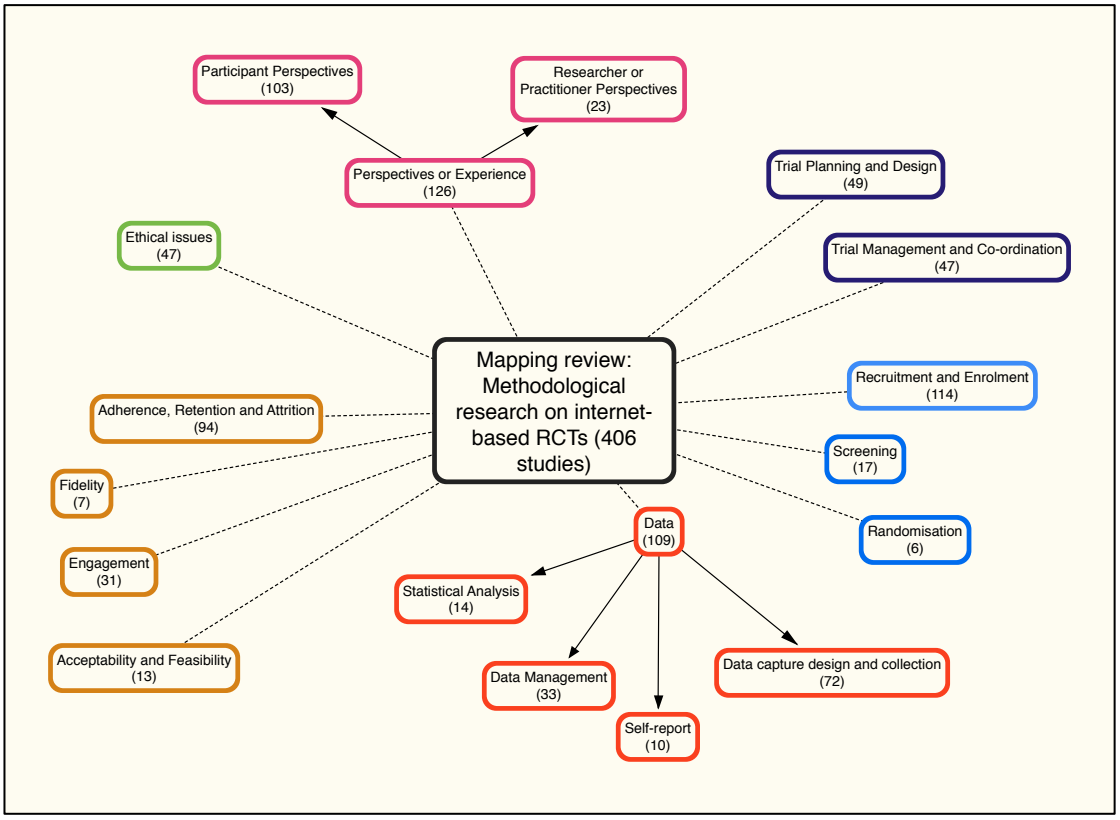

Figure 4.4 Summary of descriptive map themes

4.8.1 Key papers

Thirty-one papers were identified which provided key practice-based summaries or overviews of the methodological, ethical and technological issues. These were considered to be central to the development or understanding of the topics in the framework. Early studies contain concepts relating to the potential benefits of internet-technologies including lower costs [47, 48, 59] and increased size [47]. Studies include the impact of the internet on common methodological areas, including randomisation [48, 59, 132, 133], and recruitment [48, 59, 134-138]. Adherence issues were reported in 5 studies [59, 135, 138-140], and fidelity in 4 [59, 138, 141, 142]. The relationship of internet use to the planning of multi-site and international trials was identified in 3 studies [132, 136, 143], and in terms of compliance with regulations in one study [133].

Themes relating to data management and collection were identified in 11 of the key papers, with specific themes relating to general data entry [132, 134]; data security and confidentiality [47, 48, 136, 143-145]; authentication [135]; data quality [59]; and self-report [133].

Unanticipated additional costs of developing trial technologies were reported [141, 143]; the lack of reported cost data [146]; as well as themes relating to reliance on technical expertise [48, 142, 145, 147]. Concepts relating to ethics were identified [133, 138, 141, 144, 145]; with specific reference to trial reporting and the sharing of knowledge to avoid duplication [44, 148, 149]; and concepts relating to inequalities [150].

More specific themes emerge in later key papers, as experience in internet-based trials develops. These themes include concepts relating to design frameworks, models or modalities, and user characteristics [151-153]; reach and representativeness [138, 139, 145, 150]; and tailored and blended interventions [137, 139, 141, 151, 154, 155].

An emerging theme relating to the role of the human in internet-based trials was coded in 7 key papers from 2009. Sub themes include face-to-face versus online contact [147, 149, 152]; human contact or support [142, 153, 154]; and changes in the nature of the role of the therapist [155].

Four key papers explored participant or researcher experience [133, 134, 143], and one paper reported a two-stage realist synthesis [156].

4.8.2 Trial planning and design

Forty-nine papers contained general concepts relating to trial planning and pre-trial requirements, or discussions on trial design, piloting or feasibility studies.

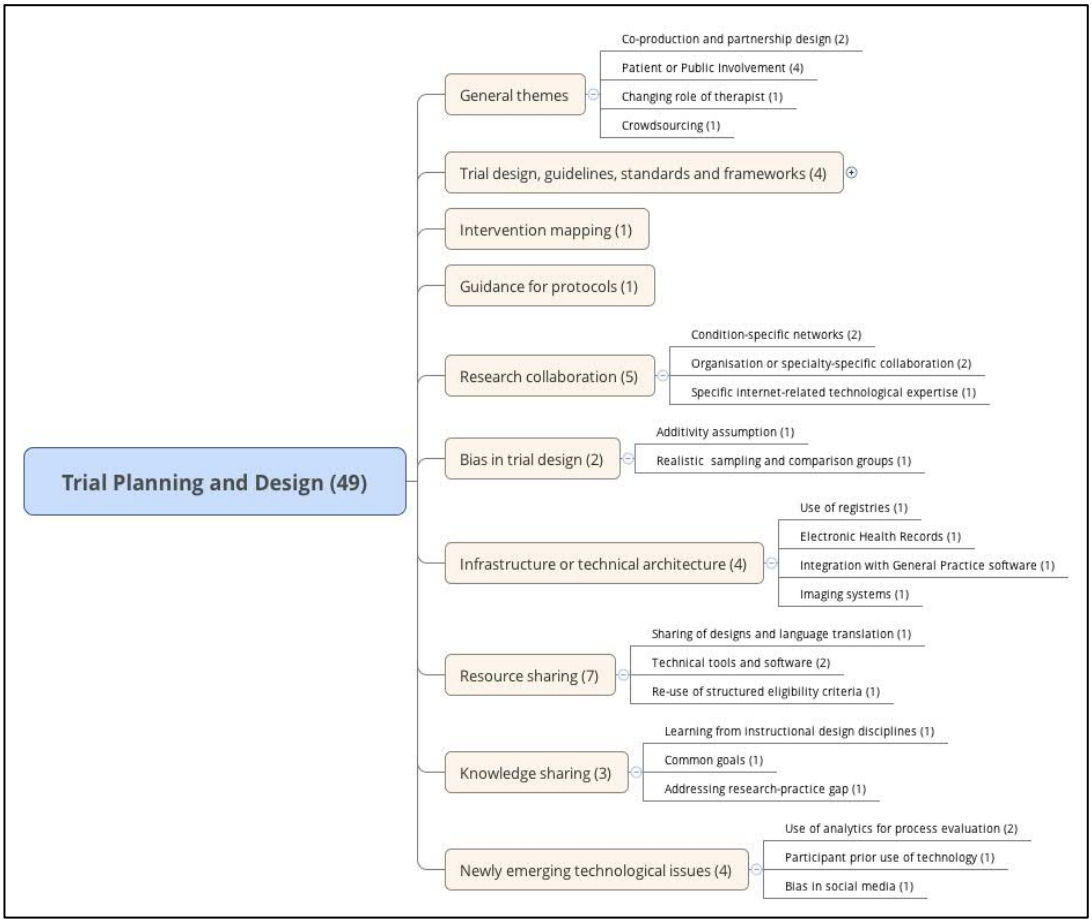

Figure 4.5 Map: trial planning and design

Co-production and partnership design themes were featured including professional collaborative or shared-care [141, 157]; involvement with patients or the public [158-161]; the changing role of the therapist [162]; with one study introducing the concept of crowdsourcing in trials [159].

Themes relating to trial design guidelines, standards and frameworks were identified [163-165]; intervention mapping [166]; and guidance for protocols [167]. Concepts relating to research collaboration ranged from condition-specific

networks [168, 169]; organization, or specialty-specific collaborations [170, 171]; and expanding teams to include specific internet-related technological expertise [172]. Bias in trial design was highlighted relating to additivity assumption and research participation effects, realistic sampling and comparison groups [173, 174].

Infrastructure or technical architecture themes included the development and use of registries [175]; Electronic Health Records [176]; integration with general practice software [157]; and imaging systems [177].

Resource sharing themes include the sharing of intervention designs and translation of relevant documentation to other languages [150]; technical tools and software [157, 170]; and re-use of structured eligibility criteria [178].

Knowledge sharing concepts include shared learning from other disciplines such as instructional design [153]; common goals [168]; and addressing the research-practice gap [179].

Emergent technological issues relating specifically to trial methodology were reported in 4 papers, including use of analytics for process evaluation [180, 181]; participant prior use of technology [182]; and bias in social media [183].

4.8.3 Trial management and co-ordination

Forty-seven papers were included in this code set, of which 34 discussed the concept of quality assurance.

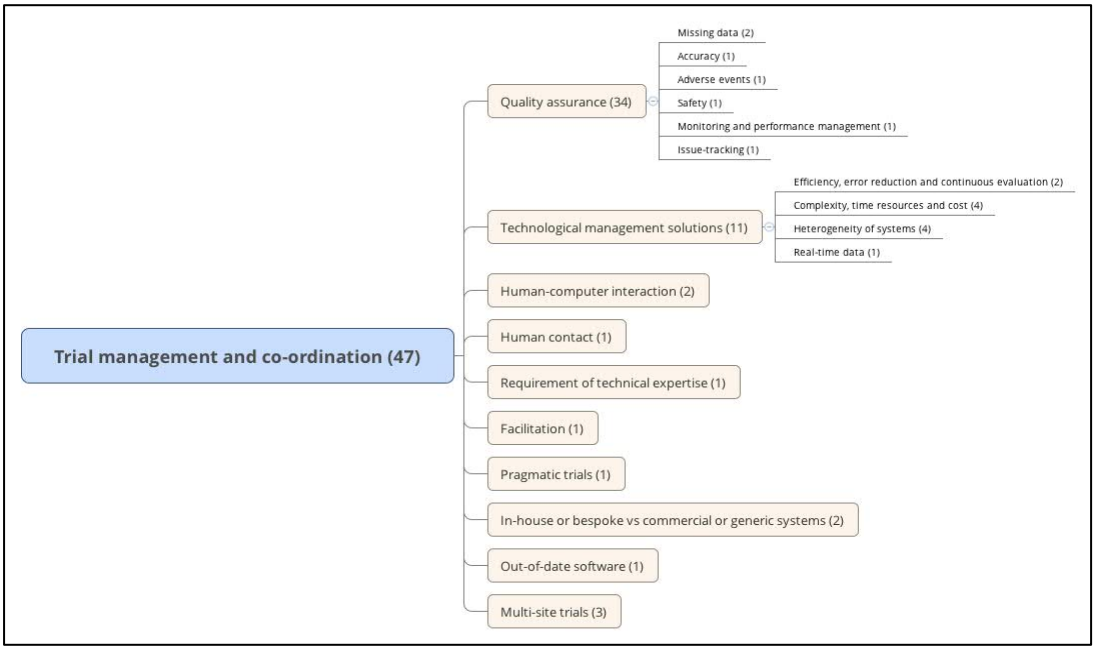

Figure 4.6 Map: trial management and co-ordination

The impact of technological management solutions included themes of efficiency, error reduction, and continuous evaluation [184, 185]; complexity, time resources and cost [186-189]; heterogeneity of systems [187, 190-192]; and real-time data [193]. Papers included themes relating to human-computer interaction [194, 195]; human contact [192]; the requirement of technical expertise as a component of trial management [188]; facilitation [142]; and the management of internet-based pragmatic trials [192]. Choices between management systems developed in-house or bespoke versus commercial or generic systems were noted [191, 193], and problems relating to out-of-date software [157].

Themes were identified relating to the management of multi-site internet-based trials in 3 studies [191, 196, 197].

Quality assurance as a component of trial management included themes relating to missing data [198, 199]; accuracy [188]; adverse events, safety, monitoring and performance management [195, 197, 200, 201]; and issue-tracking [196].

4.8.4 Recruitment and enrolment

One hundred and fourteen studies were coded as being primarily concerned with recruitment and enrolment.

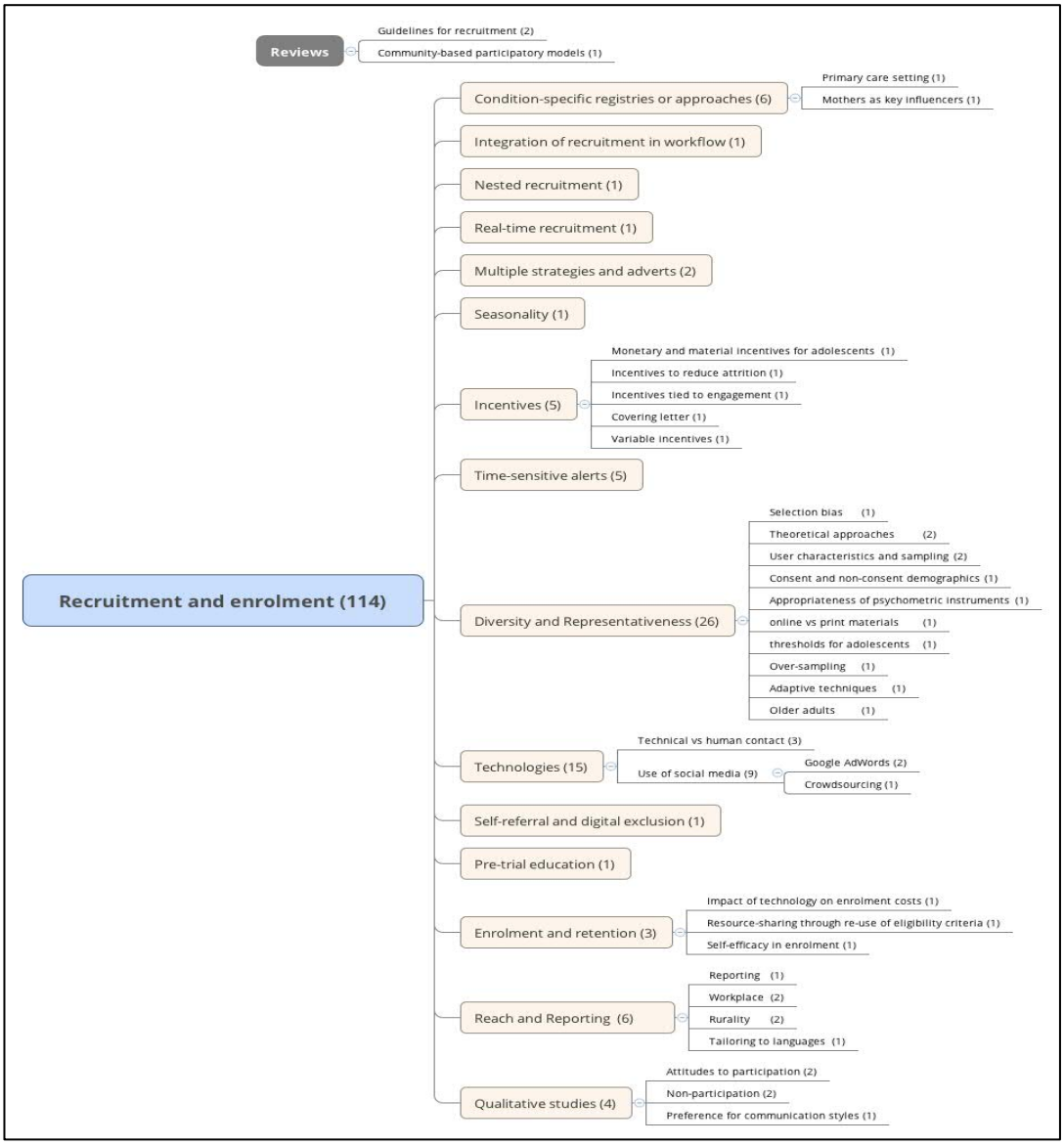

Figure 4.7 Map: recruitment and enrolment

4.8.4.1 General

Four studies were identified as reviews of recruitment methods, including two systematic reviews [149, 202], a narrative literature review [203], and an overview [145]. Themes were identified relating to the development of guidelines

for recruitment [204]; the use of community-based participatory research models [205]; and a comparison of multiple strategies and adverts [185, 206].

Six papers described the use of condition-specific registries or approaches [207-211]; in settings such as primary care [212]; or with key influencers such as mothers [213]. Integration of recruitment in workflow [214]; nested recruitment [215]; real-time recruitment [185]; and seasonality [142] were included as themes.

Codes relating to the type of technologies used in recruitment included comparisons between technology and personal contact [212, 216, 217]; use of social media [155, 203, 208, 209, 213, 218-221]; with two studies specifically investigating the use of Google AdWords [222, 223]; and one with crowdsourcing [149]. Self-referral and digital exclusion were reported themes [155], as were pre-trial education [224].

Impact of recruitment techniques on other stages of the trial were identified in relation to enrolment and retention [203, 225]; impact of technology on enrolment costs [225]; resource sharing through re-use of eligibility criteria [178]; and self-efficacy in enrolment [226].

Five studies were coded with the theme of time-sensitive recruitment through alerts [227-231].

4.8.4.2 Diversity and representativeness

Twenty-six studies were coded for diversity, reach or representativeness. Studies relating to recruitment strategies to enhance diversity included themes of selection bias [232]; theoretical approaches [233, 234]; user characteristics and sampling [235, 236]; and comparisons between consent and non-consent demographics [237]. Other concepts included appropriateness of psychometric

instruments [238]; online versus print materials [239]; recruitment thresholds for adolescents [240]; and over-sampling [241]. One systematic review included a summary of adaptive techniques [242], and a practice-based summary reported strategies for recruitment of older adults [138].

Concepts relating to reach and reporting [243]; reach through workplace recruitment [244, 245]; rurality [246]; perceived barriers to recruitment [247]; and tailoring recruitment to languages [248] were recorded.

4.8.4.3 Incentives

Five studies were coded with concepts related to incentives, including monetary and material incentives for adolescents [209]; incentives to reduce attrition [249]; incentives tied to engagement [250]; incentive with covering letter [251]; and variable incentives [252].

4.8.5 Screening and randomisation

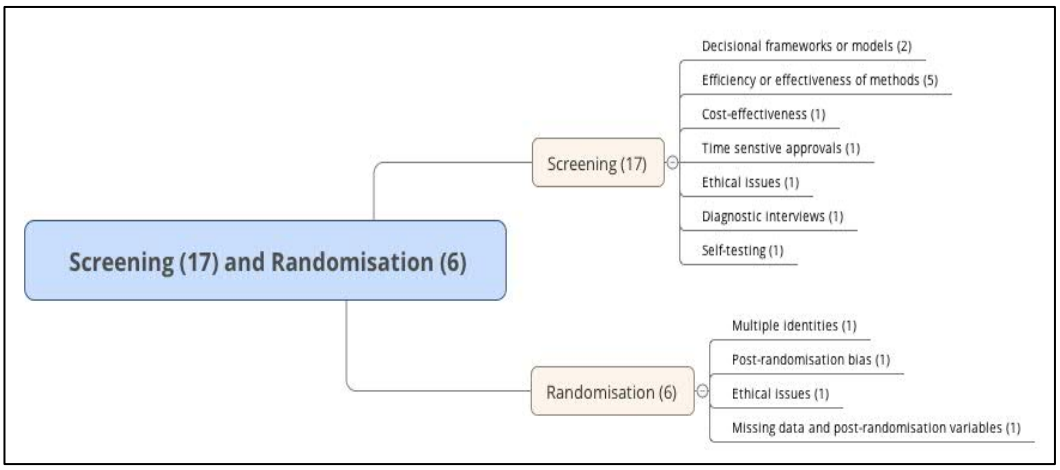

Figure 4.8 Map: screening and randomisation

Seventeen studies contained concepts relating to screening within studies [253]. Themes identified included the use of decisional frameworks or models [254, 255]; efficiency and effectiveness of methods [216, 253, 256-258]; and cost-effectiveness [259]. Time sensitive approvals [260]; ethical issues [261]; diagnostic interviews, and self-testing [262, 263] were identified themes. One paper included the issue of duplicate patients in trials [264], and researcher perspectives were explored [255].

Six studies included concepts relating to randomisation methodology, as opposed to a historical or descriptive report. Themes included those relating to multiple identities, and post-randomisation bias [59, 173]; ethical issues [141]; and missing data and post-randomisation variables [265].

4.8.6 Data

One hundred and nine studies reported issues concerning data.

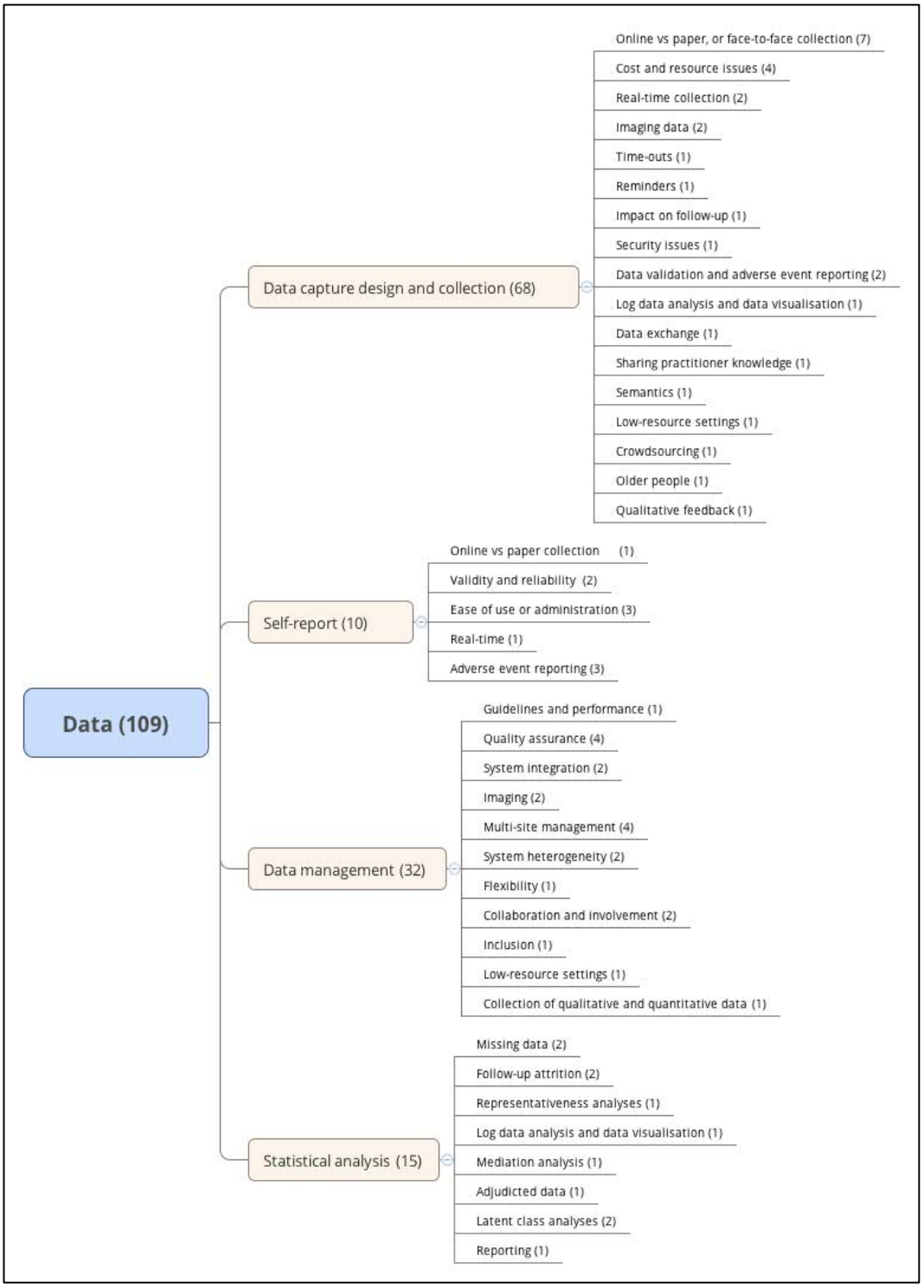

Figure 4.9 Map: data

4.8.6.1 Data capture design and collection

Sixty-eight studies contained themes relating to data capture design, and data collection. Themes included the comparison of online versus paper, or face-to-face data collection [199, 266-271], and cost and resource issues [192, 272-274]. The concepts of real-time collection of data [193, 275]; imaging data [177, 276]; time-outs [277]; reminders [278]; and impact on follow-up [279] were identified. Security issues [274]; data validation and adverse event reporting [201, 280]; log data analysis and data visualisation [281]; a theme relating to data exchange [282]; sharing practitioner knowledge [274]; and semantics [282] were found.

4.8.6.2 Data management

Data management themes were coded in 32 papers, including guidelines and performance [200]; quality assurance [187, 188, 196, 197]; system integration [259, 283]; imaging [189, 259]; multi-site management [187, 191, 193, 284]; system heterogeneity [187, 191]; and flexibility [283].

4.8.6.3 Self-report

Ten papers contained the concept of self-report, including comparison of online versus paper [285]; accuracy [286]; ease of use or administration [164, 285, 287]; validity and reliability [288, 289]; real-time [287] and adverse event reporting [201, 290, 291].

4.8.6.4 Statistical analysis

Fifteen papers contained concepts relating to statistical analysis, including missing data [198, 292]; follow-up attrition [293, 294]; representativeness analyses [243]; log data analyses and data visualization [281]; mediation analysis [295]; adjudicated data [296]; latent class analyses [297, 298]; and reporting [243].

4.8.7 Acceptability and feasibility

Thirteen studies included concepts relating to acceptability and feasibility, including tailored advice [299, 300]; use of video messages [301]; incentives [250]; face-to-face versus online designs [299]; and training [302]. Co-production [158] and content validity [303] concepts were identified. The use of focus groups featured in one study [304].

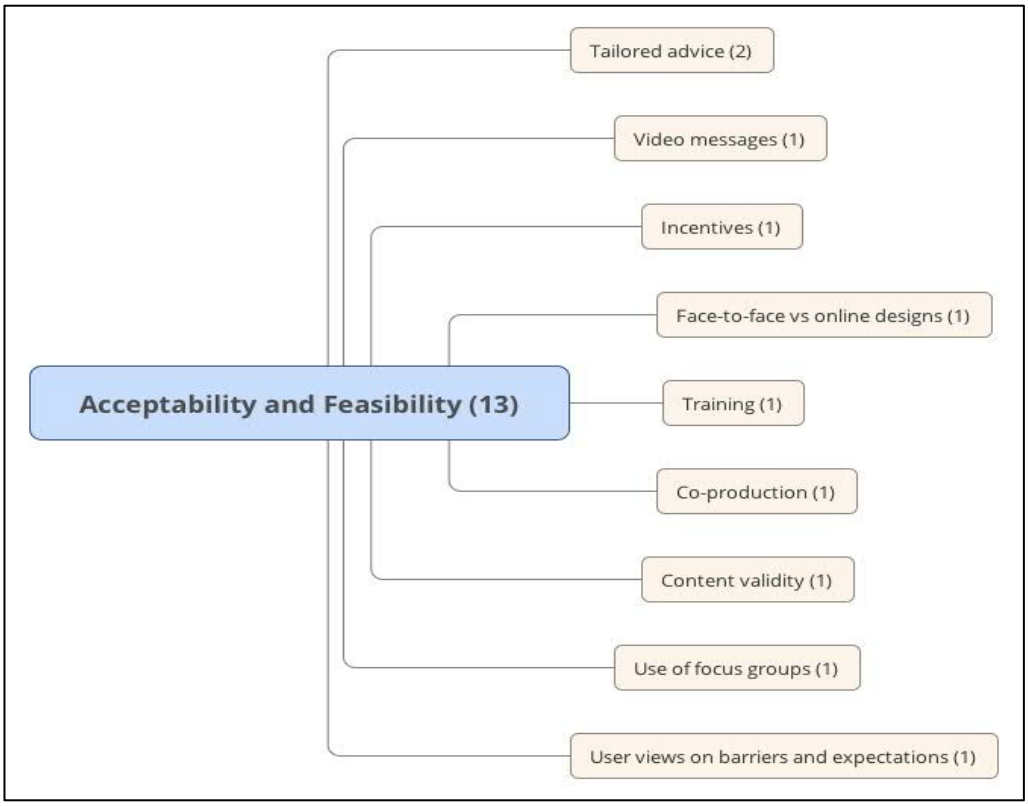

Figure 4.10 Map: acceptability and feasibility

4.8.8 Engagement and fidelity

Thirty-eight studies were coded with themes relating to engagement and fidelity.

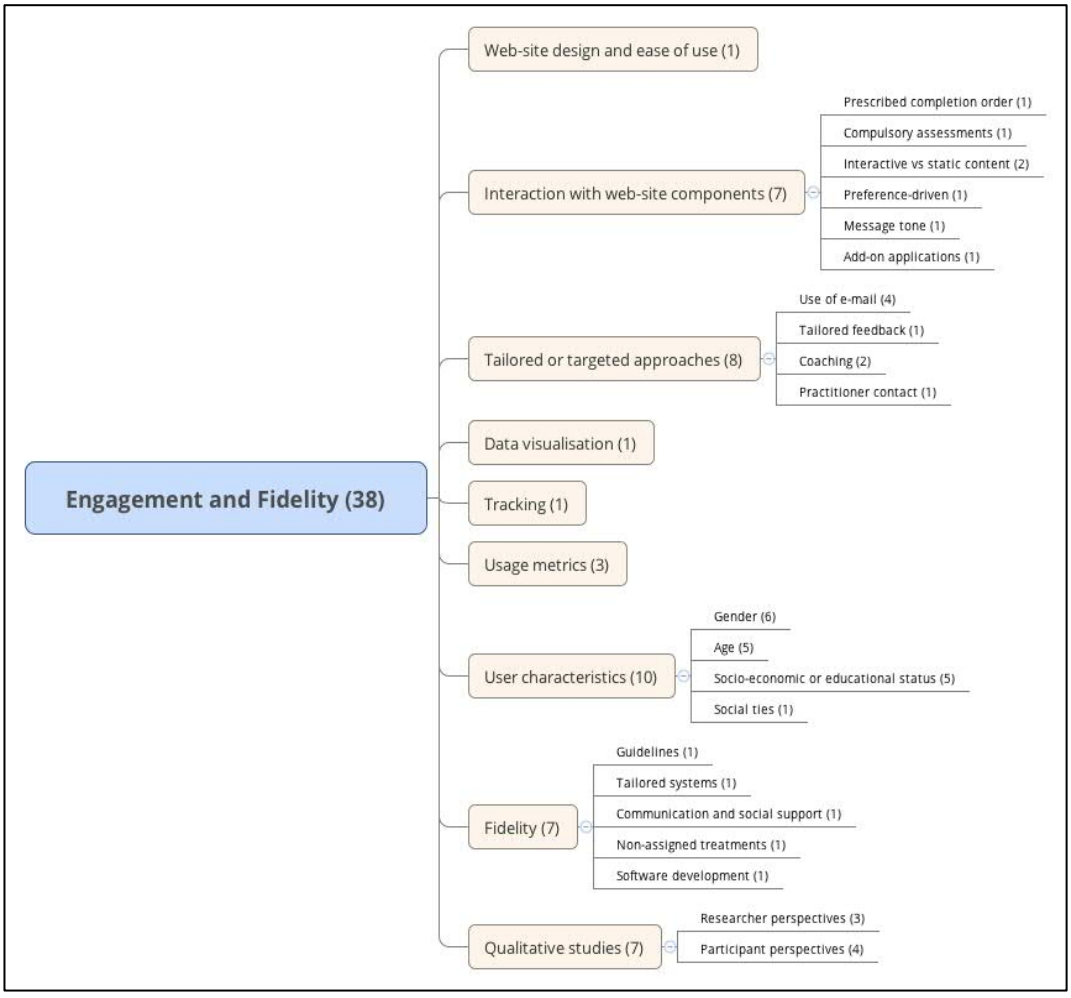

Figure 4.11 Map: engagement and fidelity

4.8.8.1 Engagement

Themes relating to engagement included usage metrics [203, 304, 305]; tracking [306]; data visualization [281]; website design and ease of use [307, 308]. Concepts relating to interaction with the intervention components included prescribed completion order [309]; compulsory assessments [310]; interactive versus static content [305, 311]; preference-driven [312]; message tone [309]; and add-on applications [313]. Tailored or targeted approaches included e-mails

[217, 307, 309, 314]; tailored feedback [308]; coaching [315, 316]; and practitioner contact [217]. User characteristics, such as gender, age, socio-economic or educational status were identified [217, 236, 297, 298, 306, 311, 313, 317, 318]; and social ties [319].

4.8.8.2 Fidelity

Seven studies contained themes relating to fidelity, including guidelines [320]; tailored systems [321]; communication and social support [320]; non-assigned treatments [322]; and software development [188].

4.8.9 Adherence, Retention and Attrition

Ninety-four studies included concepts relating to retention, attrition, and adherence.

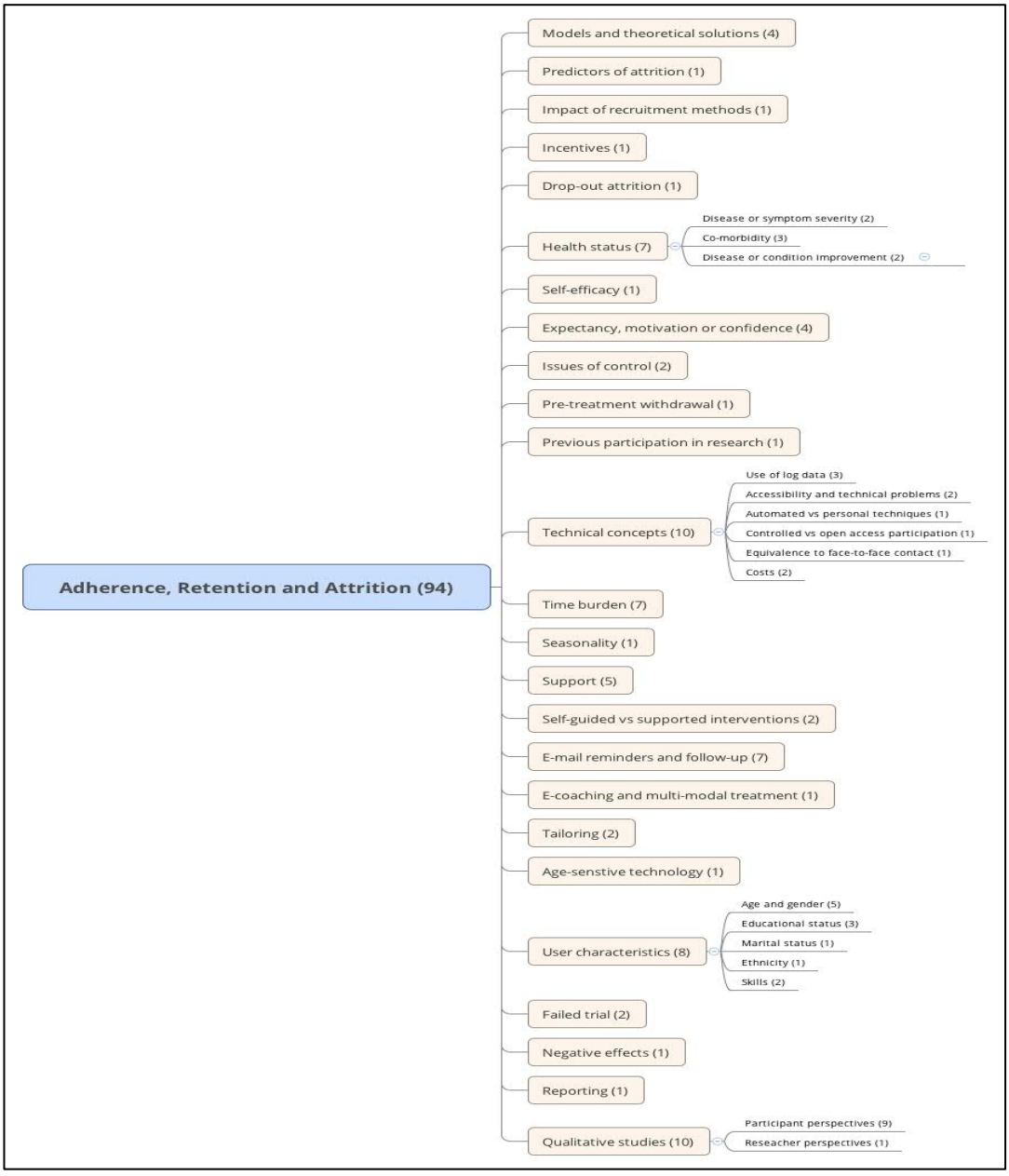

Figure 4.12 Map: adherence, retention and attrition

The concepts identified across these themes were very similar, therefore they have been combined for this summary. Five studies relating to adherence, retention or attrition were systematic reviews [323-326].

Concepts relating to models and theoretical solutions were identified [233, 327-329]; to predictors of attrition [330]; impact of recruitment methods [331]; incentives [332]; and dropout attrition [323]. Health status concepts were identified including disease or symptom severity [323, 327]; co-morbidity [327, 333, 334]; and disease or condition improvement [335, 336]. Other concepts included self-efficacy [226]; expectancy, motivation or confidence [337-340]; issues of control [327, 328]; pre-treatment withdrawal [341]; and previous participation in research [342].

Technical concepts related to use of log data [324, 343, 344]; accessibility and technical problems [336, 345]; automated versus personal techniques [346]; comparison of controlled versus open access participation [343]; equivalence to face-to-face contact [347]; and costs [348, 349].
Concepts were identified relating to time burden [323, 333, 335, 350-352]; seasonality [353]; support [325, 327, 332, 345, 354]; self-guided versus supported interventions [355, 356]; e-mail reminders and follow-up [324, 340, 342, 343, 357-359]; e-coaching and multi-modal treatment [360]; tailoring [345, 359]; and age-sensitive technology [138].

Similar to the section on engagement, themes relating to user characteristics were identified [233, 330, 336, 343, 344, 361-363]; including age and gender [138, 334, 340, 364, 365]; education [340, 353, 366]; marital status [335]; ethnicity [367]; and skills [335, 345]. The concept of the failed trial [361, 368]; negative effects [329]; and issues in relation to reporting were noted [369].

4.8.10 Ethical issues

Forty-seven papers discussed issues relating to ethical issues in internet-based trials. These included 21 relating to consent, 3 to issues of health equity or inequalities, and 11 to trial reporting.

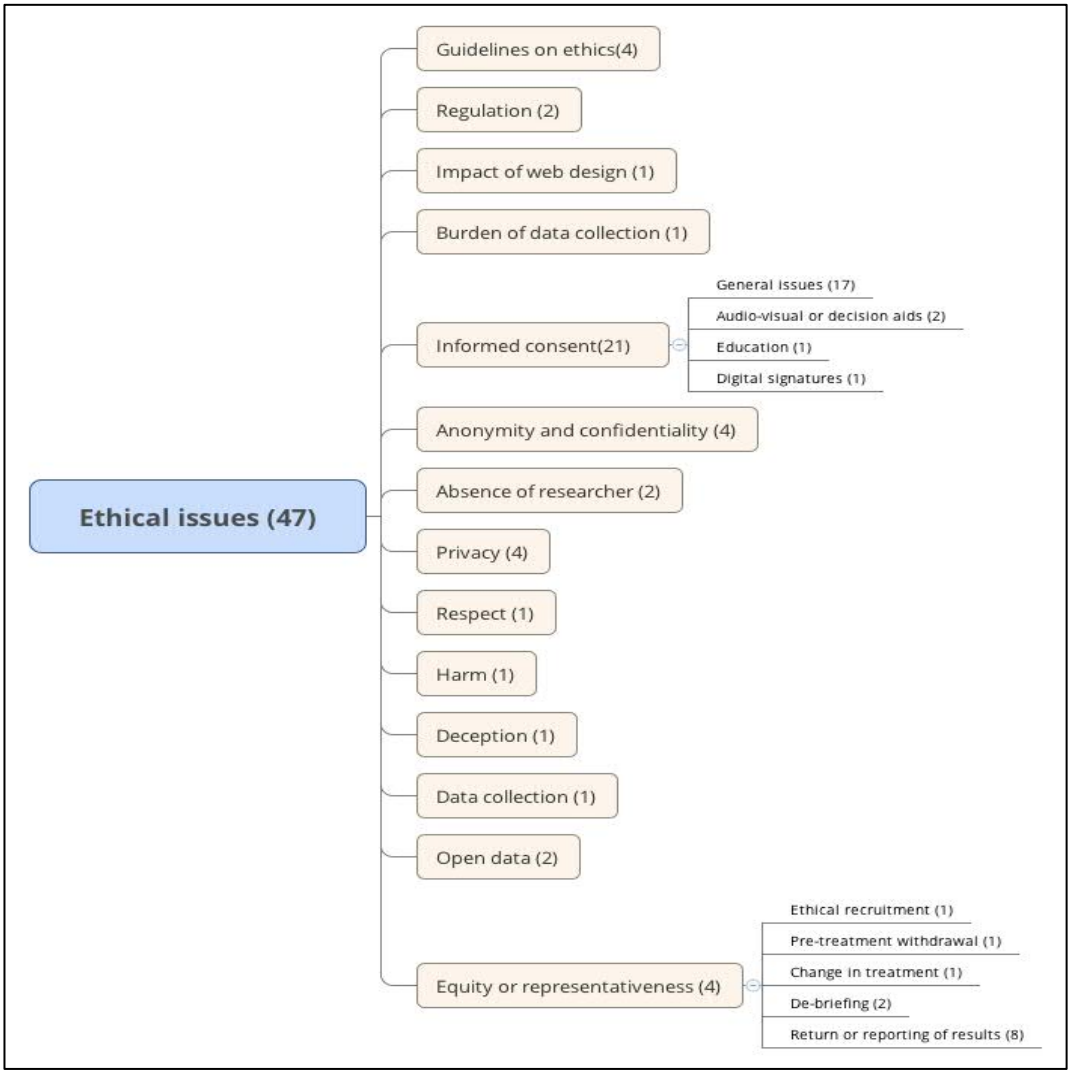

Figure 4.13 Map: ethical issues

Concepts relating to guidelines on ethics were identified [143, 163, 370, 371]; regulation [145, 155]; impact of website design [141]; and burden of data collection [143].

General issues relating to informed consent were identified [59, 133, 134, 138, 145, 371-382]; audio-visual or decision aids [383, 384]; education [385]; and digital signatures [48].

Ethical concepts were identified relating to anonymity and confidentiality [143, 144, 341, 386]; absence of researcher [144, 171]; privacy [134, 143, 145, 171]; respect [372]; harm [143]; and deception [387]. The ethics of data collection [138], and open data [388, 389] were described.

Concepts included equity and representativeness [143, 150, 165, 366]; ethical recruitment [390]; pre-treatment withdrawal [341]; change in treatment [141]; de-briefing [144, 391]; and return or reporting of results [166, 391-397].

4.8.11 Perspectives or experience

Themes exploring researcher, practitioner or participant perspectives and experience were included in 126 qualitative studies.

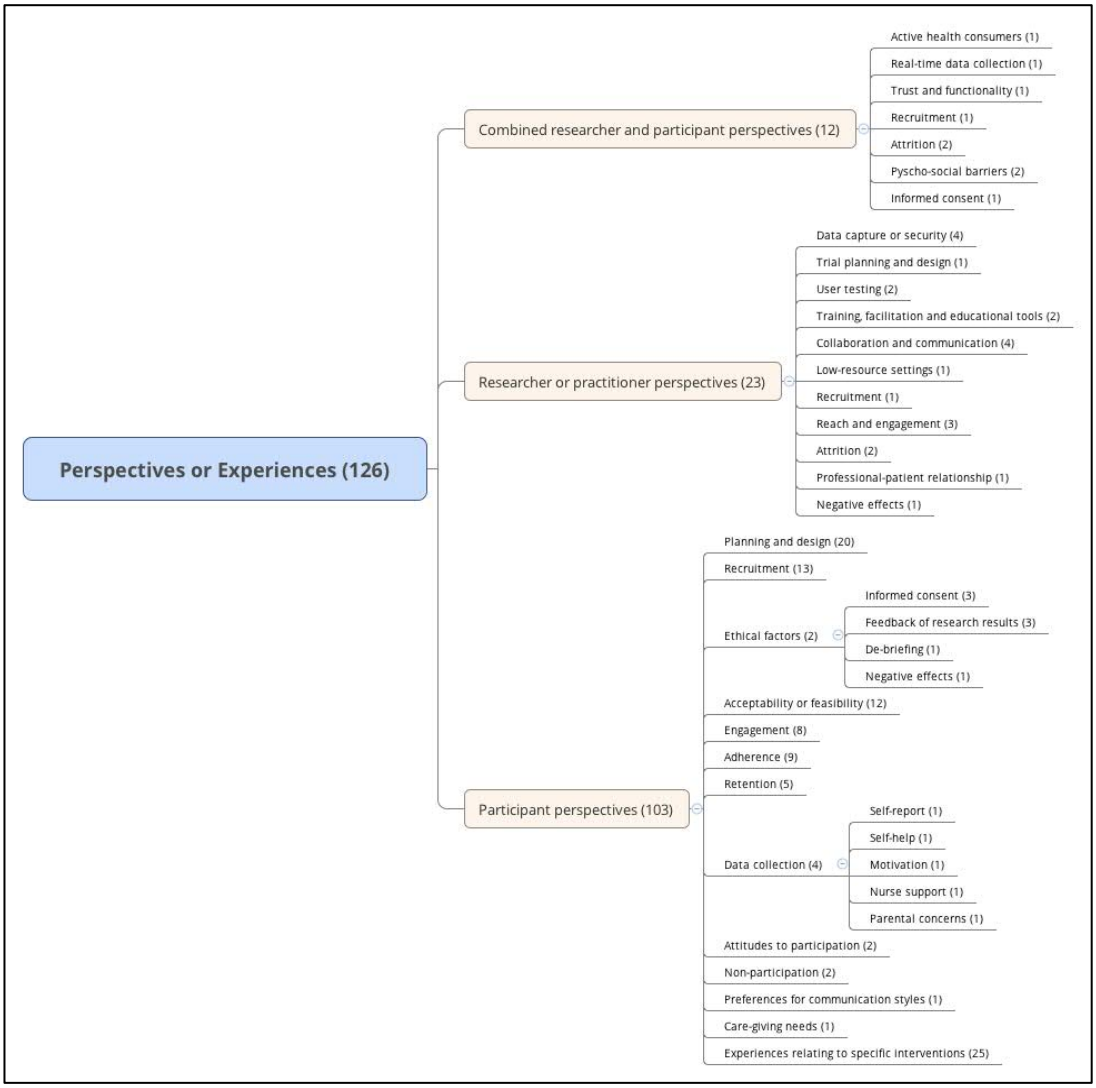

Figure 4.14 Map: perspectives or experience

4.8.11.1 Combined researcher and participant perspectives

Twelve studies reported both researcher/practitioner and participant perspectives, including the concepts of active health consumers [398]; real-time data collection [275]; trust and functionality [399]; recruitment [176]; attrition [352, 400]; psycho-social barriers [224, 400]; and informed consent [371].

4.8.11.2 Researcher perspectives

Concepts relating to data capture or security were identified [275, 401-403]; trial planning and design [172]; user testing [157, 159]; training, facilitation, and educational tools [179, 352]; collaboration and communication [170, 400, 404, 405]; and low-resource settings [403].

Researcher perspectives related to recruitment [224]; reach and engagement [308, 399, 406]; attrition [352, 400]; professional-patient relationship [400]; and negative effects [148].

4.8.11.3 Participant perspectives

Themes identified in qualitative studies reporting participant experience included planning and design [407, 408], and recruitment [234, 381, 409-419].

Ethical factors were identified [144, 370], including specific themes of informed consent [133, 383, 389]; feedback of research results [392, 394, 420]; de-briefing [391]; and negative effects [421].

Participant perspective themes relating to acceptability or feasibility [158, 161, 247, 299, 301, 304, 413, 422-426]; engagement [304, 316, 413, 427-431]; adherence [329, 338, 343, 345, 351, 355, 399, 426, 432]; and retention [335, 341, 354, 364, 433] were identified.

General data collection concepts were coded [268, 278, 389, 434]; and also featured self-report [435]; self-help [436]; motivation [338]; factors relating to nurse support [437]; and parental concerns [438].

Qualitative studies reported on attitudes to participation [412, 413]; non-participation [414, 439]; preferences for communication styles [440]; and care-giving needs; and reported on experiences related to participation in specific intervention trials [405, 408, 421, 424, 441-461].

4.8.12 Setting or participant characteristics

Eighty-five studies reported on trials undertaken in specific settings or on participants with specific characteristics.

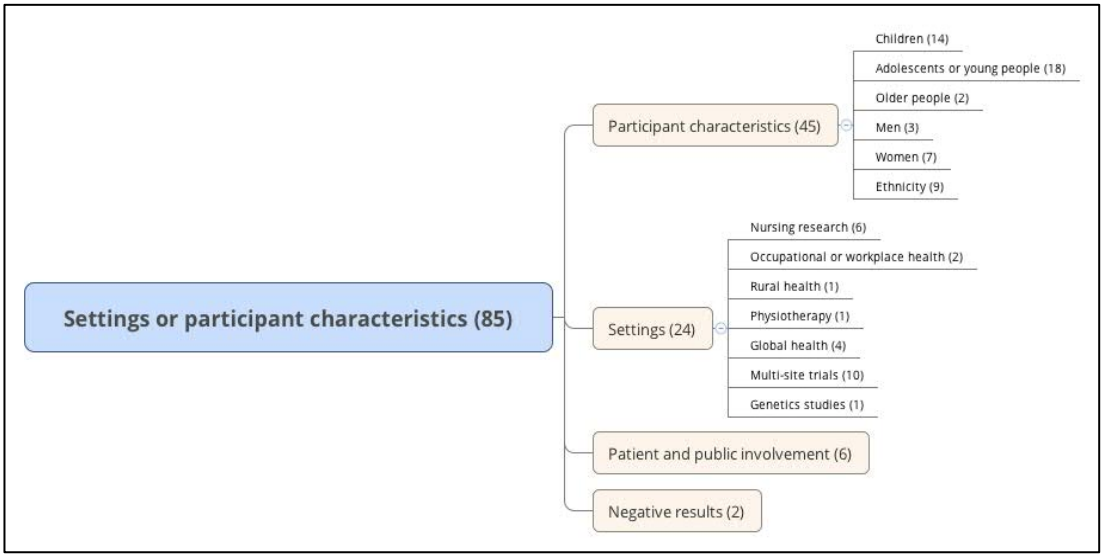

Figure 4.15 Map: setting or participant characteristics

Fourteen studies focused on children, and 18 on adolescents or young people. Two studies reported a specific interest in older people. In terms of gender focus, 3 studies reported a specific interest in men, and 7 related to women (not including papers coded specifically to women's health).

Nine studies reported an interest in ethnicity, and 4 in global health concepts. Six studies included the concept of patient and public involvement; ten reported aspects of managing multi-site trials, and two on the concept of negative results. Six studies reported from the specific perspective of nursing research, one on physiotherapy, 2 on occupational health or workplace health, one study on rural health, and one genetic study setting.

4.9 Discussion

4.9.1 Inclusion of studies

Due to the large number of results, it was necessary to restrict inclusion and analysis to reports of methodological and qualitative studies. This meant that relevant data embedded within the reports of individual trials, although potentially useful, was not included. In future studies, the emerging technique of text-mining could be used to search for relevant data embedded within the reports of individual trials. The potential to update ORCHID and mine the included studies for specific methodological issues will be included in recommendations for further research.

4.9.2 Coding

Finding a suitable coding structure for the map proved to be complicated. Using the scheme derived from ORCHID provided an initial framework, but the limitations of using this became apparent as screening and coding was undertaken. Included studies used a wide variety of terminologies and approaches to describe methods and findings, and the amount and type of information contained in abstracts was also a limiting factor. Studies were retrieved from a wide range of sources, and contained different epistemological perspectives on research methods and language. This meant that the code sets within the review had to be constantly iterated, and revised several times. This also led to issues in judging appropriate sensitivity and specificity for allocating codes, and to a tendency to apply too many codes for each study, which contributed to the complexity of coding and difficult in arranging the results in a logical way.

Following the completion of screening all the code sets were subject to a final review, and re-coded where necessary. This was driven by the need to present the findings in a pragmatic manner relevant to the review question, and the core researcher audience. This may have led to coder bias in this highlighted selection, however the full list of coded papers is available, and items can be selected via cross-cutting topics or themes.

4.9.3 Dates of studies

Some papers, particularly those focusing on specific software products, or web sites tools, were of interest only in a historical context, and not relevant to current research practice. However, due to the fact that some concepts remain relevant, despite the date of the study, different cut-off periods for inclusion were set for different codes. The studies excluded from inclusion in the analysis for this reason are available via the ORCHID database.

Some issues raised in very early studies, for example in the key papers, have had less additional investigation than other factors. Nosek [144] raised the issue of ‘absence of researcher’ in an early paper on internet-based trials in 2002, which was not considered again until a study by Wu in 2014 [171]. Similarly, McAlindon conducted a feasibility study on glucosamine for the treatment of osteoporosis of the knee in 2003 [135], however the number of reports of non-behavioural trials identified in ORCHID is much less prevalent. Trials using psychological or behavioural interventions account for approximately 46% of included studies.

This may reflect a number of issues relating to the research-practice gap. Poor reporting of studies, as found during the searching and screening for this descriptive map, may prohibit easy identification or sharing of concerns and

knowledge. Publication bias, and the reluctance to publish all trials, regardless of the direction of the results, may also inhibit learning about what works in trial methods, or help ensure that only questions of known uncertainty are investigated. A resistance to the publication of negative results may have led to relevant studies being missed due to an unwillingness to report on what are perceived as common problems. A theme concerning the need to share researcher knowledge emerged, and a range of factors identified in the mapping exercise will be explored through systematic synthesis in the next chapter. The need for the development of better protocol and reporting standards for online trials indicates that there are ethical as well as practical concerns around methods and quality. This will be important to consider, if researchers are to meet the three requirements for internet-based trials outlined by McAlindon of 'feasibility, efficiency, and validity' [135].

4.9.4 Ethical issues

Internet-based trials are likely to share the ethical issues found in traditional clinical trial methodologies, but may also engender a new set of concerns. The findings of the mapping exercise raise some uncertainty about whether the ethical implications of internet research have been explored with researchers and participants. It would be helpful to determine how this may affect motivation and participant experience. This could help ensure that future strategies for the conduct of good quality research, including that which is patient-led, are informed by appropriate qualitative research.

Finally, the development of a more consistent taxonomy and use of terminology within the research community could be informed by this descriptive mapping process. This could be further enhanced by taking a co-production

approach, involving researchers, funders, patients and public communities, which could also help the promotion of better reporting and dissemination.

4.9.5 Limitations

4.9.5.1 Search strategy and sources

The broad nature of the topic meant that it was not possible to search all the potential databases and sources, and therefore the search strategy was restricted to the major health databases. As with the previous ORCHID search, the broad concepts also restricted the precision of the search, and this was compounded by poor indexing and reporting.

4.9.5.2 Screening

Due to the number of results (16248), and the nature of the mapping review, double screening was only undertaken for 10% of the search results, which may have led to bias. The double screening was done in two stages, with an increase in inter-rater reliability of 60% between the two batches (266/700 and 107/700). Resolution was achieved without the need for a third reviewer.

4.9.5.3 Coding

As with the screening of results, coding was primarily undertaken by the author, with a small sample of 10% being double coded by another researcher. The coding structure was iterated to reflect the concepts in each study, however lack of clinical or subject expertise may have led to some studies being coded to the wrong topic or intervention area. Challenges were also experienced due to the wide nature of the disciplines and terminologies used to describe studies, and perspectives may not have translated accurately across studies.

4.9.5.4 Patient and public involvement

At the planning stage, it was envisaged that participatory methods would be used to engage with key partners and stakeholders actively throughout the mapping process. This was possible with other researchers, but not directly with patients or the public due to constraints of time and access to resources.

4.10 Conclusion

Too much current research is not informed by prior research, and leads to waste of time and resources, not least of those who volunteer to participate. The development of a descriptive map to review the existing evidence on the conduct, challenges and experiences of internet-based RCTs identified a range of themes for further investigation. Mapping methods used in this study have identified a range of existing methodological research relevant to trial researchers, but also qualitative studies with themes relating to researcher and participant experiences of conducting or taking part in trials. In order to improve understanding of these factors, a systematic synthesis of the relevant evidence was deemed to be a useful and instructive next step. As well as increasing the understanding about the potential benefits, or barriers, to participation in internet-based trials, it could also inform further primary research, help reduce uncertainty, and become an additional resource to share learning.

4.11 Chapter Summary

- The need to bring together different types of knowledge to inform policy and practice has led to the development of new techniques for evidence synthesis. These enable reviewers to address a broader range of questions than traditional quantitative systematic reviews or meta-analyses.
- The benefits of a two-stage systematic review design include help in managing the scope and resource costs of a review, and in identifying uncertainties for further synthesis or primary research.
- A descriptive mapping methodology was used to identify and categorise studies about the use of internet technologies in RCTs, to establish the size of the literature, key themes and concepts.
- The process builds on the methodological studies retrieved during the development of the ORCHID database, supplemented by additional searches. The broad scope of the topic required the use of a wide range of search techniques and sources, and a range of techniques to optimise sensitivity.
- The map identified 406 relevant studies, dating from 1997- 2016, with the largest number of studies originating from the USA (178), followed by the UK (57), Australia (43), The Netherlands (29), Germany (20), and Canada (18). Included studies were mapped and coded using an iterative thematic approach.
- The map helps build an understanding of the potential methodological, ethical, technical or experience-based issues for both researchers and participants engaged in this type of study, to inform practice and provide focus for further methodological research.

- The findings raise some uncertainty about whether the ethical or experience-based implications of internet trials have been fully explored with researchers and participants, and how this may affect trial conduct and participant participation.
- In order to further improve understanding of these factors, which might influence the likelihood of participation in internet-based clinical trials, and therefore improve trial success, a systematic synthesis of the evidence was planned. This would also help to inform further primary research, as well as become a resource to share learning.
- The results of the mapping exercise provide the basis for refining the topic and scope for the second stage of the review.

5 Factors influencing patient and public experience in internet-based RCTs: a qualitative evidence synthesis

5.1 Overview of Chapter

This chapter reports the second part of a two-stage systematic review on the methods, conduct and experiences of internet-based clinical trials. It uses qualitative synthesis methodology to explore and analyse the views, attitudes and experiences of participants and researchers.

5.2 Background

Research conducted to explore the views, experiences and preferences of participants in clinical trials has identified a number of factors which influence recruitment, engagement and attrition [78]. There has been less consideration about how these factors translate into an internet-based trial setting, or to determine any emerging themes. Understanding these factors in more depth could help researchers design studies that take the preferences and behaviour of participants more fully into account, both from an ethical and practical perspective. More emphasis is also being placed on the importance of patient and public involvement in research, and how this might lead to an increase in public-led approaches to trial design and conduct. One of the benefits of using technologies, the flexibility and convenience of new channels of communication, could be seen as a possible facilitator in this and other trial processes. To help establish what is already known, this chapter will explore evidence relating to the views, attitudes and experiences of participants, the public, and researchers in relation to internet-based clinical trials, so that these factors can be better understood. Qualitative studies identified in the descriptive mapping exercise reported in the previous chapter (Fig 4.14), provide a starting point for more exploration of this theme.

5.2.1 Rationale for Qualitative Systematic Reviews

Acceptance of the importance of qualitative research in health care, and a growth in the numbers of published qualitative studies, has led to a growing interest into how this evidence could be combined, using systematic methods, for better translation into practice. Systematic reviews have been crucial in the development of evidence-based healthcare and have spread to other domains such as social care and education, helping to make sure that research is set in the context of what is already known. Developing new techniques to address a broader range of questions than was typical in systematic reviews has meant facing a range of methodological challenges, for example, integrating data from experimental studies with data from other study types, and conducting qualitative syntheses.

There is debate about the nature of qualitative synthesis and the different approaches it can take [108, 462]. As demand increases there is a need to increase understanding of the theory and methods, and to specify the methodological rigour and skills required. Whereas in quantitative synthesis results are based on meanings derived from numbers, data collection results in numerical and standardised data, and analysis is conducted through the use of diagrams and statistics, qualitative synthesis is based on meanings expressed through words, data are non-standardised and requires classification into categories, and analysis is conducted through the use of conceptualisation. Qualitative synthesis can be approached through either a deductive or inductive perspective, and reviewers need to consider analytical strategies and procedures that commence with theoretical propositions to test against the data collected. A range of inductively based analytical strategies and procedures, some of which

are likely to combine deductive and inductive elements need to be considered. In terms of methods, qualitative synthesis is a more exploratory and iterative process, and less well defined or agreed than quantitative methods. However, as more knowledge is shared, and awareness of the benefits realised, training and skills development initiatives have helped increase understanding of, and access to, this form of research synthesis.

5.3 Aim

To explore the views, experiences and expectations of participants and researchers about taking part in internet-based clinical trials, and how these might impact on the design, conduct and improvement of research.

5.4 Methods

A systematic review and thematic synthesis of qualitative literature was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [463]. The review was informed by the scope, definitions and results undertaken in the descriptive mapping stage, described in the Chapter 4. An analytical framework was developed to draw out the key messages about internet-based controlled clinical trials from the perspectives of the public, participants, and researchers.

5.4.1 Identifying studies

Qualitative studies identified in the descriptive mapping exercise were retrieved, and the search strategy updated and re-run prior to screening. Reference checking was undertaken for key papers, and citation searching carried out using Web of Science, and via the '*Related Citations'* facility in PubMed. No date or geographical limits were applied.

5.4.2 Selection of studies

Inclusion and exclusion criteria for the in-depth synthesis was informed by the review question, and are provided in Table 5.1.

Inclusion criteria • Studies using qualitative methods to explore recruitment to an internet-based clinical trial where the research includes attitudes, views or experiences • Studies exploring participant experiences of taking part in an internet-based clinical trial, including factors relating to engagement, adherence, and attrition • Studies which use qualitative methods using in-depth or semi-structured interviews and/or focus groups • Studies relating to a health condition or topic, where the participants are patients or members of the public. • Studies published in English Exclusion criteria • Studies not related to an internet-based randomised controlled trial setting • Studies which solely report on the effectiveness of an internet-based trial intervention • Studies reporting on a health care setting or condition or treatment where the primary participants are not patients or the public • Studies not reporting primary research • Studies which do not use qualitative methods using in-depth or semi-structured interviews and/or focus groups • Studies where the topic of the qualitative data is not in scope • Studies where no primary data, or links to data, are included in the results • Exclude if the topic of qualitative data is not in scope (health and wellbeing) or participants are not members of the public. • Exclude report if no primary data is included in the results, and no link to data is available

Table 5.1 Synthesis inclusion and exclusion criteria

5.4.3 Screening

Screening was conducted by the author, and a second reviewer undertook a sample screening of 20% of results for quality assurance purposes. Decisions on the double screened set were compared. Consensus was reached so review by a third reviewer was not necessary.

5.4.4 Quality appraisal

The assessment of quality for qualitative studies encompasses a wide range of approaches and views, and a number of appraisal and reporting checklists have been developed [464-466]. No clear consensus has been reached on whether assessment of quality should be undertaken at all, or if so, what the most appropriate methods should be. However, it is still regarded as an important part of a transparent and systematic process by organisations such as the Cochrane Collaboration, and EPPI-Centre, who recommend the assessment of internal and external validity within included studies [467]. For this review, the studies were assessed for quality and rigour using the NICE Quality Appraisal checklist code set available within the EPPI-reviewer4 software, which is based on the NICE Public Health Guidance methods manual [468]. The quality assessment is provided in Appendix 5A. No studies were excluded on the basis of this assessment.

Although less common in qualitative synthesis, the extent to which studies include data relevant to the review question can be assessed by undertaking a sensitivity analysis [108]. Similarly, the CERQual (Confidence in the Evidence from Reviews of Qualitative Research) approach to assessing the confidence of review findings was considered [465]. Given the small number of studies and the

broad nature of the review question and findings, this approach was not adopted for this review.

5.4.5 Data extraction

Data on characteristics of the included studies were extracted using a data extraction form, including the study research question; study site and population; sampling and data collection approach, data analysis methods, participant characteristics, and a summary of main findings (see Table 5.2). One of the features of qualitative synthesis is the iterative nature of the process which can mean that the data extraction process can shift into analysis [108], so it was decided to keep this initial data extraction form relatively simple and to then extract the data on findings for the more complex thematic analysis and coding. In addition, data within reports of qualitative research can be complex to extract, where description of methods may be poorly reported [469]. Initial data extraction using the master extraction form was carried out by the author, and checked by a second researcher. Data extraction for coding and analysis was informed by the purpose of the review, which was to identify findings relevant to researchers engaged in internet-based RCTs. Data related to other factors present in the study reports, and which therefore did not relate to the review question, was not extracted.

A key question in qualitative synthesis concerns what constitutes 'data' in the identified studies [108]. Definition of data is important in relation to qualitative synthesis, and can impact on inclusion criteria and data extraction. For the purposes of this review a selective approach was taken, and a definition used that would include data in the primary studies in the form of quotations (1st order constructs) as well as key concepts or findings (2nd order constructs). For this

second round of data extraction, data were extracted for coding and analysis from the included studies by the author, and a sample checked by a second researcher. The full set of data is provided in Appendix 5B.

5.4.6 Data coding and synthesis

The extracted data were analysed using line by line coding, and key themes and concepts established. Initial coding was undertaken by the author, and a second reviewer conducted an independent set of initial codes. These were discussed to identify similarities and differences, and the coding set updated accordingly. The author continued with the development of new codes and the translation of concepts across studies with a final discussion with the second reviewer for quality assurance purposes. The EPPI-Reviewer4 software was used to conduct and manage the qualitative data analysis, using an initial coding scheme based on the framework established in stage one of the review. The use of software can facilitate the development of themes through coding, and also allow reviewers to examine the contribution made to their findings by individual studies, or groups of studies.

This process of thematic synthesis was based on established methods that involve the development of descriptive themes and the generation of analytic themes. This iterative approach involved reading and re-reading the included studies, data extraction and coding and interpretation. Studies were coded, and then codes reviewed across all studies, and then cross-checked against the primary study data. The iterative and inductive process was repeated in cycles in order to consider the emergent analytic themes from the perspective of the review question.

The core themes were used to generate a framework to assess the findings in relation to the relevant trial stage or methods. These themes were then used to identify barriers and motivators concerning internet-based trial recruitment and conduct, from the perspective of helping researchers understand the major issues and to address the main review question.

5.5 Results

One hundred and five qualitative studies from the results of the descriptive map and update search were imported. Citation searching identified a further 3 studies. Included studies were screened on title and abstract, and 62 excluded. The 46 remaining studies were then screened in full-text, and a further 32 excluded leaving a total of 15.

Ten main themes emerged from the studies exploring participant and researcher views and experiences related to internet-based clinical trials: (1) Choice, consumers and expectations; (2) Autonomy and self-efficacy; (3) Perceptions of roles and relationships; (4) Information as an intervention; (5) Making it personal; (6) Obligation or burden; (7) Feeling safe and secure; (8) Being supported (9) Technology, time and place; (10) Ethics and informed consent.

The themes are presented below with core extracts from the included studies. Some of the findings reported in the primary studies included aspects that are applicable to any clinical trial, particularly those relating to motivation, engagement and ethics. All of these factors were included in the analysis, but only those findings judged to be relevant to online trials as well are included in the results below.

Reference and Setting	Aims	Sample characteristics	Patient group	Technology delivered intervention	Time point of data collection	Data collection method	Data analysis method
1.Advocat & Lindsay (2010) Australia	Experiences of participant in internet-based mental health trials	2 men; 8 women; 20-66 yrs (mean 45), 9 Anglo-Aust, 1 Chinese-Aust	People with panic disorder	CBT for panic disorder 12-week computer programme	At trial completion	Semi-structured interviews	Two step coding method
2. Bendelin et al (2011), Sweden	Participant views of internet administrated guided self-help treatment for depression	6 women; 6 men; 20-62 yrs old (mean 36.3) Swedish	People with mild to moderate depression	Internet Based CBT for depression	8-10 months after treatment had ended	In-depth face-to-face interviews	Thematic analysis and Grounded theory
3. Bjork et al (2014), Sweden	Explore women's' experiences of Internet-based treatment of stress urinary incontinence	21 women, 18-70 years, ethnicity not stated	Women with stress urinary incontinence (SUI) at least once weekly	Internet-based support (email) and postal support	After the 4-month follow-up	Semi-structured telephone interviews	Grounded theory
4. Bossen et al (2013), Netherlands	Explore patient, intervention, and study characteristics that facilitate or impede usage of a Web-based physical activity intervention for patients with knee and/or hip osteoarthritis	199 participants, 50-75 yrs Subgroup of 15 from intervention group took part in qualitative interviews	People with hip and/or knee osteoarthritis	Web-based physical activity intervention	1 year after being assigned to the intervention	Questionnaires and Semi-structured face-to-face interviews	Deductive and inductive content analysis & grounded theory
5. Donkin et al (2012), Australia	Explore what influences persistence with online interventions	12 participants aged over 45, gender and ethnicity not stated	People with comorbid depression and cardiovascular risk factors	12-week online CBT intervention for depression	Between 6 and 12-month follow-up stages	Face-to-face and telephone Semi-structured interviews	Grounded theory
6. Gerhards et al (2011), Netherlands	Explore patients experience and reasons for low treatment adherence	9 men; 9 women, (mean 43.6), ethnicity not stated	People with depression	Colour your Life 8-week computer programme	Up to 1 year from start of study	Semi-structured interviews	Grounded theory
7. Johansson et al (2015), Sweden	Explore participants' experiences of non-adherence	1 man; 6 women, 21-69 (mean 39.3),	People with generalised	Internet-delivered CBT for	After the participants had	Semi-structured interviews	Grounded theory

	to internet-delivered psychological treatment	ethnicity not stated	anxiety disorder	generalised anxiety disorder	decided to leave the treatment		
8. Morgan et al (2011), Australia	Report the perceptions and experiences of men who enrolled in a weight loss program	18 men, aged 18-60 years (mean 37), ethnicity not stated	Overweight/ obese men	SHED-IT (Self-help, Exercise, Diet &Information Technology) program	2 months after completion of the SHED-IT trial	Semi-structured interviews	Thematic analysis
9. Nicholas et al (2010), Australia	Explore the predictors of attrition/non-adherence to an online psycho-education program	17 men; 22 women,	People newly diagnosed bipolar disorder, who had dropped out of the study	Online psycho-education program (8 modules)	At 6 month follow up point, participants who did not complete the program were contacted.	Semi-structured telephone interview	Thematic analysis
10. Sánchez-Ortiz et al (2011), United Kingdom	Develop an in-depth understanding of the views and experiences of people undertaking internet CBT for Bulimia	9 women, mean age 23.2, 5 were British and four were international students	Students with Bulimia Nervosa:EDNOS (Eating Disorder not Otherwise Specified)	Internet-based cognitive behavioural treatment package (Overcoming Bulimia online)	4 participants had finished all of the iCBT sessions and 5 were halfway through the treatment	Semi-structured, open ended interviews & questionnaires	Thematic analysis
11. Short et al (2014), Australia	Explore attributes that may influence user engagement of a web-based physical activity intervention for middle aged men	20 men, aged 35-54, ethnicity not stated	Middle aged men	IT-based physical activity and nutrition intervention: ManUp RCT	Throughout period of main ManUp RCT.	Semi-structured telephone interviews	Thematic analysis
12. Todkill & Powell (2013), United Kingdom	Explore participant motivations and experiences of a large fully automated internet RCT	2 men; 18 women, aged 20-64, ethnicity not stated	General population	Online CBT tool to improve mental wellbeing, as part of the PsyWell RCT	After the second follow up	Semi-structured telephone interviews	Framework approach
13. Tonkin-Crine et al (2013), United Kingdom	Explore patients' views and experiences of using a CBT-based website to facilitate self-management of IBS	15 men; 16 women 34-60yrs (mean 51) 28 White British, 2 White Other, 1 unknown.	People with IBS	Web based CBT self-management program (Regul8) for managing IBS symptoms	When participants had finished, or were close to finishing the trial	Semi-structured interviews	Inductive thematic analysis

14. Wood et al (2011), United Kingdom	Explore acceptability of and barriers to online consent in large scale, population based genetic studies	21 men; 21 women, aged 20-69	General population	N/A	Data collected by direct approach at 6 Cafés, Cardiff	Semi- structured interviews	Thematic analysis

Table 5.2 Characteristics of included studies

5.5.1 Choice, consumers and expectations

A common theme across many of the studies relates to the concept of choice on whether to take part in a trial, and suggest that modern perceptions of consumerism impact on this choice. Deciding to participate in any clinical trial involves a choice but less often involves choosing a specific mode of intervention. This was interpreted by researchers within some studies as being more of an active choice of therapeutic experience for participants, where behaviour within the online trial setting as a health consumer was experienced in much the same way as other day-to-day activities, such as in seeking health information. Findings in the studies suggested that participants were demonstrating an active choice in seeking access to interventions to suit their perceived needs; or as a way of attaining what they saw as their 'rights' to specific treatments or combinations of treatments,

> *"The participants often understood their participation in the trials as just one more way that they could exercise their choice, or even their right, to seek out appropriate expert assistance". (Advocat 2010: CBT for panic disorder: Australia)*

Participants may also be choosing to join a trial because they perceive it as a way to gain access to a specific expert,

> ***"****Indeed, the power to choose may involve shopping around for the right expert. When asked if she felt responsible for helping herself feel better, Robyn, a middle-class woman in her early 40s said 'yes', and explained how she chose treatment products from a variety of experts. "I felt like I was dealing with the mental you know the mind side of it by doing this, the physical side with the chiropractor. And the kinesiology was tapping back into perhaps the root of the problem and try and work out those points in my life that created that fear so I was taking care of how it began, the physical side and the computer side was the today and focusing and all that stuff. So yeah, covering all aspects of what needed to be done for a cure". (Advocat 2010: CBT for panic disorder: Australia)*

Choosing to participate in an internet-based trial could be influenced by previous experiences when seeking care, by specific personal circumstances, or the relationship with health status or condition. This could relate to a negative experience in another health care setting,

> ***"****Some of the women said that talking about [Stress Urinary Incontinence] with a health care provider face-to-face was embarrassing and exposing. The Internet treatment offered an opportunity to seek help with less embarrassment. Having sought care on previous occasions, some women felt they had not been taken seriously or had even been ignored. On mentioning their incontinence, they had experienced a dismissive and sometimes embarrassed attitude from health care providers: 'Well, I haven't explicitly looked for it, but since I was there I asked them and told them about my problems, but they didn't think there was much to be concerned about". (Bjork 2014: Internet-based support for Stress Urinary Incontinence: Sweden)*

Recruitment to an internet-based trial could provide immediate access to treatment through trial participation, following exposure to trial publicity while engaged in other internet-based activities, outside the confines of direct contact with the health system. While this can also be seen in internet recruitment to non-internet-based trials, it is a strong factor to consider,

> *"After his (husband's) death I was, well in a state of great grief, so browsing the net, I came across your site. I don't know whether it was through looking at sites to do with bereavement or whether it was a second phase of my sort of emotional set up, and I started to look, once I had looked at everything to do with bereavement I then moved on to positive thinking, trying to access something that might actually help, and I came across your research project and I thought it was based on CBT which I knew a little about, not much but a little and I wondered if that might help me, and that's why I accessed it and that's why I decided to go through with it to see if it would help". (Todkill 2013: CBT for Mental Well-Being: UK)*

The studies show that perception of the health condition may impact on participation, such as concerns experienced about the need or justification to seek treatment,

> *"I think that I can deal with it myself with such a thing like this programme […] I don't like to go to doctors. I feel like very hypochondriac […] I always think 'let's wait, let's wait'. […] I fear that the doctor can judge or say.. 'why you are coming here?" (Sánchez-Ortiz 2011: CBT for Bulimia: UK)*

Choosing whether or not to accept the treatment intervention emerged as an important theme, with researchers perceiving that some participants felt internet-based treatments did not constitute 'proper' treatment when compared with direct contact with a health professional, or alternatively considered an online trial an easier option for something they had been avoiding. This was compared in two studies as similar to the desire to find a "magic pill" or "wonder drug", and presents a challenge to researchers in that these can be seen as either positive or negative choices for participant to make,

> *"We identified three common obstacles that appeared to deter participants from engaging with the website. The first was an ongoing search for a 'wonder drug'... They were hoping for a treatment that would enable them to 'by and large lead a normal life' (P25) without disrupting their daily lives or taking time away from preferred or prioritized activities such as work and leisure" (Tonkin-Crine 2013: CBT for Irritable Bowel Syndrome: UK)*
>
> *"The Internet, then, can be seen as offering a particular kind of product, one that was found to be a preferred treatment choice in some ways, and one that offered participants increasing levels of responsibility for their involvement in the trial and their efforts to overcome their panic". (Advocat 2010: CBT for panic disorder: Australia)*

Once within a trial environment, choice becomes a facet of the way the participant interacts with the intervention. Perceptions about their health status

and experience of the condition can be important factors in how participants feel about engaging with the trial intervention,

> *"Participants who experienced episodes of mania during the study discussed how they became distracted by their manic symptoms and were unable to complete the online modules. 'My highs interrupt my ability to see things through, and I get caught up in my highs .. Thus, the nature of the illness itself made it difficult for some participants to continue their involvement in the program. This was the most common theme in terms of reasons for discontinuation". (Nicholas 2010: Psycho-education for bipolar disorder: Australia)*

The theme of choice can also extend to how participants make choices when performing internet-based tasks associated with the trial, in the way that they might do when engaged in other internet-based activities, and this can also impact on engagement and adherence,

> *"Due to negative experiences with some components (e.g. homework or mood diary), completers did not necessarily use all the components of each course session. These completers tailored the CCBT program to their own situation by selecting only those components experienced as beneficial. 'The most important thing for me was the theory and I did that in my own way, I did something with it and to also fill in a diary and make tasks, that was too much for me". (Gerhards 2011: CBT for depression: The Netherlands)*

In one study researchers compared the way that participants approached participation in the same way they would consume self-improvement products and activities. The nature and structure of the trial supported this attitude of consumerism, because of the very way it wanted to be perceived as similar with these other activities,

> *"We argue that while the participants straddled the role of participants in a trial and clients seeking mental health treatment, the ways in which they participated, the structure of the trials and the approaches taken by the researchers constituted participants as consumers and encouraged them to engage with the trial as they do other self-improvement activities". (Advocat 2010: CBT for panic disorder: Australia)*

On the one hand this could provide a more naturalistic setting for an intervention, and offer more control for participants, potentially helping researchers understand how well study findings could be translated into real-life settings. However, this same phenomenon can also be applied to the decision to leave a trial, which some researchers perceive as a "choice" made by participants who view the internet as separate from their perception of what should constitute treatment. The expectations of participants are driven by their existing relationship with the internet. Indeed, participants may see the combined elements as a 'package', which could have implications for trial design and management if unintended,

> *"Consequences of prioritizing a medical solution to IBS included seeing the website as unimportant within the trial and not seeing the website as a form of management in its own right. Indeed, 2 participants reported having made a conscious choice to abandon the website because they had stopped taking the trial medications". (Tonkin-Crine 2013: CBT for Irritable Bowel Syndrome: UK)*

5.5.2 Autonomy and self-efficacy

Participating in an internet-based trial generated experiences of greater autonomy and self-efficacy, and a consistent theme emerged across the studies in the way participants felt empowered by their experiences of taking part. This was expressed in terms of gaining or re-learning self-control, or improved self-esteem, often combined with being provided with usable tools,

> *"it took the approach that this is your responsibility, off you go, go and do it, with enough information to be able to do that." (Morgan 2011: Self-help for weight loss in obese/overweight men: Australia)*

How participants might be empowered through this increased sense of autonomy and self-efficacy, and how this might increase motivation to engagement and adhere to the trial is evident. A sense of online community can be engendered by

the intervention mechanism, combining with new knowledge, and this could be activated by themselves,

> *"The women were empowered by the treatment programs; the discovery that they were not alone made them see themselves as part of a group, and this new knowledge helped them feel less exposed in their everyday lives". (Bjork 2014: Internet-based support for Stress Urinary Incontinence: Sweden)*
>
> *"I sometimes find it difficult to sit down and talk to someone, who'd try to understand me, and this way I got to work with myself...in a completely different way". (Bendelin 2011: CBT for depression: Sweden)*
>
> *"Some interviewees pointed to positive and/or stimulating aspects of doing a therapy in your own time, sitting behind your own home computer. These aspects concerned freedom, enjoying computer work, anonymity and being yourself. You could make up your own mind when you did something and for how long and what you do. And you're completely free to do whatever you want". (Gerhards 2011: CBT for depression: The Netherlands)*

However, this reliance on self-efficacy could be problematic for some participants, and could lead to low adherence or dropping out of the trial as an easier option. Poor adherence may be particularly prevalent in interventions relating to behaviour change, a challenge in traditional trials of this nature, but heightened by the setting,

> *"Determining workload and work pace on their own appeared to be an obstacle and was often the reason why participants did not complete modules or dropped out of treatment altogether. Deciding not to continue working with the material seemed to function as a way of handling difficulties". (Bendelin 2011: CBT for depression: Sweden)*
>
> *"Some interviewees noticed that the flexibility meant that self-discipline and motivation were required to complete regular sessions. A sense that the programme was 'lower in the priority list' resulted in postponing the sessions in some participants. 'to do it at home, you come back, it's tiring, then 'you'll do it tomorrow' and then tomorrow comes and then 'I'll do it this week-end because I will understand better' and then during the weekend 'I'll go to the park' […] it's very easy if you don't have someone that says 'you have to do it right now'." (Sánchez-Ortiz 2011: CBT for Bulimia: UK)*

An increase in self-efficacy could be a powerful motivator to continue in a trial, but improvement in health status or symptoms could also lead to a decrease in motivation leading to poor adherence or attrition. This is experienced in other types of trial, but findings from the studies suggest that it may be easier to disengage from an internet-based trial. Participants found it harder to remember to adhere to a treatment regime when they experienced improvements or felt well. Similarly, an actual or perceived lack of improvement can decrease motivation, although being able to re-access or go back to online materials was experienced as a positive factor,

> ***"****Failing to improve from treatment made participants express a wish of going back and working more with the material hoping to profit from it". (Bendelin 2011: CBT for depression: Sweden)*

Although some of the studies report the view from researchers that choice is becoming an important factor in the way that internet-based trials and treatments are 'consumed', there is clearly a tension between participants with different characteristics, for instance between those happy to work on their own, and those who prefer more direct prescription. This may be an area where the characteristics of individual participants are difficult to accommodate within the structure of an internet-based trial,

> ***"****Some participants found the discipline required of the online trial freeing. Others, however, had more difficulty finding the balance between depending on the researchers and actively taking responsibility for their recovery. For example .. a 36-year-old mother of four who had previous experiences with face-to-face therapists, found the responsibility to access the website at her own pace confronting. She found that the program allowed such freedom that it demanded a type of discipline from her that she was not always able to maintain (Advocat 2010: CBT for panic disorder: Australia)*

Self-efficacy could be enhanced by the intervention after the trial has ended, when participants view the internet-based tools or resources tools as part of a future coping strategy,

> *"Interviewees talked about the problems they were still facing and how the tools they learned from iCBT were helping them to overcome these problems and could help them to cope with issues arising in the future. 'The programme was very helpful for me especially, it gives you alternatives, it gives you like tools to deal with it in the future." (Sánchez-Ortiz 2011: CBT for Bulimia: UK)*
>
> *"This response was associated with another issue raised in the interviews, whereby a number of participants stated that they would re-access the programs' information after the study was completed if/when they were feeling depressed. 'Things really improved for me…I just felt really good and didn't really feel like I had that much to offer in regard to finding out more about it". (Nicholas 2010: Psycho-education for bipolar disorder: Australia)*

This may provide an added benefit for trial participants, however, it does raise issues for researchers in terms of continuing to give access to content, and how this will be kept up-to-date, or expectations that the material will always be available. This may need to be made explicitly clear to participants.

5.5.3 Perceptions of roles and relationships

Variation in how the roles and relationships between researchers and participants were anticipated or experienced emerged as an important theme. For some participants, initiating contact with an unknown therapist was uncomfortable and led to them being fearful about the encounter. In the studies investigating psychological therapies, the relationship between the researcher and therapist role was perceived in a number of ways by participants, with varying expectations, and with some participants feeling unsatisfied with this difference between anticipated and actual therapeutic contact or experiences,

> ***"****Previous therapy experiences also meant that some had different expectations of the therapeutic relationship. The program therefore*

> *offered reminders and information, but not therapy as such. This meant that participants struggled to engage in the computer intervention and to see it as therapy. "because you have no feedback, they're like chalk and cheese really. Well, yes...it was educative, but I didn't feel like it was a therapy session". (Donkin 2012: CBT for depression: Australia)*

Some researchers perceived a tension between the concept of participants as consumers, and their expected relationship with researchers or therapists in a trial setting. Researchers felt a loss of control in how the relationships were managed, and how this might impact on the conduct of the trial,

> *"Not hearing from the participant or receiving all of the participants' questionnaires led the researchers to believe that the participants related to the trial in similar ways to how they related to other self- improvement activities in their lives, such as exercising … For example, Julia, a therapist, said 'it's very much up to them, it's like they have the power to turn us on, they have the power to make contact, it's up to them because they know it is very much [on] their own time, it's like going to the gym.' (Advocat 2010: CBT for panic disorder: Australia)*

This might cause variance in expectations between researchers and participants, with an expectation from researchers that participants should behave in a certain way, as a "good participant". Conflicts may occur if participants are perceived to be acting in a way that prioritises their own needs, rather than following the study protocol. These findings may reflect a general shift in the way that the relationship between choice and health care services are seen. Participants may anticipate a mode of communication with the researcher or therapist that is unrealistic in the context of an internet-based trial, and the unforeseen or hidden nature of the communication mechanism could lead to misunderstandings or unmet expectations, or causing extra work for participants,

> ***"****Other participants were concerned that their answers were being misinterpreted, which may have influenced their answers and therefore the time taken to answer the questionnaires or complete program activities. This was reflected in the number of emails participants sent,*

unsolicited, to the project team to contextualize their answers to the questionnaires". (Donkin 2012: CBT for depression: Australia)

***"**Some participants perceived that the therapists did not really care about their personal issues. The therapists were sometimes considered only to have the task of checking that the participants read the text modules and completed their exercises. Some participants told us that they realized that they sought different aspects of having a face to face contact after they started the ICBT .. Some described a need for a face to face contact when sharing difficult issues such as anxiety and depression. "I would have liked to have more of a personal contact, it became a little distant everything, to do this on the Internet, because it is so heavy stuff, it's nice to meet a real person when you're working with heavy things like this". (Johansson 2015: CBT for Generalised Anxiety Disorder: Sweden)*

The expectation of a treatment without a direct relationship with a practitioner or therapist in an internet-based setting can also be preferred in some cases, particularly when dealing with sensitive conditions,

"The barrier to applying for the non-face-to-face treatments offered in the RCT appeared to be lower than for ordinary health care. The women perceived the treatments as a possibility to do something about the leakage on their own. They also saw the treatments as time-sparing and easily accessible, which was appealing; 'I saw it in a newspaper and thought it was a good idea, because I didn't have the kind of trouble where I would have sought help from the ordinary health care providers. I didn't think I had that much of a problem". (Bjork 2014: Internet-based support for Stress Urinary Incontinence: Sweden)

The absence, either virtual or actual, of the therapist or practitioner was a factor across the studies. For some researchers, this emphasised the theme of the participants as a health consumer,

***"**Despite the fact of the treatment taking the form of a trial, implying that its effects relative to standard treatment were unknown and unproven, the participants approached the trials as something to consume. The fact that the trial existed almost entirely online (with the exception of the assessments) may play a role in such understandings". (Advocat 2010: CBT for panic disorder: Australia)*

5.5.4 Intervention as information

For some participants in the studies, access to the information resources made available as part of the trial became an effective treatment in itself, even if not intended as the primary intervention under investigation. The role of the internet as a key source of information in the daily lives of participants offers an opportunity for researchers to promote this as a benefit, albeit sometimes unconsciously, as part of their trial,

> ***"****While actively choosing their level of participation they sought both information and assistance in dealing with panic disorder …. The trial website reflects the shift in psychological treatment toward a rationalised, outcomes-based approach which provides information and encourages the participant to take an active role in using the information". (Advocat 2010: CBT for panic disorder: Australia)*
>
> ***"****When asked what they found appealing about the SHED-IT recruitment materials, respondents identified the perception that it would be non-intrusive, flexible, and compatible with a busy lifestyle in that it did not require extensive time commitments. 'it was just an information session and that's kind of all I think that you need". (Morgan 2011: Self-help for weight loss in obese/overweight men: Australia)*

This could be seen to have unintended consequences for testing the efficacy of the primary treatment, but may not be fully understood by researchers,

> ***"****Three participants identified gained awareness through reading the material as a main theme in their accounts of how they worked with the treatment material. However, they were not able to or did not want to put their newfound insights into practice, nor did they report that they applied treatment strategies in everyday life. Instead, they expressed that they had required a general theoretical understanding of treatment principals and/or themselves by reading the material" (Bendelin 2011: CBT for depression: Sweden)*

Participants may separate the notion of the trial from the information provided to them, indeed it may provide enough of an intervention in itself, and stimulate choice, consciously or unconsciously, in terms of the level of engagement. This

is also reinforced by differing expectations about the function of a particular medium, for instance a web-site, as opposed to the main trial intervention tool,

> *"Some participants reported ceasing to utilize the program after they gained what they wanted from it or once their mood had stabilized. Other participants indicated that they worked through the modules but did not complete the associated workbooks. 'I was so self-absorbed at the time that I was only interested in the information [rather than in returning workbooks]'. (Nicholas 2010: Psycho-education for bipolar disorder: Australia)*
>
> *"Participants' preconceptions about the impersonal nature of websites constituted a second obstacle to engagement. Some participants saw websites as a means to provide factual information and were expecting the website to provide extensive, authoritative, and new facts about IBS and its management. They were disappointed that the website did not meet their expectations: "it wasn't extensive information, it was quite limited, I think I expected more". (Tonkin-Crine 2013: CBT for Irritable Bowel Syndrome: UK)*

In contrast to seeing the internet as anonymous or impersonal, some participants experienced the intervention as having a persona in its own right, feeling that they were being responded to personally, and this motivated them to continue. This sense of help being available through the trial without the need to seek an encounter with a health professional was sometimes seen as being something that would not be warranted, showing a concern or lack of confidence in the justification of seeking help. It could on the other hand, be seen as being less intrusive,

> *"they wanted a less intrusive method of seeking help .. 'because it was Internet-based it is easier to put down and think about it and stuff that I may not wanted to have talk about, I am not a person who would go for counselling or anything, I'm just not that kind of person but I'm quite happy to put some stuff into the internet and let it tell me what I'm thinking if that makes sense, so it deals with me personally". (Todkill 2013: CBT for Mental Well-Being: UK)*

This may lower the threshold for achieving engagement in the trial and provide a benefit for researchers in terms of adherence.

5.5.5 Making it personal

Tailored messages can impact on the way that participants experience taking part in a trial, and this needs to be considered carefully by research teams. Benefits perceived as personal or family-related are known to be a motivating factor for taking part in traditional trials [470] however internet-based settings can require additional considerations, particularly in newer, less familiar fields of research, such as those involving genetics studies. One study in the sample investigated this specific area, and findings suggested that the expectations of participants of personal benefit, may be more of a challenge to meet,

> *"Respondents were often enthusiastic and interested in the study because they thought they were going to learn something about their own genes. They were intrigued about their own genetic inheritance, how their genes influence their health, and were both curious and concerned about learning something detrimental about their future health. When the interviewer reiterated the absence of direct clinical feedback in this study, respondents were disappointed and although this did not deter anyone from participating, it definitely reduced enthusiasm for engagement with the research". (Wood 2011: Online consent in population based genetic studies: UK)*

Participants in the included studies expressed a number of preferences for the way that the intervention could be tailored to their personal needs. Some felt that they could relate personally to the trial content, and that it was very relevant to them, while others reported that the trial content or the style of materials provided was 'not like me'. This could be the result of poorly tailored content, aimed at a different age group, educational level, or varying severity of the condition or symptoms, or it could be attributed to individual, personal preferences. Expectations when joining a trial may include views on how trials should be tailored or include personalised content or tools. Information provided could be perceived as either accessible or inaccessible, which could in turn impede or

promote different levels of engagement and motivation for different people. In some studies, poor experiences were reported relating to usability in terms of language, style and appeal of materials, level of complexity or number or questions, all of which could have an impact on adherence and attrition,

> *"The questionnaires included too many questions and some questions were hard to answer. Eventually I didn't want to make the effort anymore, so I decided to quit the program". (Bossen 2013: Web-based physical activity intervention for knee and/or hip osteoarthritis: The Netherlands)*
>
> ***"**the content was perceived as complex and abstract. In some cases the participants felt unintelligent for their inability to understand". (Johansson 2015: CBT for Generalised Anxiety Disorder: Sweden)*
>
> ***"**a lot of the stuff we did online was not new...and that frustrated me". (Donkin 2012: CBT for depression: Australia)*

The characteristics or values of individual participants therefore plays a major role in whether the trial content, activities or outcomes are perceived as being relevant or personal. The fact that the relevance of content can be experienced as a positive motivator or a barrier in the same trial with different participants, demonstrates the complexity and challenge inherent in designing an internet-based trial that has the flexibility to appeal to a wide range of personal characteristics,

> ***"**Many CCBT users had difficulties in translating and applying the homework assignments to their own social situation. The film fragments were partly experienced as good, recognizable examples. However, some CCBT users experienced these examples as incomparable to their own lives, which did not provide appropriate solutions for them personally. This is distant enough to be used as a mirror, and because it's the same people in the films each time this also gives a feeling of familiarity". (Gerhards 2011: CBT for depression: The Netherlands)*
>
> *"Go and find friends. I haven't got any friends (laughs), I don't need any friends. Not for me, the examples were nice. Nice okay, but not for me". (Gerhards 2011: CBT for depression: The Netherlands)*

At the other end of the spectrum, where examples were perceived as relevant, some participants wanted more of them, or more direction or prompts. Participants demonstrated an awareness that the successful delivery of an intervention through the internet might rest on personal suitability, and accepted that this was a feature of the medium,

> *"For most participants the content of the programme felt appropriate. Some said that certain aspects were irrelevant to them, but there was a general understanding that the programme had to be suitable for a broad spectrum of people. 'Parts of it are relevant and parts of it are not but I mean […] that was fine, I think if you got in your head that this is a computer programme for everyone, you just get on with it". (Johansson 2015: CBT for Generalised Anxiety Disorder: Sweden)*

The choice of language used in trial materials was cited as a factor in engagement, particularly when targeted at a specific population, such as men in a weight loss trial,

> *''So the real blokey thing about it I think when we all got together as men it is easier to have those blokey sorts of jokes and stuff, carry on a bit like that without women being there". (Morgan 2011: Self-help for weight loss in obese/overweight men: Australia)*

The re-use of materials, translated or shared from other interventions could be experienced negatively, and lead to feelings of being patronised, of content being aimed at a different age group, or being repetitive,

> *"One described it as repetitive and boring – 'sort of after a couple of weeks when the reminder came I thought oh no, not this again, you know, it wasn't holding my attention and I didn't want to log on". (Todkill 2013: CBT for Mental Well-Being: UK)*
>
> ***"**I just found the whole sort of process a little bit, um as I say a little bit sort of condescending, so you know it was sort of, it was very impersonal .. didn't gel with me at all". (Tonkin-Crine 2013: CBT for Irritable Bowel Syndrome: UK)*

Tailoring which is responsive to a range of preferences, but which also translates off-line, could promote better engagement and adherence, but is not often available within trials,

> *"Other participants said they were dissatisfied with the program because they expected personally tailored information or feedback, which was beyond the scope of the current program. I wanted something more about me specifically, as opposed to talking about general issues". (Nicholas 2010: Psycho-education for bipolar disorder: Australia)*

> *"The third obstacle to engagement related to poor perceived fit between the website and the individual and can be summarized by the phrase, 'the website is not right for me'…. Poor perceived fit was also related to perceived symptom severity and existing levels of knowledge .. participants politely suggested other groups for whom it might be more suitable, including patients with more or less severe symptoms". Tonkin-Crine 2013: CBT for Irritable Bowel Syndrome: UK)*

The extent or availability of tailoring could impact on the need for support, and this was recognised in the studies. However, this can create a tension in terms of expectations of researchers and participants, when the benefit of delivering an intervention online is seen as a way of promoting flexibility to the participant, the suggestion that a wider form of personal support would be beneficial challenges the rationale for the flexibility and efficiency of the internet-based model,

> ***"****Although the Regul8 website included tailoring by symptoms, some participants still felt that the website was aimed at people with different symptoms than themselves, either more or less serious. These assumptions could be addressed by changing the content of webpages, to emphasize the relevance to all patients or by increasing the ability of patients to skip information they already know. Participants who do not engage with certain sections of a Web intervention, for example the CBT aspects, may need further support and could benefit from one-on-one discussions with health care professionals as detailed above". Tonkin-Crine 2013: CBT for Irritable Bowel Syndrome: UK)*

Trial content or interventions being poorly experienced can be affected by the participant's skills and abilities, information literacy or by usability issues, with

participants expressing a need for more active support or guidance in using the web site or intervention tools,

> *"The content of the treatment modules was perceived as difficult to understand and process by individuals who considered themselves as having attention problems or limited reading and writing skills: 'I thought that it was too much to read, and I cannot read anything at all that I need to remember or learn. It goes in here and out there" (pointing at the ears)". (Johansson 2015: CBT for Generalised Anxiety Disorder: Sweden)*

The range of views and experiences suggest that it would be difficult for researchers to anticipate all the likely preferences and characteristics of participants. There was little data in the studies relating to how usability and feasibility testing was done. The situation was summed up by one researcher as an interdependence between characteristics and adherence, a complex area that would benefit from further investigation,

> *"These different conditions and characteristics, presented in interplaying pairs, seem to play a role in non-adherence to Internet-delivered therapy". (Johansson 2015: CBT for Generalised Anxiety Disorder: Sweden)*

5.5.6 Obligation or burden

A strong theme emerged from the studies relating to the phenomenon where participation in the trial is experienced as an obligation or burden. The sense of obligation can be in relation to the abstract concept of the research itself; to the researchers; or to the individual's sense of their own values. Although this is not specific to online trials, it contrasts sharply with the theme of autonomy or choice, and a tension which may be harder to reconcile in an online setting,

> *"The power of choice is balanced in the trials through the need for treatment and the lingering sense the participants had of their obligation to the trial" (Advocat 2010: CBT for panic disorder: Australia)*

An obligation to the trial can be projected onto participants by researchers, sometimes with very specific expectations of how the participants should behave,

> ***"****Researchers believed that active participation was essential for online treatment. For example, one researcher, Julia, was upfront about her opinion that participants should be actively participating in their treatment... In the case of these trials active participation meant regularly e-mailing the researchers and filling out the questionnaires as expected." (Advocat 2010: CBT for panic disorder: Australia)*
>
> *"Cindy, another researcher, commented that ''the [participants] think, 'it's there when I need it' kind of thing.'' Since the researchers needed the participants to use the information and complete the questionnaires, so that they could collect data for the trials, they interpreted this as a kind of lackadaisical attitude from some of the online participants". (Advocat 2010: CBT for panic disorder: Australia)*

This lack of understanding between researchers and participants is interpreted as a further misunderstanding about the nature of adherence in online trials, relating again to the concept of choice and preferred style of engagement,

> *"they reflect a common perception, which some of the participants referred to, of the infinite and timeless nature of the Internet. The Internet, then, can be seen as offering a particular kind of product, one that was found to be a preferred treatment choice in some ways, and one that offered participants increasing levels of responsibility for their involvement in the trial and their efforts to overcome their panic". (Advocat 2010: CBT for panic disorder: Australia)*

A sub-set of negative feelings or barriers to engagement was reported across the studies, expressed as guilt or anxiety. This can be more marked when the online intervention involves treatment for a psychological condition, in which these feelings are already manifested. Feelings of guilt are exacerbated by expectations that have not been clarified or shared between participants and researchers, and are attributed in some studies to uncertainty about self-commitment to the trial, or as self-judgements,

> *'I felt like I couldn't control it, it became something of a burden that was added to me, you could say that it created anxiety, one more thing that I*

couldn't do or complete, that I promised to do". (Bendelin 2011: CBT for depression: Sweden)

This contrasts with the perception of one participant who was capable of being self-judgmental about the way they had taken part, but had lacked a channel to express this during the trial,

***"**When asked if she would change anything about her participation in the trial she replied, ''I would be more prompt with my responses, I would really get into [it], I would get stuck into [it], I would read everything, I would do all of the assignments, I would do it properly.'' (Advocat 2010: CBT for panic disorder: Australia)*

The obligation to adhere to the intervention could be reduced by a perception that an internet-based trial has less reliance on resources in terms of people,

"Angie related that she started to feel better before the end of the trial and, not realising that she was enrolled in a trial which required her participation, she stopped being diligent about filling out the required questionnaires. She explained, 'because I just thought it was something on the computer and there was always going to be someone at the other end, I was a bit slack about it towards the end'. The fact that the trial was on the computer made her think that it would be there indefinitely, like many websites seem to be. Here, Angie was illustrating how some of the participants related to the Internet aspect of the trial as simply offering products to consume when they feel like it, as an extension of their daily lives, not as something distinct, requiring consistent, immediate attention". (Advocat 2010: CBT for panic disorder: Australia)

A sense of duty and commitment was a factor in encouraging adherence to the interventions, even when experienced as an unwanted task or burden,

***"**By contrast, patients who felt themselves responsible for their own progress were most likely to use the program. These individuals perceived the program as something that needed to be done, rather than appreciation or enjoyment". (Bossen 2013: Web-based physical activity intervention for knee and/or hip osteoarthritis: The Netherlands)*

'Of course, much of what I did, I did because I promised to do it (the treatment program) and then I felt like I had to do it'. (Bendelin 2011: CBT for depression: Sweden)

This sense of obligation to the researchers, and the trial itself, can impact on adherence, even with a virtual presence, once an agreement or contract is made,

> *"Those participants who perceived little personal benefit from the program reported persisting due to the perception of obligation to the researcher or the belief that their input would help the wider community. They appeared to hold values around completion and contributing to society that allowed them to continue to persist with the program". (Donkin 2012: CBT for depression: Australia)*

The lack of physical contact, or the effort required to participate, could contribute to this lack of engagement, seen as a feature or consequence of an internet-based trial, where costs are perceived as being lower and this can lead to less value being placed on the impact of non-compliance, and as easier to ignore,

> *"The sense of accountability was decreased, as there was no feedback or cost of engaging with the program. A lack of perception of the program being a therapeutic relationship and of someone relying on their attendance meant that several participants felt that they were able to put off completing the program". (Donkin 2012: CBT for depression: Australia)*

Researchers interpreted the impact of values held by participants, and compared them to how these values applied in more traditional treatments,

> *"The development of habit and the perception of the modules as needing to be done is particularly interesting given that participants were able to opt out of the trial at any stage. Instead, they conceptualized the trial as medicine that needs to be taken". (Donkin 2012: CBT for depression: Australia)*

As well as adherence to a specific trial, awareness about trials more generally was an important factor in studies. Previous knowledge of the research process helped to maintain a sense of commitment as well as a strong sense of altruism and helping others, as experienced in traditional trials. Findings interpreted this sense of participant obligation as pressure to adhere for the benefit of others,

> *"This research-related engagement appeared to be driven by an obligation to others, rather than an obligation and perception of the*

benefits that they might have received themselves. Participants reported that when they were completing a program for only themselves, program use was more ad hoc, as they believed that they could complete the program at their own pace without affecting others. However, when engaged in research, there was more pressure to complete the program in a timely manner and in its entirety to ensure their contribution was able to benefit others. 'For instance, with my [other program] I drop in and I drop out depending on my other commitments because I know that nobody else is involved but myself". (Donkin 2012: CBT for depression: Australia)

The nature of the internet-based trial, and the relationship between the commitment made to participate and its presence in participants' daily lives led to feelings of guilt, which may be more difficult for researchers to pick up in a virtual setting,

> *"Many women also mentioned a sense of guilt because of the inconsistency between their own goals for the training and their actual achievements. These women placed high demands on themselves, and wanted to do the right thing to meet the expectations they perceived from the urotherapist: 'Yes, toward the end there was a negative pressure. But it wasn't because of the emails I got, but because I felt that I should have done more, and this was important for me. And then I felt guilty about it and chose not to answer, because I felt that, no, I have to do the exercises properly now for a week before I can answer". (Bjork 2014: Internet-based support for Stress Urinary Incontinence: Sweden)*

5.5.7 Being supported

The rationale for conducting studies using the internet is influenced by a number of factors, including the type of condition; health status and type of intervention; expectations that using this medium will help deliver research at scale; for promoting recruitment; and making it easier for people to take part by increasing convenience. However, the way that support or feedback is offered or managed within internet-based trials, and how these interactions affect the conduct of the trial emerged as a key factor.

Support can take different forms, including the provision of phone lines, help desks or e-mail support; feedback mechanisms; and support in how data is

collected or the actual intervention mechanism used. In some studies participants valued having a choice of whether to receive support, particularly if it could be accessed on demand or answered particular needs, even if this was seen as a 'back-up',

> *"Interviewees expressed the importance of feeling supported by email during the treatment. Being aware that there was someone they could contact if they needed help played a crucial role, even for people that preferred not to use the support". (Sánchez-Ortiz 2011: CBT for Bulimia: UK)*

Some participants preferred working on their own, but others wanted more contact, or clearer instructions from the research team on how or when to engage with the intervention. The reasons for this were expressed as a need for direction, or a form of reassurance,

> ***"****You can't judge whether or not you're doing good. I find that difficult, I think that the most important thing is, that you can just ask a question like am I doing it right. Just a bit of confirmation that is actually the only thing. (Gerhards 2011: CBT for depression)*

Others wanted personal, human contact, reporting that this contact, as well as receiving prompts, led to better adherence. This was also interpreted as contributing to a sense of communicating more equally through an exchange of views. In some cases having no contact led to negative experiences of being involved in the trial,

> *"Next to self-discipline, a second reason for wanting support was to have personal contact. 'I think that that [personal talks] is not so easy to put off. That I put it off less easily. I think that it is nicer if you can exchange ideas.. I need to be with people, I can't just be alone behind my computer screen". (Gerhards 2011: CBT for depression*
>
> *"Without the email support maybe it would have been dry, the email support makes it more real". (Sánchez-Ortiz 2011: CBT for Bulimia: UK)*

This sense of need for a more personal relationship with the therapist, practitioner or researcher is complex, with some participants seeking a sense of reassurance which could impact on their motivation and engagement.

> ***"****Most women in the Internet group experienced the establishment of a relationship with the urotherapist. They described the relationship as both personal and distant, and said that it gave them a sense of being acknowledged and supported without being exposed. They mentioned many factors as important for the development of the relationship, including the fact that someone seemed genuinely interested in their concerns, gave them praise when they were doing well, and supported them when their motivation was low". (Bjork 2014: Internet-based support for Stress Urinary Incontinence: Sweden)*

> *"Some interviewees preferred feedback or wanted to go more in depth into the course through personal support. 'That thing doesn't talk back, I haven't got any contact with it. Whereas when I talk to you, then you react, and then you straightaway reach a much deeper level than with the computer'. (Gerhards 2011: CBT for depression: The Netherlands)*

Some participants found it useful to visualise a 'person', or to have more structure or options around the way communication was managed. These themes demonstrate how impersonal the care they were receiving could be experienced, and how this might reduce the efficacy of communication,

> *"Some participants found that their motivation for doing the sessions was related to the sense of having someone giving them support. 'I don't think I have the self-motivation to do it whereas .. it's just a computer but you know that at the end of the line there is people who were watching your responses and your progress and that's encouraging." (Sánchez-Ortiz 2011: CBT for Bulimia: UK)*

> *"this group also liked the nurse telephone support when it was available to them: 'I think I got more out of it by having even the interim call with [nurse], during it, because um, the website can't cater for everything without it being over-complex and pages and pages of options". (Tonkin-Crine 2013: CBT for Irritable Bowel Syndrome: UK)*

> *"Some aspects of the relationship were lost or became more superficial without face-to-face contact. For example, small shifts in facial expressions, body language, or intonation were missed, and for some women this led to an experience of a less-close patient–provider relationship. As a consequence, these women also felt less motivation to*

do PFMT: 'It is easier to cheat, what should I say, if you don't have a physical meeting. It gets more distant and it can be easier to skip, if you don't feel really engaged, because it becomes a more impersonal contact that hasn't got the same weight'. (Bjork 2014: Internet-based support for Stress Urinary Incontinence: Sweden)

Sometimes an absence of support was reported, with a corresponding impact on motivation. Again, as in other types of health research participants may value having personal contact with health professionals of researchers, but can be as a direct consequence of the online nature of a trial,

"*On the other hand, the Web-based character also had a downside. Some participants had a strong need for personal guidance. In the words of one participant: 'Although it was possible to fill out an evaluation form about pain and performance, sometimes I just needed a personal chat to talk about my progress". (Bossen 2013: Web-based physical activity intervention for knee and/or hip osteoarthritis: The Netherlands)*

"They felt that the computer offered little in terms of support, interaction, and feedback. Participants frequently reported thoughts of giving up on the questionnaires and the trial due to feeling that their information would be misrepresented and therefore not useful to the trial team. 'Because you need a bit of feedback...It's a bit of an empty system, because...you know...you put out a few stories about your thoughts and experiences, but you know...nothing comes back'. (Donkin 2012: CBT for depression: Australia)

The uncertainty of how much personal contact is needed is present in a number of the studies. Alternatively, for some participants there are negative aspects of face-to-face contact, and this may variation may need to be considered as an option at the trial design or acceptance testing stage,

"*I think I actually stopped going [to the face-to-face therapist] because well, you could say I was a bit caught up with the emotional type of you know, guff that they go on with in therapy and some of the questions that he asked me I kind of thought, you know, well, what does that have to do with anything, you know it was more looking at relationships and all that. I just wanted answers and I think the website gave me that". (Advocat 2010: CBT for panic disorder: Australia)*

"*The lack of face-to-face contact had both positive and negative*

consequences. Some women experienced the relationship as more harmless and less potentially judgmental, compared to a face-to-face relationship, and this made them feel freer to talk openly about the leakage: 'I mean, I think I developed a close relationship with her anyway. I mean, just because I could ask about things more directly than I normally would. And you got an answer the next day, she didn't try to escape. She was there, it was a comfort to have her there. And I knew that if I needed to ask about something, I could email her" (Bjork 2014: Internet-based support for Stress Urinary Incontinence: Sweden)

Ambivalence is expressed by participants across a number of studies, and these individual human factors feed into how motivation or engagement is experienced or accounted for,

"A few women said that it was more difficult to explain complex situations and feelings in written text than face to face. One woman expressed the ambivalence like this: 'Sometimes it can be tough to have a contact, get to the contact, sit face to face, and go there every week. It feels demanding and it takes too much time, so that was really positive. Sometimes it is good, though, to have someone to look you straight in the eyes and tell you what to do. It is easier to take it seriously. But I thought that the contact over the Internet worked really well". (I) (Bjork 2014: Internet-based support for Stress Urinary Incontinence: Sweden)

Even when the participant is communicating purely through an online interface, some perceive the presence of a doctor behind the trial, or find it difficult to distinguish the difference between the intervention activities and reporting outcomes,

"*The face-to-face screening and the Internet questionnaires were sometimes experienced as part of the treatment. Sometimes, the impact was directly visible: two interviewees confused CCBT with the Internet questionnaires. They thought that the questionnaires were CCBT. 'I thought that the computer program was the questionnaire, and the doctor. So however, I read it I thought computer program and doctor. That was it for me: questionnaire and doctor". (Gerhards 2011: CBT for depression: The Netherlands)*

"*Previous therapy experiences also meant that some had different expectations of the therapeutic relationship. The program therefore offered reminders and information, but not therapy as such. This meant that participants struggled to engage in the computer intervention and to see it as therapy '..because you have no feedback, they're like chalk and*

cheese really. Well, yes...it was educative, but I didn't feel like it was a therapy session". (Donkin 2012: CBT for depression: Australia)

Feedback can be an important motivator to participants, and emerged as a common theme. This requires consideration at the trial design stage, especially if participants have expectations of treatment based on previous experiences in other therapeutic encounters. Feedback could be automated or human, including the ability to receive instant or visual feedback, which can be a useful feature and perceived benefit for participants.

Reminders are a common tool in trials, but used in the online setting can have both positive or negative consequences for participants, sometimes perceived as stressful to receive, but for others helping to maintain motivation. Some participants perceive this is as active monitoring, and that someone is 'keeping an eye on me",

"*And for some, monthly questionnaires or reminder mails were experienced as helpful towards treatment adherence. 'As far as I'm concerned they can higher the frequency of the monthly questionnaires. To rub your face once more in the research It would help me to follow the lessons more regularly" (Gerhards 2011: CBT for depression: The Netherlands)*

It could also be important not to forget the impact of social support for participants, particularly as one of the potential benefits of internet-based trials is to be able to set them in the home environment. This might lead to a greater visibility and awareness of impact of the trial on participants for others present in their daily lives than in a traditional trial setting,

"*Furthermore, those who emphasized the importance of their partner, family, or friends in maintaining the Join2move program were mostly adherent. One participant commented: 'Regularly, my husband and friends joined me because I told them about the program. This motivated*

me to continue". (Bossen 2013: Web-based physical activity intervention for knee and/or hip osteoarthritis: The Netherlands)

5.5.8 Feeling safe and secure

Issues relating to concerns about privacy, confidentiality and security are consistent with those experienced in traditional clinical trials, although emerging issues, anticipated by early researchers working in the online environment, and outlined previously in Chapter 2, were identified in the studies. The nature of communication, data collection and storage within an internet-based trial has led some researchers to consider the impact that this may have on trial conduct, particularly in relation to recruitment. Findings suggest that participants make assumptions about the nature of data storage and security, that there is a variable, and often poor, level of information and digital literacy, a lack of knowledge about different types of data, and confusion about how data and personal information already stored in other parts of the health system is currently handled.

Confidentiality and privacy were common themes across a number of studies, related to the security of data, the nature of the condition being investigated, and also to the potential for disclosure without permission of personal data or health status,

> ***"****The importance of confidentiality was acknowledged by all participants. Some participants thought that receiving treatment through a computer was secure in terms of privacy, confidentiality and anonymity. 'You know that a computer isn't gonna judge you and a computer isn't gonna go and talk about your problems with somebody else". (Sánchez-Ortiz 2011: CBT for Bulimia: UK)*

Privacy is a key issue for participants, although the perception of the internet as a safe and anonymous medium for a trial was a factor in some decisions to take

part, in addition to increased flexibility, particularly again when disclosure related to sensitive topics or conditions,

> *"One could say, had she been sitting in front of me like anybody else, then I would not have asked in the same way. . . Yes, I thought so. It felt natural in a way, I did not feel as exposed and vulnerable". (Bjork 2014: Internet-based support for Stress Urinary Incontinence: Sweden)*

> *"Interestingly some felt that the website was a particularly good format for discussing a sensitive subject that some people may not want to talk about face-to-face .. "it forced you to be quite open and honest probably more so than you would be in face to face conversation, especially,…you know it's not the most pleasant of topics to discuss". (Tonkin-Crine 2013: CBT for Irritable Bowel Syndrome: UK)*

For other participants there were flaws in trial design, caused by how they accessed the intervention, that led to fears about exposure, and loss of privacy,

> *"Most participants expressed concern regarding accessing iCBT in a public place for fear of others finding out about their ED (Eating Disorder]. These concerns were often related to the heading 'Over-coming Bulimia' situated on the screen of the programme. As a result some participants had to be extremely careful when they accessed iCBT using a public computer. Others said that if they had not had a computer at home they would have not used iCBT at all. 'I felt a bit self-conscious because I had to use it in the library computer room so sometimes the big headings of Bulimia! And Fighting Bulimia! I kind of not necessarily want everyone else to know what I'm doing". (Sánchez-Ortiz 2011: CBT for Bulimia: UK)*

This suggests a need for care in the design and planning of the intervention, and although access to personal internet-enabled devices has become very common, the portable nature of handheld devices and the security of their data does not remove this problem.

Trust was identified as a core theme, particularly in how researchers are viewed by potential participants as experts involved in the pursuit of science, or assumptions about the purpose and value of the research, and this could influence recruitment. Trust is a known phenomenon in traditional trials, and the

need for participants to feel that the motives behind the research are not only trustworthy and transparent, is also found in internet-based trials,

> *"The values "trust" and "reliability" were important in the decision to engage the Join2move program. To cite one patient: "Join2move is based on an evidence-based theory. This persuaded me to participate and to continue with the program". (Bossen 2013: Web-based physical activity intervention for knee and/or hip osteoarthritis: The Netherlands)*

> *"The trust that was engendered by the brand had a dual role in ensuring participants both that there were no alternate motives by the researchers (particularly financial), but also that the organisations would have the facilities and ability to store their data confidentially... 'I suppose because the NHS has you know, my medical records and they assure me that they are confidential because I felt comfortable with that. Also I knew it was the University and they were doing some research, so I knew that they would use possibly use my information but it would be used in the right way". (Todkill 2013: CBT for Mental Well-Being: UK)*

Participants show specific interest in whether the researchers involved in a trial represent a 'trusted brand', such as a university, or public sector organisation. This factor may be more important in an internet-based trial, where a clear distinction between the provenance of different products or services in the digital space may be needed,

> *"The most prominent theme that emerged from the interviews was the importance of a trusted (offline) brand to participants during enrolment. The branding took the form of the logos of the NHS (UK National Health Service) and the lead University conducting the research. The value of this branding was in providing legitimacy to an online site and giving participants both trust in the content and that any information they provided would be used securely" (Todkill 2013: CBT for Mental Well-Being: UK)*

Views on how personal data might be stored and the impact this might have on security and confidentiality affected whether participants were willing to consent to take part in a study. Knowing how data would be used, being able to distinguish between use for research or commerce, i.e. for improving medical

conditions rather than the development of commercial products, was a concern. Factors that contributed to hypothetical decisions on whether to provide DNA samples for a genetic study included being given assurances that these would not be used for commercial purposes. However, this raises additional questions about how much reassurance is needed, or can be provided, in terms of future use of data, where the remoteness from the researcher leads to more unanswered questions,

> *"What will they do with it? Is it possible to test a sample 5 years from now? What kind of research are they going to use this for, any examples? I wouldn't want my DNA to help someone develop a 'keep you young' cream". (Wood 2011: Online consent in population based genetic studies: UK)*

In an internet age, where identities can easily be hidden behind an alias, questions were raised by research participants around authenticity, and how they could be assured, not only that the research is being carried out by a trusted organisation, but that the recruiting sites or people approaching potential participants are who they say they are. This represents a distinct feature of online recruitment,

> *"Respondents used a variety of references to trust (e.g., reassurance, authenticity, reputation, credibility). Respondents appeared to be making a quick intuitive decision about whether they could trust that the website was a product of Cardiff University or whether it could be attributed to an impostor posing as Cardiff University. In doing so, they looked for evidence to satisfy their scepticism. 'I'm very suspicious and worry as I know things can be duplicated I would need evidence that it really is Cardiff University. (Wood 2011: Online consent in population based genetic studies: UK)*

Issues relating to potential new uses for data, and advances in technology in terms of the type of data that can be collected, stored or used, for instance DNA samples, are recognised. However, the concerns are often expressed in vague

terms, sometimes demonstrating a lack of knowledge about research, and suggesting a need for better information to be provided to potential participants. Researchers may also need to place a greater emphasis on understanding the impact of health, information, and digital literacy skills. Participants could articulate different types of misuse, using examples they had experienced in other areas of their online lives to highlight concerns in areas they found more conceptually difficult to articulate, such as for eugenics, unwanted communication, or military purposes,

> *"Security of personal data was a major preoccupation of many respondents. It was feared their personal information may be misused, which might range from unwanted communication through to the use of their DNA for development of biological warfare or eugenics. 'Abuse of information: can anybody else access this information? You can't keep tabs on everything. What will happen to this information? Phone calls? Spamming?". (Wood 2011: Online consent in population based genetic studies: UK)*
>
> *"Security concerns extended beyond the security of the website itself there were concerns about how data would be handled and how any potential for it to be lost would be mitigated. Some respondents mentioned worries over laptops or removable storage with personal data on being mislaid. 'Risks? Just personal information being mislaid". (Wood 2011: Online consent in population based genetic studies: UK)*

In the Wood study, participants asked a range of questions relating to future security of data, which are rational and in some cases unanswerable. These could suggest that researchers need to think about how they express uncertainty, or manage the tension between the need to recruit by providing assurance, against the need to recognise and mitigate against this uncertainty,

> *"Some respondents were deeply skeptical about the site and had difficulty trusting the content, and its promises of safety, security and privacy. 'This separation [of names and data] is meaningless. Someone can put it back together". (Wood 2011: Online consent in population based genetic studies: UK)*

Concerns were expressed about general data security, evidenced through known events not specifically related to research, but giving rise to the same fears. This could become more of a factor in internet-based trials, if participants were made fully aware of the nature of research data collection and storage.

5.5.9 Technology, time and place

A number of issues emerged relating to internet access and usability for trial participants, themes of time and place used to express a range of experiences, which can in turn could impact on the conduct of a trial. Some assumptions were made on the part of researchers that the use of technology would automatically engage a response from participants and lead to greater compliance. However, the very fact that the internet is so present in the daily lives of participants can also provide distractions and lead to the trial being as easily ignored, and perceived as a barrier to engagement by participants,

> *"They judged themselves for not managing their participation exactly as the program suggested. One participant, with no experience of therapy before, explained 'maybe [I] would have spent more time, I was always racing around with the kids. I have three kids and all that, but um, maybe spending a bit more time really sitting down and read, like I'd read it and I'd think, 'oh, geez no, I've got something else I've gotta be doing.' And I should have spent more time sitting there, and think 'well, that can wait, this is mine and I'll give it 20 min,30 min, half an hour, this is my half hour to do this.' Cause I always seem to be in a hurry". (Advocat 2010: CBT for panic disorder: Australia)*

Findings suggest that for some the internet is perceived as always there and present, however these perceptions can vary, and can impact on the degree to which a trial is seen as being completely integrated with daily life, and the way this is perceived as a motivator or barrier.

> ***"****Although their approach to work in terms of completing home-work assignments to some extent had made it possible for them to integrate treatment in everyday life, they also expressed ambivalence, and*

sometimes scepticism, regarding practicing insights and working on their own". (Bendelin 2011: CBT for depression: Sweden)

"*Forgetfulness appeared to be particularly prevalent when the participants postponed completing a module until a later time. Many stated that they would put the module off, intending to complete it when they would be able to focus on the intervention without competing demands, but often forgot to return to it. They often forgot when other demands on their time arose or when they lacked regular computer time, resulting in a lack of visible reminders that the program was open. 'It was good, but I did especially appreciate the reminder because sometimes it came through at a busy time, um, I didn't mean to forget about it but it happens. And I was thankful for the reminder". (Donkin 2012: CBT for depression: Australia)*

Participants approach other areas of online engagement in different ways, and it is unclear how they might carry across these behaviours into a trial setting,

"*Participants who integrated the program into their day-to-day routine appeared to be less likely to struggle to be adherent ..they saw it as a task to be done with little emotional connection to it. 'I log in to my Internet every morning. I spend an hour or two hours, depending on what I have to do…and I'll always complete task as they come up. So with my emails, it's the same. I'll answer them on the same day or possibly the next day". (Donkin 2012: CBT for depression: Australia)*

Taking part in an internet-based trial usually reduces the need to travel, and can lead to a feeling of having more time, not feeling rushed, and being in control of the pace of engagement, time and place of use. Being able to return to the intervention in their own time was an aspect of benefit for one participant, and having time to reflect between sessions, to ***"****let the new knowledge sink in".* Benefits were experienced in being able to access and return to material when convenient, and therefore this may improve adherence and compliance,

"*Being able to dictate the pace in the online intervention meant that they felt they got more benefit from it. The ability to choose which activities to complete and what areas to focus on for the activities resulted in many feeling as though their agendas were catered for in the program rather than that of the therapist. Due to this, they felt that they could be more honest with the program, and this led to greater reflection. 'I think when I reflect on therapy you've got the lead up, going to [laughs] therapy, the*

anxiety beforehand, you know. You're going into the therapist's room, you're in someone else's domain, but it's like being in front of a stranger, you know, you're in front of a stranger and you feel you have to perform a little bit. [Laughs] whereas if you're by yourself, controlling it yourself, I think you can be more reflective about yourself". (Donkin 2012: CBT for depression: Australia)

"Several participants reported that they had dropped out of previous face-to-face therapeutic relationships due to the nature of the interactions. They reported feeling as though the therapist had been restrained by the amount of time available and that they were rushed by the time allocated to individual sessions. This resulted in their feeling unimportant and merely a patient rather than a person, and that their agenda was not as important as the agenda of the therapist. ...'you could sit there and just actually take your time to do it. You know you could really think. Whereas when you're talking to somebody and you've got an hour or three-quarters of an hour or something, you really kind of you know...so time to me is the important thing". (Donkin 2012: CBT for depression: Australia)

The health status of the participant, their avoidance of seeking treatment for condition or symptoms, and the nature of the condition or intervention under investigation can impact on the trial. Reports across the studies highlight a link between attrition and the nature of the condition, with studies involving trials in mental health or behavioural conditions reporting specific issues. In the Nicholas study, the very nature of the online interventions had a perceived negative impact for the participant, their self-management, or coping strategies,

"I found it quite confronting, and reading the information made me feel uncomfortable, thinking that these issues related to me—I preferred the ostrich approach".. "[I] found it difficult to sit down and do those things. I got into an anxiety and went off to do other things. I didn't really want to sit down and think about it". (Nicholas 2010: Psycho-education for bipolar disorder: Australia)

Having to use a computer could help adherence for some participants by providing structure, or discipline in the way they were required to use it, but this can again also be a barrier. In terms of an improved experience, specific features in online trials, such as having more structure in how exercises are completed,

automatic recording or recovery of input, or not being able to skip specific sections in order to progress, may suit some participants. Conversely, for some the self-motivation that is needed to complete some interventions may not suit their preferences or individual behaviours,

> ***"****All participants reported that the website took time to complete, and several mentioned that a user had to be self-motivated to work through the material: 'I found it time consuming, you know, to log in, and I'm not one of those on the computer all day. I found it a bit time consuming and sometimes I must admit I thought I can't be bothered to do this today". (Tonkin-Crine 2013: CBT for Irritable Bowel Syndrome: UK)*

The concept of providing greater convenience to trial participants is cited as an advantage of internet-based trials, and this theme emerged in the studies, sometimes as a positive factor, but also as a barrier. The convenience associated with avoidance of travel and time savings was expressed, but forgetting to complete the programmes was also a feature, and could lead to increased feelings of anxiety and pressure,

> ***"****Forgetfulness appeared to be particularly prevalent when the participants postponed completing a module until a later time. Many stated that they would put the module off, intending to complete it when they would be able to focus on the intervention without competing demands, but often forgot to return to it. They often forgot when other demands on their time arose or when they lacked regular computer time, resulting in a lack of visible reminders that the program was open". (Donkin 2012: CBT for depression: Australia)*
>
> *"that I've got to do this" and "I've got to do that," and "I can't do my [program] now, I'll do it later," and really there is nothing that can't wait. Nothing at all. I have a set routine. I'm retired. But I get myself into such a state of anxiety that I can't relax and do my [program]. So I leave it and go and do my silly little things such as taking my dog for a walk and doing my shopping. All sorts of, you know, mundane things that are not important, well they are important, but I could give myself the time to relax and do it..". (Donkin 2012: CBT for depression: Australia)*

Flexibility within the trial design could aid adherence, specifically the ability to fit activities in with daily life,

"The ability to be flexible in the completion of the program also meant that participants were able to overcome time-related barriers, allowing them to complete modules in sections, when time allowed. Sometimes this appeared to be prompted by reminders that were part of the program. 'I remember doing a long one and thinking, "Oh yeah! I missed one! I can go in and do that one again". It always good because you know you can go in and do it again. That's the first time I actually left the memory one and come back and do it again and I'm going "I'll do that later". (Donkin 2012: CBT for depression: Australia)

"Many interviewees had busy schedules associated with their university courses. The flexibility that iCBT offered in terms of time, place of access and having both the computer programme and the workbooks covering the main parts of the sessions was seen as an advantage for all participants. "You can do it whenever, any day. Like you can just to do it anywhere in time and that was good." (Sánchez-Ortiz 2011: CBT for Bulimia: UK)

For some the prior use of technology, usability, or connectivity issues could impact on their ability to interact with the research. This can relate to poor broadband access or speed, download times for data, or poor connectivity in rural areas, and could be exacerbated by the nature of the condition,

"*A few participants had problems getting to a computer on all days or found Internet connection speed unsatisfactory: 'if you had an application that you could download and that would be run at the speed of your own computer that would help . . . but that was a great facility but it was a challenge to use.'' (Morgan 2011: Self-help for weight loss in obese/overweight men: Australia)*

"*The first trial began in 1998, with some participants living in rural areas, where they had little access to high speed or reliable Internet service, or the skills to solve any technical problems that arose. The researchers explained that some of the participants began the trials unfamiliar with the most effective ways of using the Internet as a tool to overcome their panic disorder and therefore they had trouble fitting the use of the Internet for the trials into their busy lives. The online participants did not have to make an appointment to contact their assigned therapist or engage with the material on the website. One researcher stated, 'if they had a [face-to-face] appointment there was at least somewhere they needed to go to do stuff [but instead] they have to organise it amongst the chaos of their world to dedicate it time and for some of them it struck me that that was too difficult to do.'' (Advocat 2010: CBT for panic disorder: Australia)*

5.5.10 Ethics and informed consent

Ethical themes run throughout the studies, similar to those experienced in traditional trials, but also confirming emergent issues highlighted by Murray [59], relating specifically to the nature of the internet trial. One key theme relates to participant understanding of clinical trials and the research process more generally, and the impact that this has on informed consent, expectations and roles and relationships. As with the previous theme relating to technology and place, the presence of trial recruitment adverts and the subsequent delivery of a trial intervention online could lead to a blurring between the perception of common usage, and what people think they are signing up for as part of a trial,

> *"Not only did Sue misunderstand the purpose of the trial but, despite signing an informed consent form, when asked, she did not really feel that she was even participating in one: ''No not really. It was more like answering [quizzes in magazines], you know like in the T.V. Week and Women's Day". (Advocat 2010: CBT for panic disorder: Australia)*

> ***"****Before the treatment started the participants received written information about the treatment. They were also encouraged to contact the staff for additional information if needed. The concept "insufficient awareness of the treatment" is based on statements from participants explaining they were offered and recommended to test a treatment but without getting or trying to find sufficient information about it. 'I had no idea at all really about what the treatment would be like; I was only interested in doing anything that might help me". (Johansson 2015: CBT for Generalised Anxiety Disorder: Sweden)*

In many studies participants demonstrated a lack of understanding about how clinical trials work, which could be a major area of concern in terms of gaining informed consent, and could impact on recruitment and attrition. Expressed concerns that relate directly to the internet environment demonstrate different levels of understanding about the process of clinical trials including randomisation, use of comparisons, the need for specific outcomes, or the purpose of the trial,

“The participants did not always show an understanding of the scientific underpinnings and rationale of the trials, despite signing informed consent forms. This lack of understanding is reflected in their reluctance to engage with the online program, particularly when they were feeling better. In the interviews, participants were asked about their understanding of the trials and few of them conceptualised their involvement as participation in research. Instead, almost all of them understood their participation as a convenient way for them to get treatment, for which most of them were desperate. In the interviews, participants reflected on the term ‘‘trial,’’ explaining how they understood a trial to work and the reasons one would undertake such a project”. (Advocat 2010: CBT for panic disorder: Australia)

“*Participant altruism was a frequently cited motivator to enrol in the trial. 10 interviewees discussed altruistic reasons and were interested “in participating in research which might help others in the future” ..when asked about their feelings about participating in the trial”. (Todkill 2013: CBT for Mental Well-Being: UK)*

Researchers can underestimate the need to fully explain all the mechanisms involved in trial participation, from the rationale and reasons, to the very practical matter of what people will actually have to do, and then a further issue is how to gauge whether real consent is given.

“Some participants did not remember what kind of information they had received and others had just entered the program out of curiosity. Insufficient awareness of content and outline of the treatment appeared to be an aspect that influenced participants' decision to terminate the treatment”. (Johansson 2015: CBT for Generalised Anxiety Disorder: Sweden)

In the genetic study sample, participants also raised issues relating to governance, looking for a clear separation between what was perceived as the ‘state’ in the form of the government, and the more trusted ‘universities’ conducting the research. Views were expressed that showed distrust of ‘government’ use of data. The fact that a significant amount of health research is already funded by the public purse was not distinguished by participants, and

questions were asked about who holds 'ownership' of data collected as part of a study.

The theme that emerged in relation to feedback and reporting is particularly important as science and research develops in the digital age. The concerns expressed correspond with current debates about open data, the ethics of reporting results, and the phenomena of incidental findings. In terms of reporting, there was a strong personal interest present in decisions about potential trial participation, views on whether information and feedback should be provided. The specific issue of whether incidental findings should be communicated was an emergent concern in the Wood study, where people felt that trial participants providing samples should be told about findings personal to them,

> *"Some respondents questioned the ethics of the absence of clinical feedback and considered whether or not participants in the study should be told if a genetic marker was found in their DNA. C1:" If by any chance they do discover something wrong with you will they tell you? Yes I think they should". (Wood 2011: Online consent in population based genetic studies: UK)*

> *"Respondents were often enthusiastic and interested in the study because they thought they were going to learn something about their own genes. They were intrigued about their own genetic inheritance, how their genes influence their health, and were both curious and concerned about learning something detrimental about their future health. When the interviewer reiterated the absence of direct clinical feedback in this study, respondents were disappointed and although this did not deter anyone from participating, it definitely reduced enthusiasm for engagement with the research". (Wood 2011: Online consent in population based genetic studies: UK)*

Potential participants were disappointed at being told that they would not receive direct clinical feedback in this type of study topic. This was seen as reducing motivation to join such a study, but not necessarily deterring them to take part. These are issues that will require further consideration, particularly as the

questions of open data gain momentum, and researchers will need to ensure that a wide range of participant and public views are taken into account, and fed into trial design, planning and conduct.

5.6 Discussion

5.6.1 Choice and expectations

Being regarded as an active health consumer and choosing a therapeutic experience is cited as a change in the way people engage with research with an internet-based trial design, although the potential of gaining more access to treatment is also a motivator in traditional trials. It is not clear if this phenomenon is a consequence of the internet-based trial or common to all trial settings. The expectation of expert support and advice is a powerful motivator for participants however, and this may not be made clear or expressed at the feasibility or recruitment stage if the emphasis is placed on the convenience of the channel. There is a sense that the expectations of researchers and participants are different, and not well understood by each other. The relationship between the researcher and the mode of intervention delivery may be less clear than in a trial setting that involves face-to-face contact.

5.6.2 Security and data

An interesting question emerged relating to whether researchers can provide adequate safeguards or assurance about data security and privacy in an era where technology is advancing rapidly, and where major threats to data are experienced even in the most well controlled sectors such as finance, government and commerce. One study included in the review had a major focus on how participants feel about the security of their personal data in the context of these new challenges, although themes specifically around trust do appear in

other studies in the sample. Although the premise in this study is quite abstract, it does use the device of a tangible 'sample' in terms of a DNA 'swab' to help potential participants envisage the circumstance of the use and re-use of data, to make it easier for participants to conceptualise their views. Although this study was specifically set up to explore attitudes towards genetic research, the themes could be relevant to other types of research holding personal data in internet-based studies.

5.6.3 Open data

The increasing complexity of science in relation to digital media, open data and genomic research may become a concern for participants. Perceptions of the research environment, the ownership of information and the role of the 'state', can appear confused, and require better understanding on the part of researchers about how they provide information to participants, and on the nature of trial information, consent and support. A question could be posed whether researchers are tempted to be less explicit in naming potential threats or uncertainties in case it puts people off from agreeing to take part in a study.

The range of views and experiences in the studies suggest that it would be difficult for researchers to anticipate all the likely preferences and characteristics of participants. There was little data in the studies relating to how intervention usability and feasibility testing was done, but in the light of this complexity this crucial stage could be supported by experts in digital presentation and digital behavioural insights as part of the trial team.

Although the changing digital environment and data storage and use issues are also a factor in traditional trials, the level of expectation in internet-based trials

may lead to an increased need for very specific and clear information for participants and a means of checking expectations and understanding.

5.6.4 Limitations

The search sources were restricted to health-related databases, and therefore could have missed relevant content in the wider social science research literature. This was mitigated by the use of reference checking and citation searching of key studies. A selective approach to data extraction could have led to missed findings, but this was balanced by ensuring a transparent approach to the description of the methods.

The establishment of a framework for coding, based on the previous ORCHID and descriptive mapping findings could have led to bias in terms of the initial coding structure, and have hampered the identification of unanticipated themes. This was mitigated by constant comparison of emerging themes with core data from the primary studies, and analysis and discussion with a second researcher. These issues reflect a number of similar characteristics found more generally in information science and qualitative research, including determining research quality, retrieval of relevant studies, and the need to search through an increasing range of knowledge sources in a wide variety of disciplines to find relevant material.

5.7 Conclusion

The concepts of choice and consumerism emerged as important factors within internet-based trials, contrasting to the observations that participation is perceived as an obligation or burden. Participating in an internet-based trial could promote a feeling of greater autonomy and self-efficacy, and a consistent theme emerged across the studies in terms of participants feeling empowered by their

experiences of taking part. The greater convenience an internet-based trial offers is often cited as an advantage for trial participants, and researchers. Findings suggested that this was a consequence of the way that the internet is perceived as always there and present, which can be seen as a positive factor. However, experiences vary, and the degree to which a trial becomes completely integrated with daily life can be a potential barrier as well as a motivator for participants.

Variation in how roles and relationships between researchers and participants were anticipated or experienced emerged as an important theme. The relationship between the researcher and the intervention may be less apparent than in a face-to-face trial, and the expectations of researchers and participants may differ, and are not well understood by each other.

Participant concerns about privacy, confidentiality and security were consistent with those experienced in traditional clinical trials, although a new set of issues, anticipated by early researchers working in the online environment, are emerging. Questions remain as to how researchers can provide adequate safeguards or assurances about data security and privacy in an era where technology is advancing rapidly, and where major threats to data security are experienced even in well controlled sectors such as finance, government and commerce. Although understanding data storage and use is a concern in all trials, the changing digital environment may lead to an increased need for very specific and clear information for participants. New ways of confirming understanding and expectations may be needed, particularly as the drive towards open data gains momentum.

Ethical themes run throughout the studies, and highlight some emergent issues. Participant understanding of internet-based trials, and the research process more

generally, impact on informed consent, and this in turn impacts on adherence. The fact that one study reported that participants were not even conscious they were taking part in a trial reinforces this concern. The online environment has the potential to present supplementary information cost-effectively, tailored to different needs to address accessibility and equity. This could enhance better public understanding of science, particularly in testing treatments, and help mitigate some of the issues experienced within these studies. Themes relating to participant's fears and uncertainties are present but not always well articulated, being expressed as more general concerns, but they do express a desire to know more about the nature of research in general, and the impact it has on them personally.

The range of views and experiences in these studies suggest that it would be difficult for researchers to anticipate all the likely preferences and characteristics of participants, but it is not clear how much these considerations are part of the planning process. The impact of the online environment needs to be better understood, and the views and ideas of participants combined with those of researchers and funders, and fed into trial design, planning and conduct. The themes were used to inform a qualitative study, reported in the next chapter, to make sure that the views of researchers and participants were brought together.

5.8 Chapter Summary

- The second part of a two-stage systematic review used qualitative synthesis methodology to explore and analyse the views, attitudes and experiences of participants and researchers in relation to internet-based clinical trials.
- The thematic synthesis was based on methods that involve the development of descriptive and analytic themes, using an iterative and inductive process.
- Fourteen studies were included in the review, and ten main themes emerged from the studies. These comprised choice, consumers and expectations; autonomy and self-efficacy; perceptions of roles and relationships; information as an intervention; making it personal; obligation or burden; feeling safe and secure; being supported; technology, time and place; and ethics and informed consent.
- The range of views and experiences in these studies suggest that it would be difficult for researchers to anticipate all the likely preferences and characteristics of participants, but it is not clear how much these issues are routinely considered as part of the trial planning process.
- The impact of the online environment needs to be better understood, and the views and ideas of participants brought together with those of researchers and funders.
- The findings from the synthesis were used to inform the final part of the thesis, which was a primary research study to further explore the emergent themes.

6 Understanding participant experience in internet-based trials

6.1 Overview of Chapter

This chapter presents the findings from a primary qualitative study to explore the attitudes, views and experiences of people involved in internet-based RCTs, including patients and the public, participants, and researchers. The study builds on the findings of the systematic review, and aims to help improve the design, recruitment, conduct and relevance of internet-based clinical trials.

6.2 Background

Previous chapters have aimed to identify the extent of activity and the most important questions or uncertainties about internet-based clinical trials. This has provided a better understanding of how often internet technologies are being used in clinical trials, how this has changed over time, what types of clinical topics and interventions are being investigated, and what methodological research has been undertaken in this area.

Qualitative research makes an important contribution to the understanding and practice of health care [61], and is now commonly included in health care research strategies, where the application of specific qualitative research methods are informed by the nature of the research question. Qualitative research can be used to understand the meanings that relate to people's experiences, or to interpret social phenomena, such as behaviour or interactions [471]. The qualitative synthesis reported in the last chapter identified some key themes which would benefit from further investigation to help ensure that both researchers and participants' attitudes and experiences are better understood, and used to inform future practice.

6.3 Research Question

To explore the attitudes and experiences of people involved in internet-based clinical trials, including patients and the public, study participants, and researchers, to help improve the design, recruitment, conduct and relevance of health research.

6.4 Methods

This was a qualitative interview and focus group study, using a modified grounded theory approach, including thematic analysis with constant comparison, and aimed to explore attitudes and experiences of a range of people involved, including patients and the public, study participants, and researchers. Nineteen semi-structured interviews and one focus group were conducted between 2015-2016. Topic guides, based on the literature review, were prepared for the focus group and the respective interview schedules for researchers and the public, to outline the main areas for discussion, with sample questions and concepts to be discussed (see Appendix 6A). Questions were designed to elicit individual experiences and understanding on the main focus of the research question, but also to prompt conversations that allowed participants to expand on areas of interest to them. Criteria and content for the topic guides were informed by the systematic review reported in chapters 3 and 4, including the descriptive map and qualitative synthesis.

Focus groups and semi-structured interviews were held with:

- Internet-based trial researchers and methodologists
- Patients and the public involved in research
- Patients and the public not previously involved in research

The results from the different population groups were then analysed and compared.

6.5 Sample size and recruitment strategy

A purposive sampling approach was taken, and a sampling framework developed to include potential and actual trial participants, and researchers with experience in internet-based clinical trials. Sample size reflected the heterogeneity of the study population, and the aim of reaching data saturation. The primary recruitment strategy for researchers was planned through the 2014 Med 2.0 International Conference; EBHC Teachers and Developers network; and the PLOT-IT web platform for online trials. Members of the public were recruited through the Involve Co-ordinating Centre and Network and People in Research network. Participants agreeing to take part were invited to take part in a focus group, or semi-structured interview conducted in person, by telephone or using web-based media. Information sheets were provided for the researcher and public participants, and are provided in Appendix 6B.

Thirteen interviews were held with researchers, ten using Skype and three in person. Six interviews with members of the public, five using Skype and one in person. One focus group was held with four patient representatives. Interviews were held for an average of one hour for researchers, and 30 minutes for the public. The focus group and individual interviews were located in community centre premises to ensure a safe and comfortable environment. Public participants were offered a small value (£25) voucher to recompense for their time. The study participants were assured that all information will remain strictly confidential and any published data would be anonymised. Ethics approval was

obtained through the Central University Research Ethics Committee (CUREC), University of Oxford. The consent forms are provided in Appendix 6C.

6.6 Data analysis

The analysis used a modified grounded theory approach. The results from the systematic review were also used to help interpret the data. All focus group discussions and interviews were recorded and transcribed, with accompanying field notes. Data were organised initially using NVivo [472] and then transferred to the EPPI-Reviewer [473] software to facilitate development and iteration of a coding structure. Field notes were imported into the software to help provide context and additional observations for the analysis. An initial coding scheme was used to categorise data, and anticipated and emergent themes were identified. Constant comparison was used to ensure the representation of all perspectives in the analysis. A mind mapping techniques (OSOP one sheet of paper) was used to help explore patterns in the coded data [474]. An example is provided in Appendix 6D.

The ethical principles of voluntary participation, anonymity, confidentiality and informed consenting were adopted and strictly adhered to.

6.7 Results

The main anticipated themes, identified from the research so far, included choice, consumers and expectations; autonomy and self-efficacy; perceptions of roles and relationships; information as an intervention; making it personal; obligation or burden; feeling safe and secure; being supported; technology, time and place; and ethics and informed consent. Emergent themes were identified both in addition to, and within, these categories, such as understanding research; the tension between convenience and intrusion; rapport; control; sharing

knowledge and learning; the extent of patient and public involvement; the wider impact of technology on society, and the impact of this on research.

To maintain confidentiality, direct quotes from participants are anonymous. For ease of reporting, all references to members of the public taking part in the study, as distinct from 'researchers', whether previous trial participants, members of the public or lay representatives, are referred to as 'public'.

6.7.1 Understanding of research

Participant attitudes to taking part in online trials are similar to those in traditional clinical studies [78], and feature themes such as altruism, reciprocity, and an interest in trials testing conditions and treatments personally relevant to them or their families. Similarly, participants want to be provided with information on the main purpose of the study, potential side-effects, time commitments, and to receive assurances regarding the use of data. Concerns or fears regarding the risks of joining a trial are often attributed to 'others', rather than as a personally held attitude,

> *"there might be some people who might be really worried about – not worried, but they might be reluctant to provide some details because they might not be fully aware about the research study and how the study goes on, and they might think that, later on, it might, like it might risk them in some way. It's because of the lack of awareness. If they are made fully aware that, okay, that your research study would be used for some specific purpose and the results, the data would be destroyed, so I think …then they should not be reluctant to provide their details" (Public Interview 4)*

The representation of concerns as things that 'others' may be worried about were sometimes owned as a personal view when participants were asked for more specific examples in later stages of their interviews. Medical language or

terminology used by researchers was perceived as a potential barrier, and also attributed to something 'others' didn't understand,

> *"I don't think people are much aware .. they are not aware about the…like basic stuff, like if you say blood donation or body mass index, this is quite common, but if it's quite technical, a bit of it, then it's very hard for them to understand, because biological terms are very technical" (Public Interview 4)*

In an online study, there was an expectation from some researchers as well as from some participants that a lack of understanding might be increased in this setting,

> *"I mean, it has its advantages and disadvantages... it does have the advantages of it was designed to be self-guided in that manner, which is fantastic, but it also means that a lot of participants didn't really have an understanding of what they were signing up to [laughing] but didn't care, but I think that's not necessarily specific to internet trials, but I do think that there's more of a risk of it" (Researcher Interview 4)*

Patient representatives in the focus group had previous knowledge of clinical research, or the health care system in general, and demonstrated a wider understanding of why using the internet in clinical trials might help researchers, such as in the need for trials to recruit 'large numbers' of people. Their perspectives, influenced by the nature of their previous involvement, experiences or conditions, demonstrated how previous positive or negative experience in health care, of a treatment or service, could impact on attitudes towards taking part in research. Both the patient representatives and other public respondents found it difficult to differentiate between different types of clinical trials, and were influenced by high-interest media stories, such as the problems experienced as part of a Phase 1 trial held at Northwick Park Hospital in 2006 [308]

> *"M1: But I want to know about the side-effects and that, I want to know about the freedom to withdraw, stop, and all that stuff.*

F2: Yes, unfortunately, you often read about the one-off bad experience and one always remembers what happens at Harrow…" (Focus Group)

In the wider sense, from the researcher perspective, there was a concern that the way that online trials are developing could pose a risk that participants would potentially learn 'less about science' than in a traditional trial. Whether this would be as a result of changes in the way researchers communicate, or whether technology itself could be used to increase the accessibility of information about clinical trials in general, was not clear. One of the major stated benefits of online methods, that of making it easier to join a trial, may in itself negatively impact on participant awareness and understanding. Making it too easy to join a trial may lead to participants not even being aware that they are participating in a trial. Researchers may feel they are representatives of the research community and talk about the role with a sense of responsibility: and one researcher suggested that scepticism about research in the general population could increase without the rapport that can develop in contact-based trials.

6.7.2 Ethical issues

Anticipated themes concerning ethical issues were identified by researchers and the public. These included the use of incentives, the nature of informed consent, issues relating to bias and waste, and the reporting of results. Emergent themes included problems relating to ethical approval, transfer of online research into practice, and issues relating to sustainability and equity.

6.7.2.1 Ethical approval

Some researchers using internet technologies in clinical trials had experienced difficulties when seeking ethical approval, and felt that ethics committees lack understanding about the specific nature of online trials. Although it was felt that

this would improve with time, there was a fear that the pace of change in technology is so fast that this improvement would always lag behind that of researchers and emerging trial methods,

> *"I'm very positive in using technology, so I would definitely recommend using technology in research, eh, for sure. At the same time, I would stress on issues like ethics and security and things like that when you are using it, and also the pace at which the technology goes" (Researcher Interview 10)*

These concerns are characterised by researchers as a lack of understanding of technology within ethics committees, which can cause delays in trial development and conduct,

> *"but there's a general lack of understanding in …everybody regulating what we do, about sort of how differently things work in terms of it being an online intervention. So, for example, … ethics committees, or R&D Departments…they don't really have enough understanding about it, so it's quite difficult when you're trying to get them to approve your research, trying to get them to understand it I guess, so that's certainly a barrier, which I would hope will improve with time, but I'm not sure" (Researcher Interview 4)*

Where delays had been incurred this was seen as increasing costs and slowing up the progress of the trial itself. In one particular study the ethics process had impacted on the trial design by changing the extent of clinical involvement, through fears that the original protocol showed a lack of 'duty of care' – this was seen as fundamentally challenging the rationale for the online design of the trial, and affecting the results,

> *"ethics was quite interesting to get through because they didn't know anything about it, and so one of the things that came up very strongly with Ethics, which probably ended up being why our groups didn't show any difference, was that they were very concerned about duty of care and about what would happen if people became suicidal …, because we weren't taking any clinical responsibility. So we ended up developing a sort of red-flag system" (Researcher Interview 8)*

Public interviewees acknowledged the importance of ethical approval, and the need to be provided with sufficient information about the trial and the potential risks, but were sometimes less concerned about the impact on this personally than indicated by the researchers,

> *"Yeah, I'm quite easy-going. I know like that, you know, like ethics, everything, you have to have like all your participant information sheets and give loads of like warnings and stuff like that, but I'm always quite carefree about, like taking part. I never really have too many concerns anyway. So I think that would be something I would consider taking part in". (Public Interview 2)*

6.7.2.2 Informed consent

Concerns about the nature of informed consent were consistent with those experienced in traditional trials. Specific concerns for online researchers included a fear that the medium generates additional problems in terms of how much information is understood or even read by participants,

> *"But the main reason for them taking part in the trial was just to gain access to the website, and in the interviews, it was very clear there that many…not everyone had realised they'd taken part in a trial .. even though there was several pages of information [laughing] and consent forms and blah, blah, blah. They actually didn't really understand that that's what they'd entered into". (Researcher Interview 5)*
>
> *"I think there's always the question of who's paying attention, right, and that's true with everything over email – I mean, are they reading the email properly, are they reading the instructions, are they reading the consent form, right? It just…people are distracted. You know, it's like an internet class versus a class in person, right? There's a lot of other things on their mind and you never know that you're getting their full attention, and that can be an issue" (Researcher Interview 12)*

Similar to the suggestion from one member of the public that they did not care about potential risks, one researcher felt that patients 'cared less' about reading information online and skimmed over important information. Trial participants felt that personal contact could lead to a better explanation of what taking part in a

trial would involve, and help in managing expectations, although this is often also expressed as 'other people's needs', and not their own,

> *"I guess that could happen where people don't quite understand something that's being asked, or answered not quite as well as if they haven't read it correctly, you could get people who sign up then get half way through something and not quite get to the end, haven't submitted, or have good intentions when they sign up, but they haven't found the time to do it, but where you have an appointment, it's more likely someone's going to turn up because they've made that I guess, that initial you know, they've gone out of their time to make that appointment and they don't want to let someone down". (Public Interview 6)*
>
> *"I do think that people might take things less seriously when they sign up for them online than when they sort of sign, hand-sign, a consent form in person" (Researcher Interview 4)*

Researchers did report difficulties in their ability to manage the expectations of participants, consistent with the findings from the public. The public had some preferred ways of receiving information, or seeking reassurance, that conflict with the potential benefits of increased efficiency that researchers said online recruitment provided,

> *"I'd also like someone to call me, as it's a clinical trial, like it's quite serious, in my opinion, so I would like them to call me, definitely." (Interviewer: So you'd actually want to talk to a person, in person) … "Definitely, 100 percent". (Public Interview 5)*
>
> *"if just the information sheet is given to them, then they might not read completely, so the researcher themselves should make them aware and put each and every point very clear in front of them. Then…because, if they are made fully aware, it's just with the one-to-one communication, that would make them aware, because sometimes they might just, misunderstand it and stuff" (Public Interview 4)*

Common to both groups, reading detailed information online, whether for research purposes or not, was seen as difficult. The view that explanations were better conducted one-to-one, and that a human 'voice' provides clearer meaning was present in researcher and public responses,

"You know, the big thing for me is they need to fully understand the study, and they need to be very clearly presented …., your information needs to be crystal clear….and we do have websites for projects and they can go on and get more information. They can email the researchers and get more information. That's absolutely fine. There's no problem there. If you see somebody face-to- face, you can clarify things, but if everything is written or even like…we're going down the route of even now…even a voice recording. It's more personal. We're finding that now, using like podcasts and stuff, it's more personal, which is fine and I think that's a good idea" (Researcher Interview 2)

Both researcher and public interviewees suggested that the new technologies themselves could aid 'getting full attention'. Researchers know that the lack of understanding about consent is an issue, but did not all demonstrate an ability or motivation to address this, or to put different mechanisms in place. Rather it is seen as something that just has to be done to get to the next step in the trial process. This is also recognised by participants as a 'tick-box' exercise, confirming findings from the qualitative synthesis of participant experiences,

"M2: But we tick the box, oh yes, because you can't go any further without ticking the box!" (Focus group)

6.7.2.3 Reporting research

Themes relating to the reporting of research were raised, with the public clear that joining a trial, motivated potentially by personal relevance and being curious about the outcomes, should mean that results are reported back to them, despite any barriers due to language or terminology. One participant reported an absence of this in previous trial experiences,

"So, on some of the consent forms, I've seen that you can tick it if you want to receive the report afterwards, and I always do tick that, but I've never, ever, ever received anything" (Public Interview 1)

One researcher wondered whether the transient nature of an online intervention would mean that participants would not be interested, which was in contradiction to a view from a public interviewee that it should happen as a matter of course,

> *"I can't remember [laughing]. I think we've said that the results will, …yeah, I think we've said that we'll send them a summary of the findings, and we tried to, when we were struggling with the follow-up rate, we did try to say that again in emails at 12 months, "so we'll send you a summary of the findings", but I'm not sure how interested… I know in other research studies that people are quite keen to know, but I think, given this…because this is a transient problem, I don't think that people are overly interested [laughing]". (Researcher Interview 4)*

In terms of more general reporting, one researcher said that they thought publication bias was worse in online trials, where the enthusiastic adoption of new technologies led to fewer negative studies being published,

> *"based on the literature review I'm doing now, there is not much, out there about negative I'd say effects of the use of technologies… I would say 95% of the available literature – I'm talking about 500 papers – 5% talk about or report negative or actually no effects on behaviour. In most of the cases, probably it's more a publication bias in this case. They tend to say, ah, no, yeah, clearly there's an effect, you know, there's a lot of potential about these technologies. Of course, we need to differentiate, but in general…yeah, positive bias towards use of technologies". (Researcher Interview 1)*

6.7.2.4 Equity

For researchers, issues of equity emerged in relation to internet-based trials. These were expressed as negative factors in relation to access to technology and connectivity, for instance in rural or other disparate communities; impact on those with certain disabilities if accessibility is not considered; or for participants without the language or expertise to share or exploit existing skills, software or other resources. Particular difficulties were associated with funding and conducting internet trials in low-income countries, where populations may have poor access to technology or connectivity, and older versions of equipment.

Researchers in these settings may have poorer infrastructure or capacity, and this was felt to deny the potential benefits from increased internet-based research for people in this setting, exacerbating existing inequity,

> *"So, for example, like in a lot of less economically-developed countries, often, there's really good mobile phone coverage but there's not such good smartphone coverage, so therefore, if you're doing an intervention in that population, then you wouldn't choose an app, for example, because it would just be ridiculous" (Researcher Interview 4)*

> *"it was in a rural setting, so you know, of course we had to screen people definitely who were able to read and write, you know, to be able to use that ... in Africa, people have mobile phones, but not necessarily of course smartphones, so we had to budget that for that particular study….It's something that is emerging, like eHealth, and the use of mobile apps and stuff like that … we did a process evaluation, and it was quite challenging to some people, especially the older ones, and of course most of them, because they're traditional healers…they had to like undergo a lot of, like training, …like you have to get into certain software … these are the things that may also be costly, and you need to know somebody who can do these things" (Researcher Interview 13)*

6.7.2.5 Representativeness, sustainability and waste

One researcher said that choosing an online design was important to them as an ethical researcher, as it could increase exposure to behaviour change interventions. A divergent view was that use of technologies could potentially decrease the likelihood of achieving better representativeness, as those populations more familiar or comfortable with taking part in research would still benefit most.

The issue of sustainability was raised as a further ethical issue, if there was no accountability for future adoption or use of the interventions being tested, again contributing to waste. One researcher feared that the move to online meant losing touch with participants and the public, and that there would be a lack of community benefit from trial activities,

"I think that can be a problem with a lot of interventions is that they can be flash-in-the-pan and it can kind of be 'What happened to that?'. I think the sustainability of it has to be a key consideration and what's going to happen to it, after it's been…after the grant is finished, …what's the long-term plan and, what's the plan for quality improvement, and how, yeah, how will it be accessible to people in the community who could benefit from it". (Researcher Interview 7)

6.7.3 Trial design and appropriateness

The decision on whether to use an online design for a clinical trial has a number of component themes, including appropriateness, planning and trial management. The advantages for trial management are consistently identified by researchers and the public, including less bureaucracy and use of paper; the need for fewer human resources; time savings through the automation of processes, particularly data collection; and a perception that these factors contribute to lower overall costs.

6.7.3.1 Characteristics

Characteristics such as age, type of workplace, and type of condition or treatment were seen as important factors influencing the appropriateness of using an online design, and the ability to recruit and engage participants, by both researchers and the public. Designing online trials for older people, for example, was viewed by one public interviewee as inappropriate or unlikely to be successful, although a researcher stressed that these populations should not be ruled out. Children were viewed as being a particular target group for online designs, and one researcher had used 'gamification' to successfully increase engagement. In terms of workplace trials, the impact of timing and the way the trial activities are designed were seen as potential limiting factors. Researchers questioned the acceptance of certain beliefs about online trial methods, and how these were affected by participant characteristics,

"we compare usual care with e-health and see, okay, we see that e-health is working better, when we don't actually know if it is. At the moment, of course, we might have some ideas, but… so far, there's no…I couldn't have found, [laughing], a review that investigates different aspects of technology and compares them with the outcome. I would like to know more about within a group. So, if there are sub-groups that participate in a trial, I'd like to understand what are the different components. Yeah, before developing actual intervention, I would like to understand more about these things, and as I said before, I'm not going to do .. test trial just because I'm interested in the technology. If people that are affected by the issue are not considering using technology, then we're not going to use technology". (Researcher Interview 1)

6.7.3.2 Convenience and cost

Specific factors relating to recruitment and screening were expressed.

Researchers thought that although online recruitment appeared to be convenient and effective, there was still a need to ensure the trial had a representative sample, and the convenience should not replace good practice,

"and that's something to be really aware of, that if you're going to be doing online recruitment or online anything, that you have still got to put good practice in there in terms of making sure that your sample is representative, if that's what they're looking for. You can't just expect the internet to kind of filter and sort for you. You still need to pay close attention to it". (Researcher Interview 6)

Researchers specified cost savings as a motivator for developing their online trials, for instance reducing the need to resource health professionals or therapists, and reducing costs in comparison to the resources and time used in traditional trials. One researcher compared their online experience to previous trials using paper-based questionnaires, time-consuming use of post, and time spent 'stuffing envelopes'. It was felt that the management burden of the whole process had improved, with increased efficiency,

"doing it all online and therefore emails going out, automated, and all the data just coming in and it just being there on the database, all ready, and you've not got to worry about the accuracy of putting it in and the time it

takes, I think…that's really fantastic, just from a practical point of view" (Researcher Interview 4)

"Well, I guess in terms of data collection… the smoothness of the process was definitely enhanced by having it online. We had access to people's activity. Because we were …tracking people's behaviour as they actually went round the websites, we were able to sort of see it, you know, live, and we were able to monitor things very quickly and able to, also be aware of things that were not going well in terms of not any kind of patient outcomes, but in terms of actual technology. So we were able to keep a very close eye on the running of the trial and keep a close eye on the data and, that was definitely a benefit" (Researcher Interview 7)

However, a counter view was held that this may not be the case when looking at the whole trial process, and there were experiences of unanticipated or hidden costs, especially for new interventions,

"I guess that's the trade-off. I said it was cheaper, didn't I? But it is expensive to set up a website in the first instance probably, not as much to maintain it, but there…yeah, there are sort of…some hefty start-up costs, and I know it wasn't cheap to do ours…but we didn't really have a clue as to sort of how much it would cost… So yeah, perhaps we were sort of…inexperienced I think" (Researcher Interview 7)

In some cases, for instance due to the conditions imposed by ethics committees, through unforeseen developments, or even self-imposed in response to concerns or fears researchers have themselves, extra costs had been incurred.

6.7.3.3 The rise of technology

A sense of inevitability about the need to choose an online option, caused by the ubiquity of technological change, was expressed by researchers, and sometimes conflicted with concerns about appropriateness,

"I know that I'm also involved now in a [condition] trial, which is about using additional intervention, but I know that the trial managers there, and other people are curious about the fact that so much of it is done online because they are so used to that personal contact…. So, there's a little bit of me that wonders, you know, whether we're trying to fix something that isn't even broken by just taking it online because we think it might make it easier, but actually it will create its own set of problems" (Researcher Interview 6)

Researchers experienced in using technologies in their trial design differentiated between different channels or media, seeing some as less appropriate, even though these conversely are sometimes seen as most likely to engage participants,

> *"I don't see social media as important as, for example, smartphone applications for a delivery of an intervention …I don't see them…as a good choice because … I mean, social media are not made for important content, social media as such …That might be an option for recruitment, yes, definitely. It might not be a good option for actually conducting an intervention because, on Facebook, …there's a lot of noise, okay, something that you can't really control in a…in a supposedly controlled trial [laughing], and because it's not the media, the medium, sorry, for relevant important content, the way it is now. The technology might evolve in a different way, but as it is now, Facebook, it's not the right medium for serious content" (Researcher Interview 1)*

Some researchers were enthusiastic about their work, and acknowledged the personal 'excitement' of using online methods. They felt that they were at the forefront or boundaries of knowledge, although they recognised the potential problems the medium might cause. This excitement could be expressed in altruistic terms, such as in the potential benefits for increasing accessibility, and making research less exclusive,

> *"We really wanted to make it more accessible. I mean, everything, you know, is criticised for being ivory tower-based research, doesn't really represent the real world, especially, you know, in psychiatry and what we do, that whole sort of observer bias and how that influences people, and especially in Australia when we've got such huge rural and remote communities …so, being able to open it up to everybody, that was really quite exciting" (Researcher Interview 8).*

But some researchers also acknowledged that this should not be at the expense of being underpinned by a clear theoretical framework, and questioned their own practice, and frequently used the notion of the 'trade-off',

"I completely agree that you shouldn't necessarily just choose the technology because it's exciting and new. You should choose what's going to be best for your participant group …and your disease that you're targeting" (Researcher Interview 4)

A divergent view relating to the choice of online design was noted from one researcher who was concerned that the trial they had been involved in could have been done 'more simply', and there were other contradictions expressed within the researcher sample, where a feeling emerged of knowing that some problems exist, but being powerless to prevent or overcome them. There was a sense of self-deprecation or uncertainty in some responses from researchers, often with the use of ironical laughter, particularly when talking about the problems they had experienced with engagement. One researcher suggested that online interventions required researchers to 'think in an adaptive way', a further challenge for ethics committees, and called into question the extent to which randomised controlled trial methods and principles could be applied in this setting,

"I mean, as researchers, if we want to be helpful, probably a randomised control [sic] design is not the best way because some people might not like being assigned to a specific group. So, I'd say more in a natural experiment, it would be maybe better to say…it's an observational study basically .. Still, let's say, even think about N of 1 trials, still randomised but randomised to a specific content maybe, not to the choice of medium, so people freely decide "I want to have this, this, this and that, I want to receive the information in this way, rather than this way" might improve the final outcomes, or at least the experience of the intervention itself" (Researcher Interview 1)

6.7.3.4 Reach and hard-to-reach

There was a view that online trials had the potential to increase recruitment, including traditionally hard-to-reach groups, although some expressed concerns that there could also be a risk of increased bias due to the self-selecting nature

of some trial recruitment, or lack of exposure to the relevant technology or channel. One researcher felt that recruitment through internet channels provided better results by increasing access, but in the same study noted that those recruited through direct recommendation from a general practitioner might have had a higher level of commitment to the trial.

For the public, contact directly with the researcher, when participants are recruited through a health care setting, either in primary or secondary care, was seen as an enabler, helping to allay fears about taking part. Recruitment may need the 'force' of recommendation to be successful, and some researchers sought active designs that included the use of primary care or clinical settings to increase recruitment in this way.

One researcher felt that access might be increased, but that there was a risk of decreasing representativeness as a consequence. This risk was raised by the public as well as the research community, with one public interviewee expressing a concern that ease of recruitment through online means could be increasing numbers at the expense of a more representative sample, and also contributing to attrition,

> *"there's a temptation to send it to like everybody that you know, and then, you know, but is that representative of a certain sample? So, I think that…you still have to… Even though you've potentially got like an international audience with these surveys, you still have to be really patient and wait for the responses, in the same way as you'd have to if you were doing it in person, and I think that, sometimes, you know, because there's not a face of a researcher or a hospital or something associated with it, then it's kind of easier to ignore, whereas if you were asked the same questions, for instance, walking down the street, then you might be more inclined to participate" (Interview Participant 1)*

There were other concerns that the relationship between motivation to change and the interest in technology required for a successful intervention introduces a

risk of bias or lack of representativeness across a recruited group, or problems when participants self-select but don't meet the trial criteria. Unintended recruitment was also experienced as a problem by one researcher, due to the lack of control over geographical boundaries when using internet channels.

The opportunity to engage more indirectly on sensitive questions was a key finding in the review synthesis [443, 452]. Some researchers felt that the increase in anonymity afforded by an online design could attract specific groups of participants, such as those with stigmatising conditions, through the avoidance of personal contact with the researcher or health professionals, or having to admit personally to having a problem.

6.7.3.5 Engagement and adherence

In terms of how trial design approaches engagement and adherence, there were concerns that online interventions are easier to ignore, despite being easier to access or use. This risk was recognised by one researcher who suggested that it is easier to ignore requests for follow-up, compared to being approached by a health professional,

> *"Well, it's easy, isn't it? The obvious thing is that it's just easy to drop off the face of the earth if you've got no one to be accountable to. So if, you know, your participation doesn't involve having to tell someone that you're leaving, it's just that simple, you know, psychological shift between having a face, not having a face, so I think that it's easy to drop out, when there's no one to explain why, etc. to, but it's also the fact that I think so much of online methodology just simply doesn't get the fact that it has to be…it still has to be appealing [laughing] to the person who's viewing it or doing whatever with it". (Researcher Interview 6)*

These barriers to adherence are seen as ubiquitous factors in anything to do with the internet, although this could also be a concern in any trial with remote contact. There was a sense that if participants don't have to explain, or feel they

need to explain, through a specific physical or personal encounter why they are leaving a trial, this will increase attrition. When this combines with technical difficulties the situation is made worse, multiplying the issues normally experienced in traditional trials,

> *"I found, if you don't interact with people much or…if test technologies are used in simple, plain ways, eh, people tend to ignore it, so … when you expect an intervention to work online for a longer period, you should definitely have strategies to retain the participants, otherwise, they wouldn't, you know…people would just start ignoring these technologies because it becomes a part of them. You know…they keep using a lot of apps, they keep using a lot of websites, and this intervention would become just one other thing that comes up in their schedule, so they tend to ignore it". (Researcher Interview 10)*

As mentioned earlier, qualitative research can help improve trial design and conduct, helping researchers understand the attitudes and views of their participants. Researchers gave mixed responses when asked whether they had conducted qualitative research alongside their own trials, acknowledging the potential usefulness, but not always actually having carried this out. One researcher felt that this was a particularly important feature of planning internet-based studies, where the lack of personal contact could make prediction of acceptability and engagement difficult,

> *"qualitative work, particularly in our Department, is seen as a critical component of designing materials for the intervention, particularly on the internet, because if you don't do that, people won't…often don't use it… and particularly with internet interventions, you don't often have the chance to kind of, you know, persuade someone of why they should use it, so if people don't want to use it, they'll just stop". (Researcher Interview 9)*

6.7.4 Roles, relationships and rapport

In a traditional clinical trial, delivered through a health service or setting, one of the reported perceived benefits for participants is an increased contact with a

health professional, and a feeling of being better 'looked after' [83]. In an internet-based trial, the nature of the relationship between the researcher and the participant is changed. The relationships expected, or experienced, between participant and researcher emerged as a key theme in the interviews with both groups, whether in relation to the clarity of role, or terms of impact on feelings of being really connected,

> *"I think like, on the screen, there's more like anonymity … I don't feel guilty because I don't think…they'll know me. Like even in the [name] study that was completely online, like I'd never met the researcher, like so I didn't have like a sense of guilt that I would do if I did it in person and didn't do it properly, so that, yeah, I always feel I take them much more seriously if it's in person" (Interview Participant 2)*
>
> *"That's kind of tricky because actually then you're trying to get the … person to interact on the personal level and they, the researcher, becomes potentially a therapist, and that's not what they're meant to do, so I think there's a real difficulty for them to get the balance. But, you know, I think .. you do need sometimes the face-to-face at certain points, but I think it's a tricky one for the researcher, and ethically, it could be difficult" (Focus group)*

Researchers still experienced a need to make a personal commitment, such as employing strategies to increase engagement through named contacts, or by providing e-mails or phoning participants directly, even if this is outside the main study protocol. They viewed establishing rapport as a positive factor in conducting an online trial,

> *"when I started my study, … I didn't think of establishing trust, but I thought giving a personal call at the start of the trial, would help in one way, though you might not contact the participants all along the trial. You just give them a call and talk to them, tell them about the study, and then, you know, let them know that there is a team, there is a human sitting behind all this work, and that might, help to retain them and also to, you know, to establish trust at the start of the study.. I shared my mobile number and I shared my email address, so I get emails from them in the initial stages, and …I tried to call participants at…any opportunity I get, I tried to call them, and then I have a casual chat.., just*

to, you know, to make them feel comfortable" (Researcher Interview 10)

Indeed, some researchers felt that the loss of an immediate or personal connection with participants, leading to a lack of rapport, would have a negative impact on them, a theme that emerges strongly across the researcher sample,

> *"I mean, as both a researcher and as a potential participant, I would be very uncomfortable about not being able to speak to somebody or have a named contact that I could approach if I had a question or a concern, and although all of our materials for our trial did feature the PI's name and indirect contact details, I know that there was a perceived gap between the participant and being able to make contact. I mean, admittedly, people didn't need to make a huge amount of contact, but there were a couple of situations where there were technical issues, if nothing else, where they needed help, and, it made it quite a sort of grey area, about sort of, you know, what does help look like when you're doing an online trial, and who delivers it, and so there were some questions that came up of sort of should it be the trial manager or, if it's a technical question, should it go to the developer, and should a developer be even talking to participants, that kind of stuff". (Researcher Interview 6)*

With a divergent view, one researcher suggested however that the establishment of rapport can be a disadvantage, particularly in mental health research,

> *"I think actually also a disadvantage of building rapport, but then everything that I'm saying is sort of very related to the research that I do, is that, there may be a therapeutic benefit of me talking, even if I'm just talking through somebody's, screening questions with them, that in itself, the fact that they've actually got somebody, like a friendly face to talk to, that…there may be additional therapeutic benefits of that encounter that you then…are difficult to distinguish between just the website as an intervention in itself. So, yeah, …there's always pros and cons, I guess" (Researcher Interview 5)*

Public interviewees experienced the absence of human support or contact in a number of ways, including the view that this caused them to 'care less' about how they participated, and suggested that researchers should find ways to make contact more personal. They saw the researcher in the role of an expert, and

having contact with a person in this way as being a preferred way of seeking reassurance,

> *"but I think the interface needs to smarten itself up and it needs to be… you know, "I need help" – you need to have a voice behind that rather than press the dot… button, yeah…" (Focus Group)*
>
> *"if there are no side effects something online would be fine, the possible side effects would make me hesitant, it's a bit more reassuring if you've been asked to take this medication, and you know someone's going to see you in a week or two weeks, it's a bit more reassuring if you know that you're definitely going to have someone look at you, and someone to have someone to speak to about what you've been doing". (Interview Participant 6)*

A lack of personal contact can reduce feelings of guilt participants might experience if their engagement is low. Although having less contact than expected could be experienced in all trials, the specific nature of the internet, with its potential for anonymity and people hidden from direct view, provided another 'trade-off' between convenience and engagement for all those involved. One researcher was concerned that they are forgetting about 'people',

> *"I think that what we forget is that, particularly in the trial methodology, which really is about, fundamentally, at its heart, it's about people, that there's something around… We are losing contact with the very people who are doing the hard work, and those are the participants, and for me, that…that did come across actually. I did feel very remote from the participants, even in what was an appropriately digital trial". (Researcher Interview 6)*

Researchers also reflected on how they felt they were perceived by their own participants, adding to a sense of uncertainty about overall roles and responsibilities within the trial. The absence of support, and the consequences that a lack of personal contact could have on motivation and trust, confirm findings in the synthesis reported in Chapter 5. A divergent view on the more

remote nature of the relationship was cited as a potential benefit by one researcher, suggesting that the trial would as a result be closer to 'real life',

> *"I think that probably is a slight downside, the fact that some patients may feel slightly out of touch with the research team if the whole thing has been conducted online, but I think that may have some merits from the research sense because often the interventions or the aim of the trial can be influenced by the methods you use to kind of achieve it. So, if you have a lot of face-to- face meetings and contact with the research team, you can start to influence patient outcomes just through that contact, even if your intervention hasn't started. So if you have a really lovely trial team who you have three meetings with before you actually start whatever the trial is, that can actually start to bias your trial slightly. So, I think it's kind of a toss-up…… So, I think it definitely does impact the way you communicate and I think it probably has some slight cons for the patient, perhaps, but some pros for the research team in the sense that they can be more sure of the fidelity of their intervention" (Researcher Interview 9)*

6.7.4.1 Researchers and health professionals

In online trials that included a component in a clinical setting, the nature of the relationship with health professionals in online trials was raised by researchers. Positive factors from the researchers' perspective included reducing the burden of involvement or data collection for health professionals. However, health professionals were perceived as being 'conservative' in relation to the use of technology, or fearful that the nature of the intervention being tested could threaten their roles,

> *"I think they felt a little bit put out by the fact that we might be trying to replace them…which we weren't, and we tried to make it quite clear that this was sort of additional .. as opposed to healthcare" (Researcher Interview 4)*

It was felt that some of these tensions could have negative consequences for implementation of interventions, once the trial had concluded, and also some trial protocols had required major changes or delays following lack of integration of recruitment in the clinical setting.

6.7.4.2 Social support

Researchers were concerned that online trials could reduce the potential benefit of wider social support for participants,

> *"I mean, a single session is good, but some of the stuff we targeted was social norms and, you know, we targeted it on a very individual level, and I guess that can be another disadvantage of an internet-based intervention, …it's difficult to get a group of friends around a computer, whereas you can get a group of friends to come to a focus group, not that you deliver an intervention in a focus group, but people might sign up for workshops together and go along with their friends and sort of be exposed to that social element of things" (Researcher Interview 7)*

However, one public interviewee suggested online trials had the potential to create communities in themselves, whether this was intended as part of the design or not,

> *"But maybe what might be good is to have some kind of hang out area, that they can talk to other people thinking about joining the study .. often you want to do these kind of things with your friends, but I know in market research you can't really do them with your friends, because then they say that you have the same opinion, so if you can't do it with your friends, you could do it with someone else who're interested .. but then they're going in there, do you know what I mean, to be under god knows and you know they might feel like a bit scared, and if you can meet other people thinking about doing it beforehand that might be helpful" (Interview Participant 5)*

The interface itself becomes an important element in the transfer of this role, with participants needing to know the 'person behind the button' and researchers understanding that if it is not well designed it will not 'hold' people, therefore adding to the importance of design,

> *"I think things like the site design and whether it looked professional, and whether it had the right logos on it, would definitely play a big part. I think if you went to take part in an online trial and then the website was...looked like a two-year-old had designed it and it just didn't look very professional, then that would impact on your decision- making as well" (Interview Participant 1)*

Researchers reflected on their previous studies and suggested that they would do things differently in the future, such as including features such as contact lines, to help establish trust, and improve rapport.

6.7.4.3 Personalised and tailored

The way that participants receive communications was a key concern, as in all trials, and the public provided specific experiences and attitudes that had, or would, influence their behaviour. The lack of personalisation is regarded as having a negative impact, with generic messages seen as reducing a feeling of engagement, and participants also reported the importance of using their names on any communications received. In addition to the use of personalised or tailored communication, some public participants felt that the lack of seeing someone face-to-face could be mitigated by having access to images of the research team. One researcher felt that they should be taking responsibility for this, rather than accepting the situation as a normal consequence of technology, stating that it was ‘our problem’ rather than just accepting the situation, and that more could be done to mitigate the situation.

On a very personal level, being thanked is also regarded as important by participants, a view not raised by any of the researchers I interviewed. Researchers did agree however that people need to feel ‘noticed’ and that this lack of personal contact may be an issue for the success of the trial.

6.7.5 Feeling safe and secure

Themes that emerged relating to confidentiality, privacy and identity in online trials reflected those present in attitudes to technology in daily life, covering a wide range of views, attitudes and preferences. Within all trials participants need to feel confident that their involvement in the study will not cause them any harm,

and that data and results will be held anonymously and securely, now and in the future, not be misused or disclosed, and their privacy maintained. The view of researchers in the sample was that online technologies provide a good environment for the collection of sensitive data, and may even be preferable for some participants. The potential to be anonymous was seen as helping in terms of disclosure of sensitive information, but at the same time, led to fears concerning identity and fraud, being traced or tracked, and could lead to greater or lesser honesty in providing data,

> *"they thought that…the internet was a safe place and they were anonymous, … There was nobody looking at them when they talked, it could, you know…which I find problematic because I think anybody could be on there making it up, but they just felt that it was the best way to get the information" (Researcher Interview 11)*

Online contact is seen as 'fleeting', and also causes problems with identity and persistence of any contact, for instance due to the challenge of changing e-mail addresses.

6.7.5.1 Trusted brand

Trust was important to the public, and as in traditional trials [381, 450], having a 'trusted brand' increased the sense of safety, viewed as a way of ensuring data security and stopping information getting into the 'wrong hands'. Public and researchers agreed that this can increase feelings of reassurance,

> *"I think…like if you see it's associated with a university, especially like a really reputable university, you have an element of trust in that organisation, and you kind of separate things like universities and hospitals and anyone who might be conducted this research from sort of corporate online shopping sites" (Interview Participant 1)*

The theme of identity emerged from the researcher and public perspectives, with researchers, for instance, expressing concerns about multiple registrations, and

the public about peoples 'true' identity online, and the potential for fraud. Researchers suggested that the issue of data security would be a major concern for participants, and although it is mentioned in the public interviews, there appears to be more confidence in the process than researchers expected, especially when the research was to be conducted by a 'trusted brand'.

As with the findings relating to online consent, public interviewees demonstrated a lack of understanding of trial processes, in this case related to what happens to data collected as part of the trial. Although they expressed confidence in the process, they did not always fully understand what might be involved,

> *"like some of the bits that I read about data, I feel like I'm confident within my rights, like if any of it's abused, so I actually feel like… If they said, oh, they're not going to use my data for the original purpose and they did use it, I actually feel confident that I could like claim some compensation or whatever because, although I don't want my data to be used, I'm confident in my own rights.. if it is used" (Focus Group)*

6.7.5.2 Secondary use of data

The themes relating to secondary use of data identified in the synthesis were used to probe this area with the focus group. One group member had experienced being asked whether they would allow their data to be re-used, and had agreed predicated on a belief that the same ethical frameworks and safeguards would be applied as in the original use,

> *"I was asked that and I said yes. I mean, because it seemed to me…you've given it to one. You would assume that they would pass it on again within a sort of ethical framework, that it wouldn't be misused or abused, so I would say yes". (Focus Group).*

One researcher suggested that the real concern was less about re-use of data, but in loss of confidentiality,

"I think the issue is not a follow-on use of anonymised data but a concern that somebody in the chain is going to break the anonymization, right. That's I think the key issue. I think the idea that data can be used for more than one study and studies that you can't even imagine, I think that's actually great because data…one of the things about data is you don't know what it's going to be good for, and you probably want…the data to be able to accumulate". (Researcher Interview 11)

Others in the focus group were concerned that previous information they had provided in a health setting had been used without their agreement, raising the important point that data collected in one study might not be understood out of that specific context. The data collected by supermarkets or other internet-based organisations was used as an example of potential misuse, but conversely participants could see potential benefits of mining data,

"And the other thing that's getting is this data-mining, right, of data-mining on another higher society level is that, in reality, Google knows a lot about each one of us currently, and that's a huge, huge problem because they were not meant to do any evil and this is not happening.…you know, they've picked up people's medical events just from Tesco spending [laughing]" (Focus Group F1)

"But on the other hand, data-mining, I am technically-inclined but I don't know much about the maths of data-mining. You can't rely on it too much, I don't think, and it would tend to be too expensive to indulge in everything being analysed, but clearly, there must be more emphasis on trying to focus research, of all sorts, in solving the main priorities that we have as individuals or as a population. It is a difficult area…" (Focus Group M2).

6.7.5.3 Data and validity

As well as needing to be certain about the identity of trial participants, the focus group members expressed concerns about the validity of self-reported data, suggesting that 'people' may not be accurate. These factors are also common in many other types of trial, and there were inconsistent views as to whether this may be more of an issue in online trials,

"M1: If you like visit a counsellor and you do it on the phone or on the computer, there's a difference between doing it face-to-face. You get so

much more effects.
F1: I disagree. In lots of ways, by computer, you're going to be flat-out honest. Be honest about it, and that you can be an anonymous person [laughing], without that photo, and you can really hit hard if you need to with some of your responses because you feel quite safe behind the internet curtain [laughing].
F2: That's an interesting point and I think it sort of slightly contradicts what you were saying because you were saying you'd like to…you're happy to say anything online". (Focus Group)

The public suggested that "people" can be "funny", views not portrayed as their own, but possibly based on their own experiences,

"There's always a chance that someone doesn't do it accurately… people can be funny about things about weight and body measurements, and people will, probably not intentionally, fudge it a little bit here, and a bit there, and so what the researcher is getting is what the person filling out the survey thinks the researcher wants to see" (Interview Participant 6)

Self-report in online trials was viewed by researchers in a number of ways, with some feeling that it could increase the potential for inaccuracy, for example by the requirement for participants to have a device with them at all times. They questioned how the use of reminders, or other technical and non-personal ways of engaging participants could affect data collection,

"And then there might be…sort of an incentive to just, you know, do it quickly and, "Oh gosh, you know, they keep reminding me that I've got to do this and I'll just make it up and…" you know, whereas, that's obviously going to be less likely if you're talking to somebody in person" (Researcher Interview 5)

This was supported by responses from the public, demonstrated through the experiences of one former trial participant, who rationalised the lack of accuracy in terms of the absence of personal contact,

"I don't fill things in as accurately as I would in person, like if I was trying to do it really quickly, which is obviously bad for their data, but I just, you know, I just do it to sort of get it out the way, whereas, if I was doing it in person, and I like I had the researcher there, I would actually like spend

more time and do it, do it properly. I think like, on the screen, there's more like anonymity, so like you can… I don't feel guilty because I don't think…they'll know me. Like even in the [name] study that was completely online, like I'd never met the researcher, so I didn't have like a sense of guilt that I would do if I did it in person and didn't do it properly, so that, yeah, I always feel I take them much more seriously if it's in person" (Interview Participant 2)

Respondents in both groups saw the potential of smart devices which could track data as a way of overcoming accuracy problems, but one researcher with direct experience of this viewed the technology as creating its own problems. This supports the previous view from researchers that sometimes, with new methods and technologies, it is not possible to know if you are doing the right thing or not. One public interviewee had taken part in a study where tracking was used to increase adherence, using the threat of withholding financial incentives. Although this was not within a clinical trial setting, the interviewee suggested this as a strategy that could be used for 'others', despite potential damage to the relationship of trust or commonality between researchers and participants,

"they asked you a questionnaire at the end to obviously test whether you had tried the products out because it was – you wouldn't have known the answers otherwise, and it said something like "Please note, if it doesn't seem like as if you've taken part…like as if you actually used the app over the time and did the tasks that we required, then like you won't get your payment", so that did make me use the app properly because I thought, well, they can definitely tell that I'm…by the questions that they ask, and I suspected it would be something like that, that sort of made me do it properly because I knew, yeah, that they'd be able to tell and that I wouldn't get my incentive otherwise. That wasn't a health one, but that could be a strategy that others could use to make me sort of do them a little bit more properly online". (Participant Interview 2)

6.7.6 Technology and Control

The introduction of internet technologies into clinical trials has led to a new set of challenges and experiences for researchers, relating to technical expertise, and how this is brought into the trial. The reliance on commercial expertise was a

concern for researchers, who felt that external companies lacked an understanding of the research process, creating issues relating to trust. Using an existing system without being able to customise it (using shared software and development being one of the stated advantages of online); slow processes and response times; and the lack of a shared culture and language, had all impacted on this relationship. This reliance on others could lead to a feeling of lack of control, which in turn impacted on how researchers perceived their ability to respond to, or form a relationship of trust with their participants "giving power to an automated system" instead.

As well as knowing the limits to their own knowledge, the reliance on external technologists led to pressures including timescales and delays, and reliability of results. Most commonly the lack of understanding of requirements, including the need for rigour, by experts from outside the research environment led to serious concerns and the need for alternative strategies,

> *"I had someone who helped me construct my website, and I've had different people, what I've discovered while doing this is that you need to know, or at least learn different languages and that there are research issues that maybe a web expert won't understand, with all the ethical issues, the confidentiality, all these things. So, the cooperation there was something …that I was made aware of very early, that, you know, we need to…put things straight really early and be very clear about…what is needed" (Researcher Interview 3)*
>
> *"We had difficulties, and because of that…we lost participants, even though it wasn't essential, he said it was good practice to go through the information governance toolkit, and so we ended up having to make a number of changes to the software, and also it ended up with it being so secure that actually it was really difficult just for people to log-in …it's an off-set, it's a balance between the security and the usability, which was quite difficult. I'm not sure we really solved…yeah, so that was challenge …what's really hit us hard is all the technical difficulties that we've had … They're the things that we're not in control of. So, we can find things out or participants report things, but all we can do is report it back to the developers and hope that they can fix it … I think my main note of caution is, just from a technical point of view, making sure you're using*

tools that are fit for purpose and that work, and test them to absolute death, because it's just a headache that you don't need" (Researcher Interview 4)

This expressed lack of 'control' in one case led to the development of an in-house team, which improved the situation, but decreased the potential cost savings seen as a major beneficial factor for online trials,

"one needs to be very cautious that the technology in place is running correctly and has been fully tested…so we build all elements in-house. We have some support from the IT people who built it initially, but it's minimal. So, that has pros and cons. The cons are, because it's not being developed by a professional team of, you know, let's say web developers, it can take longer to test it because we're perhaps less experienced. But the pros, which I think do outweigh the cons, are we have complete control. We don't have to send off scripts to web companies and then, you know, six months later, we get it back and it's not how we expect it. So we do all our internet interventions, which have their own back-end which runs the trial essentially in- house, which I think …. can be quite stressful, but I think, again, the benefits outweigh the costs" (Researcher Interview 9)

6.7.7 Convenience versus intrusion

The intrusion into daily life experienced by trial participants can represent another type of lack of control. Increased flexibility and a reduced need to travel are reported as advantages by researchers and participants, but these benefits are modified by experiences of intrusiveness. Therefore, the convenience of taking part in an online trial in one sense is offset by feelings of burden, and particularly related to data collection,

"I think the more complicated issue when you're talking about stuff like collecting information through phones and things like that is people may not understand…the intrusiveness of the information collection effort. Right? I think that's probably hard for people to understand". (Researcher Interview 12)

"the like other negative might be like, yeah, they're intrusive a little bit. Like, I mainly use my phone for like leisurely things, and so it might be like a little bit of an interruption – if you can't control when you're getting notified about things, for example" (Patient Interview 2)

Participants and researchers were concerned about the intrusive impact of reminders, and doubts about what was expected,

> *"I've had three email reminders about it, so now I do feel quite guilty… Like it's easy to forget like an email and sort of be like, oh, I'll do that later, but not get round to it… like the text one was probably the most annoying one, because like, when you're trying to concentrate on your work and stuff and you see you've got a text, or if you're waiting for an important message, for example, and then you're getting these texts throughout the day" (Public Interview 2)*
>
> *"but, you know, it's the time commitment that would be…that's the intrusion I worry about most" (Researcher Interview 11)*

There is a feeling that the bar is raised in an internet-based trial, in terms of acceptability of intrusion, due to the nature of the medium, and the threshold of burden therefore lowered. The nature of the time commitment has specific features, particularly for longer terms studies, and requires fitting in with daily life to sustain the convenience factor. However, this requirement is at variance between researchers looking to demonstrate long-term outcomes, and participants for whom a two-week commitment can be seen as being 'too long', and for whom dropping out from an activity is very easy. One researcher thought that participants did not feel as accountable for their compliance as in other types of research. This finding is supported by studies on internet-based trials with a high rate of attrition, and where non-response is reported to be an easier option for participants.

Connectivity, another facet of daily online live, can also impact on the way an online trial is experienced. The commitment to take part, and therefore designs to encourage engagement, need to take into account practical issues, such as participants not always being in the same setting, for instance in the workplace or being away from home for the weekend. The public interviewees identified issues

that impacted on data collection, such as the battery life of devices, lack of mobile signal, or having older equipment, and which contributed to inconvenience,

> *"I think it was within 10 minutes of receiving it, and then if not, then they said don't … don't fill it in retrospectively, just leave that and move on to the next one, but if your phone ran out of battery for example or you had no signal, then you wouldn't have got the text reminder, so I suppose like digital technologies do like fail sometimes and quite a lot of the modern mobile phones these days like run out of battery very quickly and things like that. So, yeah, they might affect it…" (Interview Participant 2)*

This is recognised by researchers who admit that the internet 'does crash', and this unreliability may impact on engagement and adherence.

Researchers further reflected on concerns relating to usability and lack of convenience, such as problems relating to constant upgrading of devices and operating systems, and the changing expectations around website design,

> *"I mean, there were various just little things in terms of things on the intervention website, in terms of like changes of wording, things that people find offensive, things that people struggle to use in terms of usability, like buttons not being big enough and just basic UX things and stuff like that". (Researcher Interview 4)*
>
> *"it was more important to them that this was a website that had been developed by researchers … you know, in collaboration with the NHS, and the way that the website was written, it was by a clinical psychologist and very non-confrontational, so that was actually, once they got past the kind of clunkiness and the poor navigation [laughing] and the out-of-date images, they didn't mind so much. Whereas, now, …, kind of it needs to be …you know, at least look sort of fairly acceptable in terms of look and feel and that sort of thing". (Researcher Interview 5)*

Technology can be seen as a positive driver of improved access and convenience, but it is acknowledged that it brings its own problems and failures, for participants and researchers,

> *"Occasionally, we get technical hitches, but again, as we've become more experienced as a research group, those happen less frequently now because …our procedures are more ironed out. So, some patients*

will struggle a bit to get on with certain sections, and sometimes it can be difficult because it's not the programme that's causing the issue, it's the user of the technology, so maybe they've got an old computer or their browser's not quite set up, so that can be a slightly tricky element from the user's perspective in that they may not be able to access a page but we can't help because there's nothing wrong with the system and it might be their browser settings" (Researcher Interview 9)

Some researchers thought that online interventions have become almost too much a feature or part of everyday life, and are therefore a trial intervention is seen as just one of many online tools that potential participants can access. This can manifest as a concern that the activities involved in a trial are not 'different' enough to compete with other online distractions, and that new strategies are need to retain participants.

6.7.8 Sharing, learning and skills

Researchers in the sample, from a range of backgrounds and settings, expressed a need for knowledge to be shared, and for better evidence about methods and trial design,

"perhaps a central network or somewhere that focuses just …on the methodology… Because all of the interventions that we look at are internet-based, the intervention itself and the trial are very intertwined, so to just focus specifically on the methodology would be… It would be nice to have a sort of, a hub [laughing] of expertise of that sort of thing" (Researcher Interview 5)

Researchers were keen to share learning and felt that it is harder to learn in the online trial environment. Some said that they frequently had been 'learning while doing', less likely in traditional clinical trials, and although they would try to act on this learning, and do things differently in the future, there was less of a sense of validated testing,

"We would always do it differently [laughing]. Yeah, I would do it, yeah, not totally different but… No. I would improve a lot of aspects of course. I was learning. I was learning by doing it" (Researcher Interview 1)

"You know, we'd do it differently now. So, there were no sort of clear ideas about what was good about it .. and if anything, we've proved ourselves wrong [laughing]" (Researcher Interview 6)

"We just wanted to do self-report…. which hadn't been done before… one of the whole things about the study was could you run any trials just doing this self- report tool on the internet, how valid was that, because we didn't know" (Researcher Interview 8)

One researcher suggested that there was a need for more collaboration between research teams, and for breaking down barriers between different disciplines and types of expertise,

"I think that my academic life these days does seem to be spent talking a lot around the methodology, of internet trials and the pros and cons of doing trials online and just the fact that .. what we're doing online now really needs to be much more collaborative with other groups of academics in particular, that we can't just expect, .. you know, the walls are really having to be broken down between disciplines at the moment, and I've noticed that, really, really massively noticed that with my work, … huge teams of people are actively trying to collaborate now. They're not working on their own little sort of separate research groups, but the nature of online research is changing hugely, and I think that that's going to be the next big interesting change of how different groups take that forward" (Researcher Interview 6)

This researcher also stressed the need to justify use of the technology when asked what they would want to pass on to a new researcher in the field,

"first of all, don't expect the internet to do anything that you wouldn't be prepared to do yourself [laughing] .. for a lot of people, I do think that the internet is seen as a way of sort of halving your workload or it's seen as a way of doing things quickly and, that's one thing I would say to really just…you know, just get that idea out your head straightway because it doesn't work like that. I think that, using the internet is incredibly complex, and needs to be very well justified. If you could do it without using online methods, then you should do it that way, and there needs to be a very strong reason for using online methods ,...that it has to be justified. It has to be justified. It's not just about recruitment. It's not just like a tokenistic, you know, something that's slotted in to make the researchers' life easier" (Researcher Interviewer 6)

The skills and literacy of their participants was an issue for researchers. Health literacy is clearly an issue in all clinical trials, but in the online environment this is

combined with the need for digital literacy, which as well as creating problems in usability, can feature in considerations of equity and transfer to different cultures and settings.

6.7.9 Patient and public involvement (PPI)

Researchers were aware of the value of involving patients and the public in the way that trials are planned and designed, but did not always do it themselves. There was a sense of them excusing themselves through expressions such as now having 'hindsight'; 'could have improved'; seeing the process as a 'rollercoaster', and therefore maybe not in their control. This is countered by their agreement that more involvement in the process could help mitigate some of the issues they raised themselves concerning the participant expectations.

There was a feeling among some researchers that PPI was seen as an extra burden at a busy time. Where activity was reported, it was primarily to get feedback on practical considerations such as usability, or acceptability of the intervention, rather than as something that could be of value to the wider process of designing or managing the trial. Some of the public interviewees could foresee potential benefits for greater involvement, through shared ownership of the process, or as a way of helping the public understand the 'why' of research. Others expressed initial concerns about the bias that might ensue from the views of individual representatives, but on reflection changed their mind during the course of their interviews, to be more positive about the benefits. A focus group member suggested that the technology itself could be used to 'bring people together' in a communal research sense, not just as a source of data.

The public were confident in the competence of researchers, which contrasted with the researchers mixed experiences of public involvement within

their own trials. Where increased involvement was mentioned, it was felt that it could have the potential to provide solutions to some of the challenges, but would require a different way of working, and would have wider implications for the role of research in general, and in the way it is translated into practice,

> *"And I think that's what we have to do, have that one person come in, but then work with them and their organisation to help build the skills at a broader level, and to continually have these kind of engagements with the community as it goes over time …and be open to it, and listen to what they have to say, and say, you know, "Oh, we've made mistakes" when we have and…and ask for forgiveness and ways forward, and ask for help and ways forward and… And develop these strategies together because…they see things that you don't" (Researcher Interview 11)*

> *"So, I guess the community, having people involved in the development …gives you a sort of bit of accountability, in a sense, you have their voices saying to you, "Well, so what….?" You want people who are going to be really blunt and say, "So what? What difference is this going to make to people's lives?" and, at the end of the intervention, will there be discernible changes in anything, or will it just be that the researcher has more data and the researcher can publish and the researcher can get famous? I think certainly it's a good thing …in offsetting any cynicism about research, and…translating that research, because, yeah, there's so much research that goes on, but the amount of stuff that actually gets translated sort of down to the ground, to everyday people, reaching the people it's supposed to reach and it's designed for" (Research Interview 7)*

Focus group members felt that greater public involvement could help direct internet-based research towards the most important patient-focused questions, such as in areas other than drug trials. This supports what is known about the need to prioritise the most important questions for patients, carers or clinicians [71], and the concept of 'waste' in research [475], and links back to the original ThinkWell research on uncertainties concerning internet-based clinical trials in Chapter 2 [81].

6.7.10 Making sense of the digital world

For some researchers, the pace of technological development and the pace of research were seen as incompatible. The types of technology used by the public can be favoured or avoided depending on rapidly changing preferences. Some researchers said they saw Facebook as not for 'serious content', others that the 'rush to mobile' was not justified, and considerations of when to use mobile technologies rather than computer-based versions were difficult to judge in terms of the impact on participation. These issues may be more prevalent in trials using digital applications but may also impact on trials using web-based interfaces, tools or software which update versions and functionality on a regular basis,

> *"You know, with research that involves technology, the pace at which research goes and the pace at which technology goes, they're unmatchable. Okay. So you do a trial with an app or an online intervention, the time you take to publish that study and the time it takes to reach the public, it's too much" (Researcher Interview 10)*

This presents challenges in terms of making sense of the digital landscape, raising further issues about the appropriateness of using online designs. E-health was seen by one researcher as a 'black-box', while some were trying to understand potential uses as devices change. New options such as device tracking were highlighted, however potential improvements such as this also generated new concerns, such as a lack of trust in the validity of device tracking, and how it would work in practice.

Some see the inevitability of being online as just something that researchers need to keep up with, without necessarily questioning it,

> *"The whole online life is dictating how we do research, and it was very important to engage with that and to see…how we could do it, you know…what is best practice, what do you need to do to recruit well, to keep people in a trial, to what do people like and what do they not like,*

but particularly, in terms of our research question, which was all about internet use and engaging with information online, it was important to do it as wholly online as possible" (Researcher Interview 6)

There is also a disconnect between the nature of research, often necessarily cautious, slow and rigorous, and the speed with which products, tools and technologies quickly 'age' and are replaced by new versions. This represented a wider, more worrying trend for one researcher, with implications for the ethics of research in wider society,

"but in modern society, at least where I live, there seems to be less emphasis on community, and people are, you know, building houses which are not as open anymore – they have brick walls at the front. So, it certainly seems that people are willing to trade-off some community cohesion for increased privacy and things like that, so maybe they're the sorts of people who won't have any objections to participating in internet trials and using internet-based interventions because the benefits outweigh the costs. But then, some people who really value community and obviously don't care about self-monitoring, that don't have any problems to monitor and don't particularly think they need intervention, it would…probably have more negative overtones for them" (Researcher Interview 7)

Some researchers themselves experience negative feelings about the lack of contact, and perceive this as being wider than just a personal relationship in the context of a single trial,

"I think whenever anything goes impersonal, personally, for me, I think it's a bit sad, and I think it sort of…yeah, it doesn't breed…like there's sort of… I tend to have a mind-set that community should be closely linked with university and there should be university/community partnerships and there should be community-based participatory action research going on, and I tend to sort of like those methodologies, so the impersonal nature of it is…certainly one thing I don't technically like" (Researcher Interview 7)

This feeds into general concerns about how the public view both researchers and research, and a feeling that losing the rapport reported earlier will worsen this situation,

"Maybe there's some scepticism about research and researchers in general and some cynicism towards research, and collecting data and doing interventions by means of the internet doesn't really address those concerns because you don't get to meet the researchers and to develop rapport with the researchers, and so you sort of feel…cynicism isn't really addressed and so you remain non-committal, I guess" (Researcher 7).

Finally, a view that the situation will require a similar scale of change in the nature of clinical research itself, which was suggested by a focus group member, and which links the themes of trial design, patient and public involvement, and self-empowerment with the wider model of health care provision,

"I think you've got to move away from the paternalistic medical model, it's so old-fashioned and it's just not keeping up with the generations that are coming through that want to be more self-empowered. The design model needs a hell of a lot of tweaking". (Focus Group)

6.8 Conclusion

Several key themes emerged from these findings, with regard to trial design, conduct and experiences, including the understanding of research, including the nature of consent, equity and reporting; rapport within roles and relationships; control of technology, including security and identity; sharing knowledge and learning; the extent of public involvement; and the impacts of technology on wider research and society. Researchers acknowledged the need for different strategies to compensate for the changes in trial design, management and conduct that online technologies require. Although many of the themes identified were relevant to all clinical trials, some specific themes emerged which require more active consideration by researchers working in this field in the future.

One such over-arching theme is the constant 'trade-off' to be made in trial design and conduct, for instance between embedding interventions into daily life, and the subsequent need for intrusive reminders; dealing with the wide variety of

participant characteristics; or cost-effectiveness and savings versus extra time being spent on feedback or personal contact. A further balance needs to be struck concerning the technical aspects of trial intervention development, and whether this should be done in-house, or outsourced.

It is clear that the same factors that make an online trial attractive to participants, such as convenience and flexibility, can also lead to barriers to engagement, and ultimately higher attrition. There were evident concerns in both groups regarding the lack of understanding about the nature of online clinical trials, and of research in general. Lack of clarity about expectations, the need for personal reassurance, difficulties in getting a realistic understanding of what it will be like to take part in terms of timescales, intrusion and burden of data collection were consistent factors in researcher and participant experiences. Trust is an important factor, and ensuring that information provided at recruitment and consent stage is fully understood could help establish better understanding and clearer expectations for all involved.

In online trials testing behavioural or psychological treatments, the nature of the condition and intervention plays a significant role in researcher and participant experience, particularly in relation to the theme of rapport. For some researchers, there was an acute awareness that the internet medium could not replace the face-to-face therapeutic encounter, however one divergent view was expressed that a lack of personal contact could be seen as a positive feature when testing an intervention where self-management or self-treatment is intended, as it could mirror a ‘real-life’ setting in which patients would not have immediate or personal contact with a health professional or therapist.

For some the nature of technological change and the increasing adoption into all areas of society spark fears of inappropriate use in research, the ‘rush to apps’. There is a sense that trial methodologies need to be agile and to adapt to the changing norms, but that this conflicts with existing trial methods, and in order to maintain ethical standards and safety for participants, will always lag behind the pace of technological development. Whether these concerns lead to further questioning or avoidance of using the technologies is not clear, and requires further research, and community-wide action.

6.9 Chapter summary

- The findings from this study provide an insight into the views, attitudes and experiences of researchers involved in running internet-based trials and the patients and members of the public who they hope to recruit.
- Researchers fear online technologies might reduce public understanding of research.
- The main benefits of an online trial were convenience and flexibility, attractive to researchers as they reduce the burden of trial recruitment and management, and to participants because they can be integrated into daily life. However, it is this very factor, being easy to join, that also provides the biggest challenge to engagement, since it is also easy to leave.
- Researchers and the public appear anxious about losing rapport, mainly through a lack of personal contact.
- Participants said that they value personal contact, and need to be appropriately informed about the amount of contact or tailored support the trial will provide. Although this phenomenon may feature in other types of clinical trial, the nature of an online trial and consent process can result in increased difficult in fully understanding the likely time commitments or the nature of activities or data collection.
- Our increasingly online life may be dictating how research is done, and may also be contributing to an unknown impact on social cohesion.
- A counter strategy was suggested that improved patient and public involvement in the whole trial process could offset this, and improve the relevance and acceptability of online trials.

7 Discussion and conclusion

7.1 Chapter summary

This chapter summarises the thesis and discusses the themes, strengths and weaknesses of the research. It outlines the potential impact of the findings, and makes recommendations for future research and practice.

7.2 Summary of thesis findings

This thesis set out to answer a number of questions relating to the conduct, practice and experience of internet-based clinical trials. The creation of ORCHID provided a baseline understanding of the online trial environment, determining that online trials had grown rapidly in number, with 1992 included in the database to March 2015. A two-stage systematic review, consisting of a descriptive map and a qualitative synthesis, helped build an understanding of what is known about the conduct of, or participation in internet-based RCTs. A primary interview and focus group study was then undertaken to explore the views, attitudes and experiences of participants and researchers in relation to internet-based clinical trials. The primary study built on the findings of the systematic review, and identified possible improvements to the design, recruitment, conduct and relevance of internet-based clinical trials. The main benefits of an online trial were those of convenience and flexibility, attractive to researchers as they reduced the burden of trial recruitment and management, and to participants because they can be integrated into daily life. However, it is this very factor, being easy to join, that also provides the biggest challenge to engagement and attrition, since it is also so easy to leave. Researchers and the public appear anxious about losing rapport, mainly through a lack of personal contact. Findings suggest that improved patient and public involvement in the whole trial process

could help offset this, and improve the relevance and acceptability of online trials. A summary of the research questions, methods, findings and impact can be found in Table 7.1, and a summary of the development of themes throughout the thesis in Appendix 7A.

7.3 Reflexive statement

Previous research and work experiences, formed in the environment of evidence-based practice, specifically in the area of systematic reviews and qualitative research, influenced the choice of methods and topics for this thesis. Ethical considerations, rooted in patient and public-focused approaches, including the importance of dealing with uncertainty and waste in the research cycle are strongly held beliefs. Prior assumptions about the phenomena under investigation may have influenced the way the research questions were formulated, particularly in choices concerning the two-stage systematic review and consequent qualitative study.

An interest in research designs that contribute to the evidence base on 'what works', and ensuring that research is translated into practice, led to the thesis being influenced by a desire to make it useful and actionable by the research community, leading to the emphasis on this group as the core target audience.

As an information specialist by profession, and therefore without a clinical background, some aspects of analysis were undertaken without full knowledge of the clinical condition or intervention background and context, so it was important during recruitment that this was made clear to participants. The majority of interviews were conducted using Skype, without the use of video, for reasons of

convenience or resource-constraints. This was a challenge due to a preference for face-to-face personal contact, and the data was examined carefully to make sure that all data were considered equally.

To help address assumptions and encourage reflexivity researchers from different paradigms were sought to contribute to quality assurance processes, such as screening and coding, and presentations made at multi-disciplinary conferences and seminars to different audiences in order to invite challenge. A research diary was kept throughout the thesis to record thoughts and feelings, and decisions about findings and themes.

7.4 Strengths and weaknesses

The main difficulties experienced throughout the thesis were due to the nature and fast pace of the topic, combined with the constraints of part-time study. This required a constant refreshing of methods over the period of study design and data collection. However, developing the thesis over this length of time also became a strength, allowing for time to reach an interview sample of researchers who had by then gained more experience in the field. As well as significant experience, they were also able to reflect and question aspects relating to the trials undertaken, and the interviews provided an opportunity to articulate and develop these reflections. This helped the thesis explore anticipated and emerging issues, and the length and detail of the data obtained through the interviews also became a strength. This was evident in how the researchers responded in the interviews, moving from recounting practical experiences to a more philosophical reflection and self-questioning. As researchers were intended to be the main audience for the thesis, the richness of the data will hopefully

Research Question	Method	Summary of Findings	Impact of findings
Establish the extent and nature of internet-based clinical trials including: How many randomised controlled trials in health and well-being research have used internet-based technologies as part of the trial process? At what stages of the trial process have internet-based technologies been used and how might these be characterised? How has the use of internet-based technologies in randomised controlled trials developed over time	Database creation (ORCHID)	Online trials have grown rapidly in number, with 1992 internet-based trials included in the database to March 2015. The largest number of trials were conducted in the USA (49.7%), followed by The Netherlands (10.2%); Australia (8.5%); the United Kingdom (5.8%); Sweden (4.6%); Canada (4%); and Germany (2.6%). South Korea (1.5%) has the highest number of reported trials for other continents. There is a predominance of interventions addressing public health challenges including obesity (8.6%); smoking cessation (5.9%); alcohol abuse (7.7%); and physical activity (10.2%); in mental health issues such as depression (10.9%) and anxiety (5.6%); and in conditions where self-management (16.6%) or monitoring (8.1%) is a major feature of care. The internet is most commonly used in the intervention stage of a trial.	ORCHID provides a resource for researchers, as a sampling frame to mine, and add, data. Coding structure used to inform initial coding framework for descriptive map, including stages of trial; conditions; interventions; and perspectives. Results used to mine for methodological studies, and researchers for qualitative study.
Identify and explore the methodological, ethical, technological or experience-based studies relating to internet-based randomised controlled clinical trials	Two-stage systematic review: Stage 1: descriptive map	Map includes 406 studies. *Country of study*: USA (173), followed by the UK (57), Australia (43), The Netherlands (29), Germany (20), and Canada (18). *Condition, topic and subjects:* Psychological and Behavioural treatments (83); Mental Health conditions (61); Smoking cessation (31); Obesity (30); HIV/Sexual Health; Alcohol (12); Cardiovascular diseases (12); Neurological diseases (12); Child Health (10); Physical Activity (10). *Stage of trial*: trial planning and design (49); acceptability and feasibility (13); trial management and co-ordination (47); recruitment and enrolment (114); screening and randomisation (17); data (109); engagement and fidelity (38); adherence, retention and attrition (94); ethical issues (47); perspectives or experiences (138).	Map used to identify potential questions for further synthesis. Coding structure used to inform thematic framework for qualitative study.
What is known about the views, experiences and expectations of internet-based clinical trial participants and researchers, and how might these impact on the design, conduct and improvement of research.	Two-stage systematic review: Stage 2: Qualitative synthesis	15 papers included. *Main themes:* (1) Choice, consumers and expectations; (2) Autonomy and self-efficacy; (3) Perceptions of roles and relationships; (4) Information as an intervention; (5) Making it personal; (6) Obligation or burden; (7) Feeling safe and secure; (8) Being supported (9) Technology, time and place; (10) Ethics and informed consent.	Results used to inform primary qualitative study, including anticipated themes; interview and focus group schedules; experts in the field; and potential interviewees
To explore the attitudes and experiences of people involved in internet-based clinical trials, including patients and the public, study participants, and researchers, to help improve the design, recruitment, conduct and relevance of health research.	Primary qualitative interview and focus group study	19 interviews, and 1 focus group was held between 2015-2106. *Anticipated themes* (identified from the literature synthesis): the understanding of research; ethical issues including consent, equity, and reporting; trial management and design; roles and relationships; personal support; and feeling safe and secure. *Emergent themes*: convenience versus intrusion; Rapport: being in control: sharing knowledge and learning; the extent of patient and public involvement; the wider impact of technology on society, and the impact of this on research.	Public understanding of research should be improved. Researchers and the public appear anxious about losing rapport, mainly through a lack of personal contact. Participants need to be appropriately informed about the amount of contact or tailored support the trial will provide. Online norms may be dictating how research is done, and may also be contributing to an unknown impact on social cohesion. Improved patient and public involvement in the whole trial process could offset some of the challenges, and improve the relevance and acceptability of online trials.

Table 7.1 Research questions, methods, findings and impact

broaden the relevance and usefulness of the research, despite the time taken to complete it.

It is inevitably harder to conduct online studies where physical measures or samples need to be collected, although some trials in ORCHID do include self-reporting or monitoring. However, these are less prevalent in the later stages of the research, and this may limit the transfer of learning in some cases. Challenges in the development of new information science and systematic review methods were experienced, but were compensated by opportunities for collaboration, as in the case of the text-mining project.

7.5 Implications of the research

The creation of the database and descriptive map have produced a potential data source for other researchers interested in the methodologies and conduct of internet-based trials. Sub-sets of the database have already been used to inform other research studies, and could be mined for other uses [95]. It is hoped that ORCHID could continue to be updated, and become an open access resource for anyone interested in the conduct of internet-based clinical trials. The results from the synthesis, combined with findings from the primary study, will help researchers understand more about the conduct of internet-based trials, to formulate further questions for enquiry, and to consider wider factors in planning and design. The full table of findings arranged by trial stage can be found in Appendix 7BThere is also the potential to inform and engage with those outside the research community, and to encourage triallists to more fully collaborate with patient and the public, throughout the whole trial process. The combination of research methods in information science, wider systematic reviewing and

qualitative research can make effectiveness research more meaningful and answer important questions.

7.6 Research and practice recommendations

Existing methodological uncertainties, as identified in Chapter 2 (see Table 2.1) remain, but the thesis has also identified areas for research, some of which were identified by researchers themselves in the qualitative interviews. One specific recommendation is made to continue to update and refine the ORCHID as an open access resource. To help researchers view the findings from a practice-based perspective, a brief summary of recommendations is included in Table 7.2, and summary findings with recommendations for practice in Appendix 7C.

7.7 Conclusion

Our increasingly online life may be dictating how research is done, and have an impact on ethics, adherence, and the wider understanding about health research. Given the constant evolution of clinical trial methods, some of these findings may be generalisable to all trials, and the difficulty in distinguishing findings specific to online trials in the data collected as part of this thesis demonstrates this complexity.

7.7.1 Roles and relationships

Participants do not always differentiate between the role of a researcher and health professional or therapist, and this can cause problems and confusion for both groups. Although this may occur within other types of clinical trial, it is an important distinction for digital researchers, but there is a perception on their part that this is less so, or not noticed, by participants.

• **Trial planning and design**
• Researchers should ensure there is a clear theoretical framework for their online trial design, keep up-to-date with methodological research, and consider other designs where appropriate.
• Acceptability and feasibility testing should be improved, and consideration given to health and digital literacy to ensure that content is adequately tailored for the target group.
• Researchers should consider both cost and quality assurance implications when deciding whether to develop online interventions in-house or outsource them.
• **Informed consent**
• Researchers should consider developing innovative technical solutions to provide trial information and gain informed consent, tailoring to different needs to address accessibility and equity.
• **Communication**
• Planning appropriate and relevant feedback requires consideration at the trial design stage, and participants should be appropriately informed about the amount of contact or tailored support the trial will provide.
• **Data collection and security**
• Expectations need to be made clear about data collection and burden, preferences for feedback and reminders, and time commitments.
• Researchers need to consider where and how participants will be accessing interventions, and ensure that privacy and confidentiality are maintained • Participants need specific and clear information on data storage and security.
• **Patient and public involvement**
• Researchers should take more responsibility for involving patients and the public in the whole trial process, working in partnership to offset some of the challenges, and improve the relevance and acceptability of online trials.
• **Sharing and learning**
• Online trial teams should be multi-disciplinary and include digital, usability, and qualitative expertise.
• **Reporting and translation**
• Standardisation in indexing methodology could help provide transparency in research, and improve reporting and retrieval of internet-based clinical trials research.
• Researchers should ensure that participants are offered, and receive, trial results.
• Research teams should consider whether Internet-based tools or resources tools could continue to be available after the trial, but consider issues of maintenance.

Table 7.2 Summary of practice recommendations

One specific area that emerged was the predominance of trials testing psychological therapies, as interventions for mental health conditions, life-style or behavioural changes. Themes such as the relationship between the researcher and therapist role, or the absence of a known therapist, in internet-based trials formed a significant volume of the findings. Roles and relationships are likely to

be different in trials of this nature, and this needs to be taken into account when considering other types of interventions.

7.7.2 Being personal

Public interviewees expressed a willingness to take part in online trials, but also had expectations that involvement would still lead to some form of face-to-face or telephone contact. This requirement for levels of tailoring, and consequent expectations, varies between participants, and between participants and researchers, and adds an extra layer of complexity to online trial design. In traditional trials the increase of contact, or experience of being 'looked after' can be heightened, and the online researcher may also find themselves unwittingly becoming a therapist, when participants are 'reaching out for help', and also recognise the powerful impact for participants of having someone 'taking notice of them'.

7.7.3 The digital world

The pervasive increase of technology in society, and the nature of online as a normal part of daily life is mirrored in the increased development and conduct of clinical trials intended to test some forms of treatment and improve health. The nature of these developments, and the pace of change, can be seen in the changing relationship between health care and the public, and in the way research is conducted. It can provide convenient and flexible tools to collect data and track activity, but can also be intrusive, easy to join, but similarly easy to leave. That technology dictates the uptake and development of internet-based trials may seem inevitable, but researchers need to be careful that trials are planned and designed based on important patient-led questions, rather than follow technological trends as a first principle. This sense of inevitability that

researchers should adopt online designs as a matter of course emerged during the interviews with researchers, and yet they themselves expressed doubts about their ability to fully consider the impacts of this on trial conduct. What might seem obvious in terms of efficiency might not be - not through the door - unintended participant - and the findings suggest researchers need to be careful about false economies and unknown, unintended consequences of their designs.

7.7.4 Sharing and learning

Ensuring that researcher knowledge and expertise is tested and shared is difficult in a fast-paced and dynamically evolving field of research. It was clear that researchers share learning about the specific interventions in their subject field, but not necessarily about online methods more generally. This means that it is harder to share cumulative knowledge amongst the global community of researchers who produced the studies contained in the ORCHID database, or indeed to help mentor those who have yet to use these technologies in their trials. For instance, the emergent theme on the use of open data, and the impact that this might have on clinical trials, raises questions beyond those about experiences in joining and participating in trials, and will have potentially global impact. Theory building is complex in an area that changes so rapidly, where even within the life of one trial the technology can become redundant.

7.7.5 Citizens and research

Themes emerged relating to wider ethical issues, sustainability and waste, which add to the need for a more systematic and embedded public engagement and understanding. This will require a wider investment in how patients and the public are brought more fully into the research process, such as that currently underway through NIHR in England, and possibly a re-framing of what this relationship is

about. The phrase, ‘patient and public involvement’, may not convey adequately enough the need for a much wider, more systematic and embedded role for the public in research, both at policy and practical level. One suggestion has been made to alter this to ‘partnership’, but this will require further exploration.

The flow of this thesis has followed a course from practical to ethical and philosophical considerations and themes. This is to be expected when considering any paradigm shift, particularly when changes such as those in technology, outstrip behaviours and evaluation. From whichever perspective it is viewed from, the rush to technology is inexorable. In order to ensure that these processes benefit society, and avoid harm, researchers need to find more efficient and effective ways to share and learn, to ensure that they are fully engaged with citizens to plan together.

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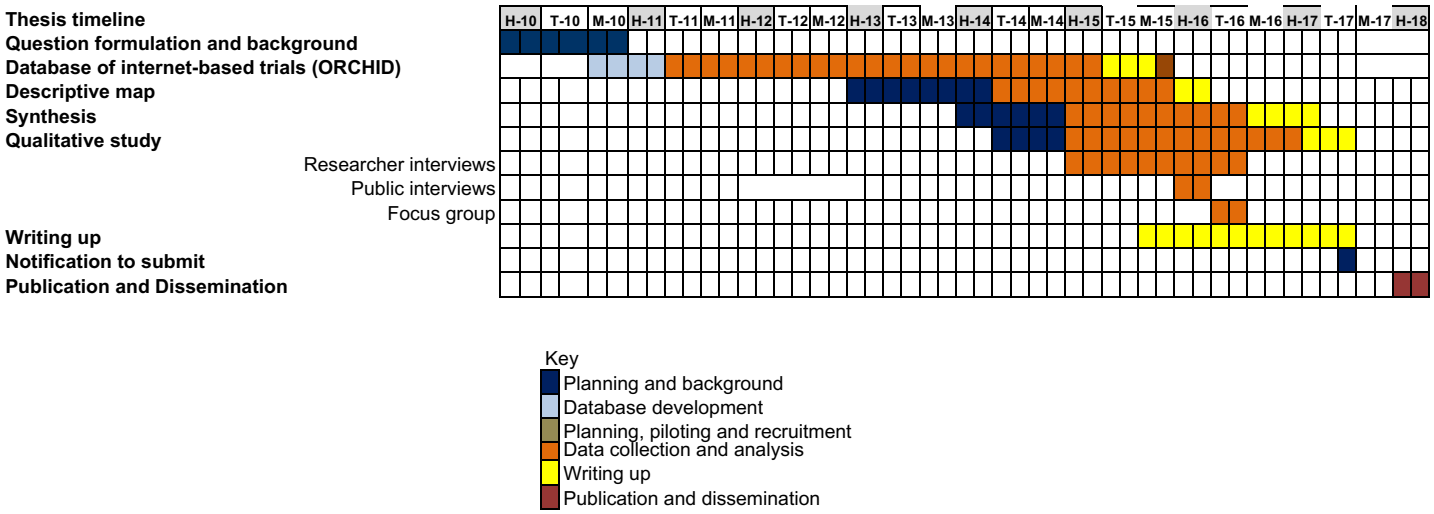
APPENDICES

CHAPTER 1 APPENDIX

APPENDIX 1.A - THESIS TIMELINE



CHAPTER 3 APPENDIX

APPENDIX 3.A - SEARCH STRATEGIES

A. MEDLINE: (Ovid MEDLINE 1948 - January, Week 1, 2011: Updates 13/01/13; 15/03/15)

1. Exp Computer Communication Networks/
2. (internet$ or web$ or online or on-line).mp.[mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
3. 1 or 2
4. randomized controlled trial.pt
5. controlled clinical trial.pt
6. randomized.ab
7. placebo.ab
8. clinical trials as topic.sh
9. randomly.ab
10. trial.ti.
11. 4 or 5 or 6 or 7 or 8 or 9 or 10
12. exp animals/not humans.sh
13. 11 not 12
14. 3 and 13

B. EMBASE: (Ovid EMBASE 1980 - 2011 Week 2: 18/1/11: Updates 13/01/13; 15/03/15)

1. (internet$ or online or on-line).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
2. random$.tw. or placebo$.mp. or double-blind.tw
3. 1 and 2

C. PsycINFO: (Ovid PsycINFO 1987 - January Week 1 2011: Updates 13/03/13; 15/03/15)

1. (internet$ or web$ or online or on-line)mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
2. (random$ adj assigned.tw.)
3. double-blind.tw.
4. control.tw.
5. 2 or 3 or 4
6. 1 and 5

D. CINAHL: (EBSCO 1981 - 01/02/13: Updates 13/03/13; 15/03/15)

1. (MH “Internet+”)
2. web* or internet* or online
3. s1 or s2
4. PT clinical trial
5. MH “Treatment Outcomes+”
6. TX randomized
7. S4 or s5 or s6
8. S3 and s7

E. ERIC: (Proquest 03/02 2011: Not used in Update searches)

1. RANDOMI* in TI,AB
2. (RANDOM* near (ALLOCAT* or ALLOT* or ASSIGN* or BASIS* or DIVID* or ORDER*)) in TI,AB
3. (RANDOM* in TI,AB) not (#1 or #2)
4. (SINGL* or DOUBL* or TREBL* or TRIPL*) near (BLIND* or MASK*)) in TI,AB
5. ((COMPAR* or CONTROL* or EXPERIMENT* or INTERVENT* or THERAP* or TREATMENT*) near (GROUP* or CLASS*)) in TI,AB
6. ((ALLOCAT* or ALLOT* or ASSIGN* or DIVID* or ORDER*)) near (#5)) in TI,AB
7. ((CROSS?OVER) or (CROSS near1 OVER)) in TI,AB
8. (LATIN near SQUARE) in TI,AB
9. ((CLINIC* or CONTROL*) near (TRIAL* or STUDIES*)) in TI,AB
10. PLACEBO*
11. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10

F. PEDro: (https://www.pedro.org.au) 26/01/11 (Not used in Update searches)

1. Internet or web or online in Abstract or Title and Method: clinical trial

G. OT Seeker (http://www.otseeker.com) 26/01/11 (Not used in Update searches)

1. internet or web or online and Method: Randomised Controlled Trial

APPENDIX 3B - TERM AND FILTER TESTING

IBRCT mapping and search term testing

Anne Brice
EBHC DPhil Seminar Week
February 2011

Sources

Databases
- Medline*
- Embase*
- Cinahl*
- Central
- LILACS
- PsycInfo*
- ERIC
- Pedro*
- OT Seeker*

Other

Search Engines
- Google, Yahoo, Copernic

Handsearching
- JAIA
- JMIR

Content experts

Reference lists & citation searching

Search strategy

For health related databases:
Internet concepts/RCT filter

For non-health related databases:
Internet concepts/RCT terms/health or well-being terms

Terms

Setting	Perspective	Intervention
Health care	Randomized controlled trials	Internet technologies
Health*	RCT filters tested as available	Internet
Health care		web
Public health		online
e-health		e-treatment
e-treatment		self-recruit*
Medical		e-intervention
Well$being		e- consent

Terms – testing

Intervention
- Tested main free-text terms from brainstorm
- Identified relevant thesaurus terms
- Text word analysis from key papers
- Web sites and personal contacts

Internet concept terms: MEDLINE

MeSH
1. Computer Communications Networks/
2. Internet/ (introduced 1999)

Free-text
1. internet$
2. web$
3. online or on-line

(use of "$" includes "internet-based" etc)

Other terms tested

- "e-RCT"
- "e-randomis(z)ed controlled trial"
- "internet randomis(z)ed controlled trial"
- "internet RCT"
- "e-health"
- "e-well(-)being"
- "e-treatment"
- "e-intervention"
- "e-ethics"
- "e-biobank"
- "e-consent"
- "e-assent"
- "e-epidemiology"
- "citizen(')s(') epidemiology"
- "self(-)recruit(*)"
- "internet recruit"
- "internet-based"
- "internet-based RCT"
- "internet-based trials"
- "internet-based randomized"
- "web-based"
- "web-based RCT"
- "web-based randomized"
- "internet-based pragmatic"
- "pragmatic internet-based"
- "self-report(s)(ed)"
- "recruited themselves"
- "randomised by computer"

Internet concepts test: Medline

Free-text	MeSH	Results
"internet$ or web$ or online or on-line or e-treatment$ or e-intervention$ or e-consent$ or self recruit$ or self-recruit$"	Exp Computer Communication Networks/	107911
"internet$ or web$ or online or on-line	Exp Computer Communication Networks/	107161
"internet$ or online or on-line"	Exp Computer Communication Networks/	80172
"internet$ or online or on-line"		71168

Search conducted on Ovid Medline 1948 – January Week 2 2011: 21/1/11

MEDLINE

Final strategy:

1. Exp Computer Communication Networks/
2. internet$ or web$ or online or on-line
3. 1 OR 2
4. Cochrane HSS sens_prec max
5. 3 AND 4

Internet concept terms: EMBASE

Emtree
1. Mass communication/
2. Internet/
3. E-mail/

Free-text
1. internet$
2. web$
3. online$

(use of "$" includes "internet-based" etc)

EMBASE concepts

- exp Mass Communication/ OR free-text AND Wil RCT Optimized = 17044
- exp Internet/ OR free-text AND Wil RCT Optimized = 7780
- exp Mass Communication/ AND Wil RCT Optimized = 12467
- exp Internet/ AND Wil RCT Optimized = 2343
- free text "internet$" OR "e-mail$" OR "mobile phone$" AND Wil Optimized = 7965

Problems

Internet concept
- Poorly controlled topic, and as use of internet has increased, almost ubiquitous in study reports, ie particularly "web" & "online" as text words
- Some terms identify large numbers of irrelevant results, ie "e-" picks up Vitamin E

RCTs
- Need to increase sensitivity, but combined with very sensitive terms for the "internet" concept, leads to huge number of results with very poor precision
- Poor and inconsistent indexing within and between databases

Filters

- Literature search for analysis of filter characteristics and performance
- Identified key web sites ie Intertasc search filters resource (http://www.york.ac.uk/inst/crd/intertasc/)
- Contacted search experts
- Criteria for search preferences
- Analysed filters for appropriate sensitivity, specificity and precision

- Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2 [updated September 2009]. The Cochrane Collaboration, 2009. Available from www.cochrane-handbook.org.
- Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE Sharon S.-L. Wong, Nancy L. Wilczynski, and R. Brian Haynes*J Med Libr Assoc. 2006 January; 94(1): 41–47.*

Search filters for RCTs in MEDLINE

Filter	Sensitivity	Specificity	Precision
Clinical Queries- sensitive	99.2	70.1	10.0
Cochrane HS RCT	98.4	77.9	13.0
Cochrane B	98.0	86.8	19.9
Clinical Queries- balanced	96.5	95.1	39.6
Clinical Queries - specific	94.0	97.5	55.5
Single term (randomized controlled trial.pt)	93.7	97.6	56.4

Ovid MEDLINE

"Internet" terms combined with:	Results
Clinical Queries- sensitive	12,085
Cochrane HS RCT sensitive	11,024
Cochrane HS RCT sensitive_prec max	4,465*
Clinical Queries- balanced	3,505*
Clinical Queries - specific	1,632
Single term (randomized controlled trial.pt)	1,534

Search conducted: Ovid Medline 1948 – January Week 1 2011: 18/1/11 using Internet terms max-sens

Search filters for RCTs in EMBASE

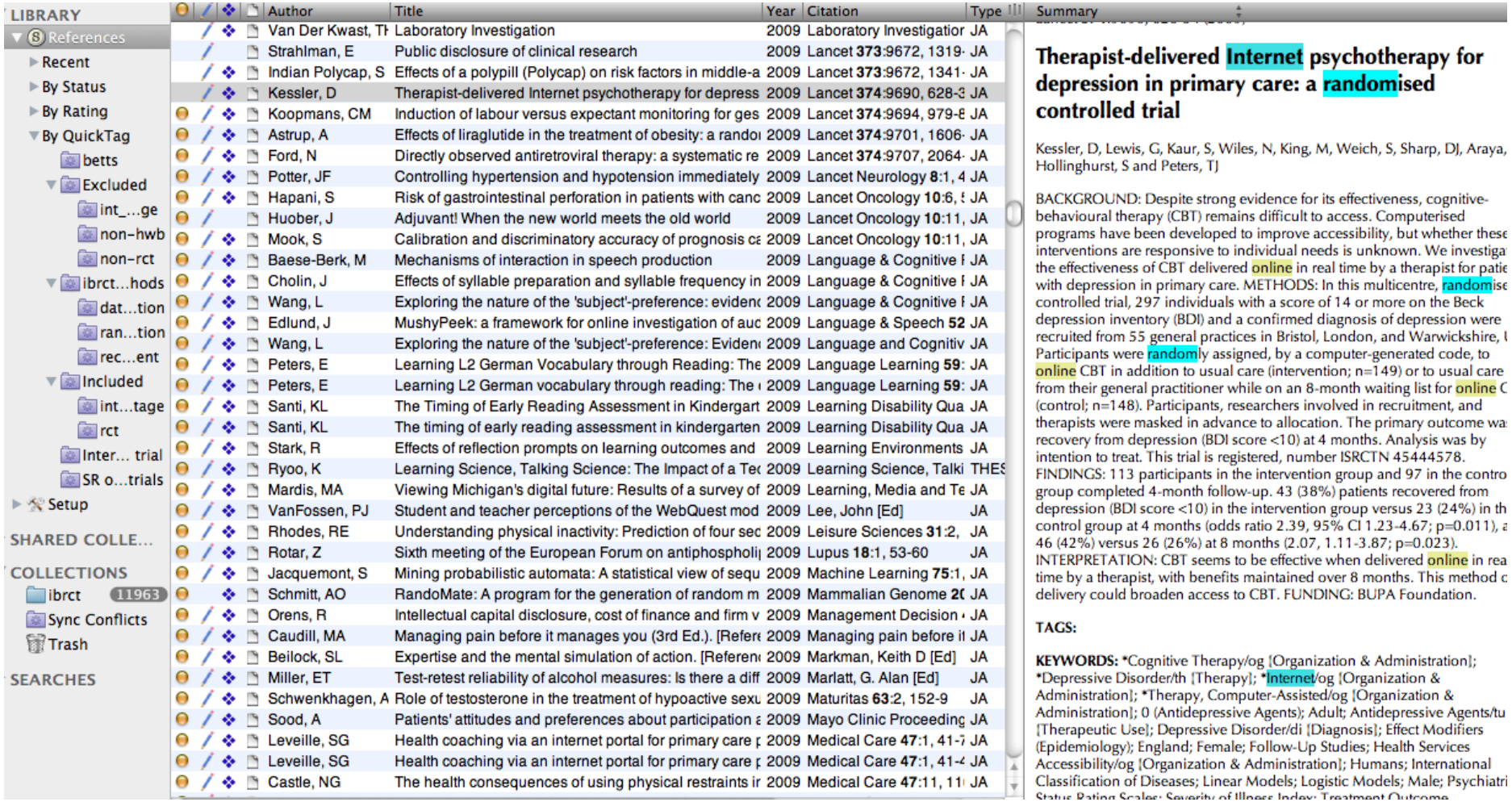
Filter	Sensitivity	Specificity	Precision
Wil - sensitive	98.9	72.0	14.3
Wil – sensitive2	98.7	77.8	17.4
Wil - specific	51.7	96.7	42.8
Wil - optimized	94.5	92.6	37.8
Cochrane H	Not calculated		
Wong	Not calculated		

Ovid EMBASE

"Internet" terms combined with:	Results
Wil – sensitive2	14,823
Cochrane H	11,967
Wil - optimized	7,965
Single term (random$.mp)	7,780
Single term (clinical trial/)	5,884
Wil - specific	1,179

Search conducted: Ovid Embase 1980 – 2011 Week 02: 18/1/11 using Internet terms max-sens

APPENDIX 3C - SENTE screen shot



APPENDIX 3D - TRIALS BY COUNTRY

Appendix 3C: Internet-based trials by country, 2015

Country		% of 2024
USA	944	46.6%
The Netherlands	202	10.0%
Australia	196	9.7%
UK	122	6.0%
Sweden	118	5.8%
Canada	80	4.0%
Germany	76	3.8%
South Korea	27	1.3%
Switzerland	27	1.3%
Spain	25	1.2%
Italy	22	1.1%
Denmark	21	1.0%
Belgium	20	1.0%
Finland	19	0.9%
Japan	19	0.9%
Norway	19	0.9%
New Zealand	10	0.5%
Taiwan	10	0.5%
Hong Kong	9	0.4%
Israel	9	0.4%
China	7	0.3%
France	6	0.3%
Austria	5	0.2%
Bulgaria	3	0.1%
Ireland	3	0.1%
Portugal	3	0.1%
Turkey	3	0.1%
Greece	2	0.1%
Hungary	2	0.1%
Macedonia	2	0.1%
Malaysia	2	0.1%
Singapore	2	0.1%
Bangladesh	1	0.05%
Czech Republic	1	0.05%
Iceland	1	0.05%
Peru	1	0.0%
Philippines	1	0.05%
Poland	1	0.05%
Slovenia	1	0.05%

APPENDIX 3E - TRIALS BY MeSH CATEGORIES

Main MeSH heading	No.	2nd level heading	No.	3rd level heading	No.	4th level heading	No.	5th level heading	No
Cardiovascular Diseases [C14]	150								
		Cardiovascular Abnormalities [C14.240]	1						
		Heart Diseases [C14.280]	4						
				Arrhythmias, Cardiac [C14.280.067]	3				
				Heart Defects, Congenital [C14.280.400]	1				
				Heart Failure [C14.280.434]	7				
				Myocardial Ischemia [C14.280.647]					
						Acute Coronary Syndrome [C14.280.647.124]	2		
						Angina Pectoris [C14.280.647.187]	1		
						Coronary Disease [C14.280.647.250]	1		
								Coronary Artery Disease [C14.280.647.250.260]	6
						Myocardial Infarction [C14.280.647.500]	2		
		Vascular Diseases [C14.907]	37						

				Cerebrovascular Disorders [C14.907.253]					
						Stroke [C14.907.253.855]	14		
				Embolism and Thrombosis [C14.907.355]	1				
				Hypertension [C14.907.489]	22				
Digestive System Diseases [C06]	26								
		Gastrointestinal Diseases [C06.405]	18						
				Esophageal Diseases [C06.405.117]	1				
				Intestinal Diseases [C06.405.469]					
						Colonic Diseases [C06.405.469.158]			
								Irritable Bowel Syndrome [C06.405.469.158.272.608]	10
						Inflammatory Bowel Diseases [C06.405.469.432]	1		
						Colitis, Ulcerative [C06.405.469.432.249]	7		
						Crohn Disease [C06.405.469.432.500]	1		
				Stomach Diseases [C06.405.748]					
		Liver Diseases [C06.552]	4						

				Hepatitis [C06.552.380]	2				
Female Urogenital Diseases [C13.351]	58								
		Genital Diseases, Female [C13.351.500]	4						
				Infertility [C13.351.500.365]	4				
		Pelvic Floor Disorders [C13.351.625]	1						
		Urologic Diseases [C13.351.968]	4						
				Kidney Diseases [C13.351.968.419]	4				
				Urinary Bladder Diseases [C13.351.968.829]	3				
				Urinary Tract Infections [C13.351.968.892]	1				
		Pregnancy Complications [C13.703]	2						
				Abortion, Spontaneous [C13.703.039]	1				
				Phenylketonuria, Maternal [C13.703.575]	1				
		Pregnancy and Childbirth	36						
		Menstruation Disturbances [C23.550.568]	3						
				Dysmenorrhea [C23.550.568.750]	1				

				Menopause	5				
				Prolapse	1				
Male Urogenital [C12]	5								
		Genital Diseases, Male [C12.294]	1						
				Infertility [C12.294.365]	3				
				Prostatic Diseases [C12.294.565]					
				Sexual Dysfunction, Physiological [C12.294.644]					
						Erectile Dysfunction [C12.294.644.486]	5		
				Sexually Transmitted Diseases [C12.294.668]	5				
		Urologic Diseases [C12.777]	5						
				Kidney Diseases [C12.777.419]	1				
						Nephrolithiasis [C12.777.419.600]			
								Kidney Calculi [C12.777.419.600.500]	1
						Sexually Transmitted Diseases [C12.294.668]	5		
Mental Disorders [F03]	746								
		Anxiety Disorders [F03.080]	111						
				Obsessive-Compulsive Disorder [F03.080.600]	10				
				Panic Disorder [F03.080.700]	24				

				Phobic Disorders [F03.080.725]	49				
		Bipolar and Related Disorders [F03.084]	17						
		Disruptive, Impulse Control, & Conduct Disorders [F03.250]	5						
				Gambling [F03.250.400]	2				
		Elimination Disorders [F03.388]	1						
				Encopresis [F03.388.300]	1				
		Feeding and Eating Disorders [F03.400]	46						
		Mood Disorders [F03.600]							
				Depressive Disorder [F03.600.300]	218				
						Seasonal Affective Disorder [F03.600.300.775]	1		
		Neurocognitive Disorders [F03.615]	33						
				Cognition Disorders [F03.615.250]	7				
				Dementia [F03.615.400]	26				
		Neurodevelopmental Disorders [F03.625]	4						
				Child Development Disorders, Pervasive [F03.625.164]					
						Autism Spectrum Disorder [F03.625.164.113]	3		

						Tourette Syndrome [F03.625.992.850]	1		
		Personality Disorders [F03.675]	2						
				Paranoid Personality Disorder [F03.675.600]	1				
		Schizophrenia and Other Psychotic Disorders [F03.700]	12						
				Paranoid Disorders [F03.700.450]	1				
				Psychotic Disorders [F03.700.675]	1				
				Schizophrenia [F03.700.750]	10				
		Sleep Wake Disorders [F03.870]	28						
		Somatoform Disorders [F03.875]	24						
				Body Dysmorphic Disorders [F03.875.149]	21				
				Hypochondriasis [F03.875.450]	3				
		Substance-Related Disorders [F03.900]	188						
				Alcohol-Related Disorders [F03.900.100]	156				
				Tobacco Use Disorder [F03.900.912]	8				
		Trauma and Stressor Related Disorders [F03.950]	79						

				Stress Disorders, Traumatic [F03.950.750]	79				
						Stress Disorders, Post-Traumatic [F03.950.750.500]	24		
Musculoskeletal Abnormalities [C05.660]	53								
		Bone Diseases [C05.116]	4						
		Joint Diseases [C05.550]	2						
				Patellofemoral Pain Syndrome [C05.550.700]	2				
		Muscular Diseases [C05.651]	7						
				Fibromyalgia [C05.651.324]	7				
		Rheumatic Diseases [C05.799]	12						
				Arthritis, Juvenile [C05.799.056]	4				
				Arthritis, Rheumatoid [C05.799.114]	5				
				Fibromyalgia [C05.799.321]	7				
				Osteoarthritis [C05.799.613]	3				
				Spondylarthritis [C05.550.114.865]	1				
Nervous System Diseases [C10]	194								
		Autoimmune Diseases of the	9						

		Nervous System [C10.114]							
				Multiple Sclerosis	9				
		Central Nervous System Diseases [C10.228]							
				Brain Diseases [C10.228.140]	78				
						Brain Injuries [C10.228.140.199]	19		
								Brain damage, chronic	
								Cerebral Palsy [C10.228.140.140.254]	2
						Dementia [C10.228.140.380]	26		
								Alzheimer Disease [C10.228.140.380.100]	17
								Huntington Disease [C10.228.140.380.278]	1
						Epilepsy [C10.228.140.490]	2		
						Headache Disorders [C10.228.140.546]	11		
				Movement Disorders [C10.228.662]	4				
						Parkinsonian Disorders [C10.228.662.600]	4		
				Spinal Cord Diseases [C10.228.854]	2				
						Spinal Cord Injuries [C10.228.854.770]	2		
		Neurodegenerative Diseases [C10.574]	4						

				Parkinson Disease [C10.574.812]	4				
		Neurologic Manifestations [C10.597]	40						
				Neurobehavioral Manifestations [C10.597.606]	38				
						Pain [C10.597.617]			
								Back pain	30
								Headache [C10.597.617.470]	8
				Paralysis [C10.597.622]	1				
				Sensation Disorders [C10.597.751]	1				
						Dizziness [C10.597.751.237]	1		
		Neuromuscular Diseases [C10.668]	3						
				Fatigue Syndrome, Chronic [C10.668.364]	3				
		Sleep Wake Disorders [C10.886]	23						
		Trauma, Nervous System [C10.900]	5						
				Spinal Cord Injuries [C10.900.850]	5				
Nutritional and Metabolic Diseases [C18]	310								
		Metabolic Diseases [C18.452]	146						

				Glucose Metabolism Disorders [C18.452.394]					
						Diabetes Mellitus [C18.452.394.750]	133		
				Lipid Metabolism Disorders [C18.452.584]	8				
				Metabolic Syndrome X [C18.452.625]	5				
		Nutrition Disorders [C18.654]	177						
				Overnutrition [C18.654.726]	177				
						Obesity [C18.654.726.500]	177		
Otorhinolaryngologic Diseases [C09]	20								
		Ear Diseases [C09.218]							
				Hearing Disorders [C09.218.458]	17				
						Tinnitus [C09.218.458.670]	7		
		Laryngeal Diseases [C09.400]	1						
				Voice Disorders [C09.400.940]	1				
		Pharyngeal Diseases [C09.775]	2		2				
Respiratory Tract Diseases [C08]	70								
		Bronchial Diseases [C08.127]	36						

				Asthma [C08.127.108]	36				
		Lung Diseases [C08.381]	17						
				Cystic Fibrosis [C08.381.187]	6				
				Lung Diseases, Obstructive [C08.381.495]	11				
		Respiration Disorders [C08.618]	7						
				Apnea [C08.618.085]	6				
				Dyspnea [C08.618.326]	1				
		Respiratory Hypersensitivity [C08.674]	38						
				Asthma [C08.674.095]	36				
				Rhinitis, Allergic [C08.674.453]	2				
		Respiratory Tract Infections [C08.730]	1						
Skin and Connective Tissue Diseases [C17]	24								
		Skin Diseases [C17.800]	24						
				Acneiform Eruptions [C17.800.030]					
						Acne	5		
				Dermatitis [C17.800.174]					
						Dermatitis, Atopic [C17.800.174.193]	2		

						Psoriasis	6		
				Skin Diseases, Infectious [C17.800.838]					
						Skin Diseases, Viral [C17.800.838.790]	1		
Environment and Public Health [N06]	16								
		Environment [N06.230]	3						
				Noise [N06.230.400]	2				
		Public Health [N06.850]	16						
				Accidents [N06.850.135]	4				
						Accident Prevention [N06.850.135.060]	4		
				Hygiene [N06.850.670]	1				
				Public Health Practice [N06.850.780]	7				
						Primary Prevention [N06.850.780.680]			
								Vaccination [N06.850.780.680.310.890]	7

APPENDIX 3F - TRIALS BY INTERVENTION (ALPHABETICAL)

Acceptance and commitment therapy	4
Aftercare	1
Aromatherapy	1
Behaviour change_wider determinants	201
Breath test	2
Chewing gum	1
Cognitive therapy	274
Communication	187
Complementary therapies	5
Compliance	62
Computer use	1
Counselling	79
Decision support	51
Diagnostics	31
Diaries	31
Drug therapy	55
Education	310
(psychoeducation)	45
Family therapy	6
First aid	1
Handwashing	2

Health information	167
Health promotion	300
Health records	10
Herbal remedies	1
Labelling	5
Lubricants	1
Mindfulness	6
Monitoring	132
Mood charts	2
Motivation	61
Neuropsychological tests	11
Spirometry	1
Nutrition	100
Occupational therapy	1
Online shopping	2
Otoscopy	1
Outcomes	2
Parenting	11
Physical activity	160
Physiotherapy	5
Prescribing	2
Problem solving	32
Programming	1

Psychotherapy	41
Rehabilitation	56
Relaxation	10
Risk assessment	101
Screening	54
Self-examination	2
Self-hypnosis	1
Self-management	251
Smoking cessation	78
Social support	123
Stretching	3
Titration	1
Video_computer games	5
Virtual world	1
Walking	12
Water	1
Web-based ambulatory care	11
Web-based care	107
Web-based feedback	136
Weight loss	121
Writing	7
Yoga	1

CHAPTER 4 APPENDIX

APPENDIX 4A - SEARCH STRATEGIES

Update subject searches for studies reporting internet-based randomised controlled trials were run in MEDLINE (OVID), EMBASE (OVID),Global Health; PsychInfo (OVID), the Cochrane Library, CINAHL (EBSCO) CAB Abstracts; and CINAHL.

Searches for qualitative research relating to internet-based randomised controlled trials were run in MEDLINE (OVID), EMBASE (OVID), PsychInfo (OVID), and CINAHL (EBSCO).
Citation searches were conducted using Web of Science. All searches were run up to 30th January 2016 unless otherwise stated.

The subject search strategies are presented below in the following order:

1. Update subject searches
2. Qualitative searches

1. Update search
The following sources were searched with no date or language restrictions applied: AMED; CAB Abstracts; CINAHL; Cochrane Library; EMBASE; MEDLINE; Proquest; PsycINFO; Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) databases; and The Campbell Library.

1.1 AMED (Allied and Complementary Medicine 1985 to January 2016
1. (internet$ or web$ or online$).mp. [mp=abstract, heading words, title]
2. exp research/
3. 1 and 2

1.2 CAB Abstracts
1. exp randomized controlled trials/
2. internet/
3. 1 and 2

1.3 CINAHL: EBSCO 01 Feb 2016
1. (MH "Internet+")
2. web* OR internet* OR online
3. 1 OR 2
4. PT clinical trial
5. MH "Treatment Outcomes+"
6. TX randomized
7. 4 OR 5 OR 6
8. 3 AND 7

1.4 Ovid EMBASE 1996 to 2016 Week 05
1. (internet$ or online or on-line).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
2. random$.tw. or placebo$.mp. or double-blind$.tw.
3. 1 and 2

1.5 Global Health 1973 to 2015 Week 01
1. exp internet/
2. exp randomized controlled trials/
3. 1 and 2

1.6 Ovid MEDLINE(R) 2012 to January Week 3 2016
1. exp Computer Communication Networks/
2. (internet$ or web$ or online or on-line).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
3. 1 or 2
4. randomized controlled trial.pt.
5. controlled clinical trial.pt.
6. randomized.ab.
7. placebo.ab.
8. clinical trials as topic.sh.
9. randomly.ab.
10. trial.ti.
11. 4 or 5 or 6 or 7 or 8 or 9 or 10
12. exp animals/ not humans.sh.
13. 11 not 12
14. 3 and 13

1.7 OT Seeker
1. internet OR web OR online AND Method: Randomised Controlled Trial

1.8 PEDRO
1. Internet OR web OR online in Abstract or Title AND Method: clinical trial

1.9 PsycINFO 1987 to January Week 4 2016
1. (internet$ or web$ or online or on-line).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
2. (random$ adj assigned).tw.
3. double-blind.tw.
4. control.tw.
5. 2 or 3 or 4
6. 1 and 5

2. Qualitative search

2.1 CINAHL
1. (MH “Internet+”) OR (internet* or online or web*)
2. interview.tw. OR audiorecording.sh. OR qualitative stud$.mp.
3. 1 AND 2

2.2 EMBASE
1. (internet$ or web$ or online$).mp
2. Qualitative.tw. OR qualitative study.tw.
3. 1 AND 2

2.3 MEDLINE
1. exp Computer Communication Networks/
2. (internet$ or web$ or online or on-line).mp
3. (e-treatment$ or e-intervention$ or e-consent$).mp
4. ((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire*))).ti,ab. or (focus group* or qualitative or ethnograph* or fieldwork or

"field work" or "key informant").ti,ab. or interviews as topic/ or focus groups/ or narration/ or qualitative research/
5. 1 or 2 or 3 or 4

2.4 Proquest
1. all(trial NEAR/9 partic*) AND all((qualitat* OR interview)) AND ab((health OR med*)) AND su(internet)

2.5 PsycINFO 1987 to January Week 4 2016
1. (internet$ or web$ or online or on-line).mp
2. ((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide or guides) adj3 (interview* or discussion* or questionnaire*)).ti,ab,id. or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant")).ti,ab,id. or exp qualitative research/ or exp interviews/ or exp group discussion/ or qualitative study.md. not "Literature Review".md.
3. exp clinical trials/
4. 1 AND 2 AND 3

APPENDIX 4B - INCLUSION AND EXCLUSION CRITERIA (FULL STAGES)

1. First screen on title and abstract
EXCLUDE ibRCT no data about methods.
Exclude report of ibRCT if no generalisable data about methodological, ethical, technical or qualitative issues

EXCLUDE non- ibRCT no data about methods
Exclude report of use of internet in intervention if no generalisable data about methodological, ethical, technical or qualitative issues relating to ibRCT

EXCLUDE on topic or participants
Exclude if the topic of the ibRCT is not in scope (health and wellbeing) or participants are not members of the public

INCLUDE based on full report
Cannot be excluded so is marked as INCLUDE. Will proceed to 2nd screen on title and abstract

2. Second screen on title and abstract
EXCLUDE ibRCT report.
Exclude report if no data about methodological, ethical, technical or qualitative issues relating to ibRCT Studies where internet intervention being tested/piloted/usability or feasibility study excluded unless generalizable methods. Exclude studies reporting comparison of data collection methods through online or face to face, unless specifically related to methodological issues for RCTs.

EXCLUDE systematic review
Exclude if report is a systematic review of topic related interventions. These will be screened separately prior to Screen on full report for generalizable data.

EXCLUDE not related to trial methodology.
Report of internet technology but not in trial setting or relevant to trial methodology. Exclude studies reporting qualitative findings if RCT not internet based. Exclude studies reporting ethical issues in trials where no specific report of ibRCT. Exclude studies reporting the development of rating scales or testing.

INCLUDE based on title & abstract.
Cannot be excluded so is marked as INCLUDE. Will proceed to screen on full-text.

3. Screen on full-text
EXCLUDE ibrct no data about methods.
Exclude report of ibrct if no generalisable data about methodological, ethical, technical or qualitative issues

EXCLUDE non-ibrct no data about methods
Exclude report of use of internet in intervention if no generalisable data about methodological, ethical, technical or qualitative issues relating to ibrct.

EXCLUDE on topic or participants
Exclude if the topic of the ibrct is not in scope (health and wellbeing) or participants are not members of the public.

INCLUDE based on full report
Cannot be excluded so is marked as INCLUDE. Will proceed to descriptive map coding.

APPENDIX 4C - CODING STRUCTURES

1.Initial coding set
Planning and pre-trial requirements
- feasibility assessment
- protocol development
- trial design: methodological and statistical
- support with funding arrangements
- obtaining ethical, R&D, and regulatory approvals

Trial management
- trial co-ordination
- questionnaire and case report form design
- data management; database design and maintenance
- randomisation
- quality assurance procedures: auditing and monitoring
- statistical analysis

Ethics
- informed consent; anonymity; incentives
- reporting

Screening
Recruitment
- Incentives

Intervention
- adherence
- engagement
- retention
- follow up

Data collection
Technology; prior knowledge; cost
Results
PPI
- Public-led

Experience: acceptance, self-disclosure

2. Final coding set
Key papers
Trial planning and design
Trial management and co-ordination
Recruitment and enrolment
Screening
Randomisation
Data
Accessibility and feasibility
Engagement
Fidelity
Adherence, retention and attrition
Ethical issues
Perspectives and experiences
- Researcher and practitioner perspectives
- Participant perspectives

CHAPTER 5 APPENDIX

APPENDIX 5A - QUALITY ASSESSMENT OF INCLUDED STUDIES

Reviewer: Anne Brice
Date: 03/09/17
NICE Quality appraisal checklist - qualitative studies

1. ID 20475309: Advocat (2010)
Advocat Jenny, and Lindsay Jo. 2010. "Internet-based trials and the creation of health consumers". *Social Science & Medicine* 70:485-92.1.
Abstract: In this paper we document the experience of participating in novel randomised controlled trials for panic disorder - where face-to-face and Internet delivery of cognitive behavioural therapy are compared. Our analysis is based on 18 months of observation and in-depth interviews with 10 trial participants and 8 trialists in Victoria, Australia. We argue that the participants are positioned as active health consumers and approach the trial as they would other self-help practices. High levels of individual responsibility are assumed of participants in these trials, which they accept by approaching the trials reflexively and searching for information and strategies they can employ while building their health literacy on panic disorder. Although the researchers set the parameters of the treatment and interaction, increasingly the participants choose the extent to which they will comply with their defined role. For the participants the trial is one of the 'pick and mix' options of available treatment and we suggest it is a compelling example of contemporary health consumption.

Theoretical approach

1. Is a qualitative approach appropriate?
    - Appropriate
2. Is the study clear in what it seeks to do?
    - Clear

Study design

3. How defensible/rigorous is the research design/methodology?
    - Defensible
      Seeks to explore the experiences of participants and researchers within the theory of 'health consumption'. However, no description of sampling approach.

Data collection

4. How well was the data collection carried out?
    - Not sure/inadequately reported
      Study reports use of participant observation and interviews, but no details given re the interview methods, other than that they were 'face-to-face'. No mention of open or semi-structured etc, and no link to interview schedule or data.

Trustworthiness

5. Is the role of the researcher clearly described?
    - Unclear
      Qualitative work undertaken by 'first author', not clear what relationship is with other researchers, or the trial that the work is linked to. No details about where the interviewer is based or their context.
6. Is the context clearly described?
    - Clear
      Context of study within the trial well described, but involves more than one trial and which one the participants are involved in isnt made clear. The research involves the study research team as well as participants, and this is assumed to be the context of the overall theoretical standpoint, that the interaction between participants and the research process needs to be seen from both perspectives.
7. Were the methods reliable?
    - Not sure
      Methods were restricted to interviews for the participants, which is acceptable. Participant observation mentioned for researchers, but no details provided

Analysis

8. Is the data analysis sufficiently rigorous?

- Not sure/not reported
  Two-step analysis conducted, to allow for complexity and thematic analysis, but only conducted by main researcher

9. Is the data 'rich'?
   - Rich
     OK, but could have been more detail
10. Is the analysis reliable?
    - Not sure/not reported
      No double coding or quality assurance of analysis reported.
11. Are the findings convincing?
    - Not sure
      A case is made for the confirmation of the underlying theoretical framework, but there is a lack of direct quotations to demonstrate statements made in the findings, and no tables or descriptions of thematic coding. So, not enough examples to be really convincing.
13. Conclusions
    - Not sure
      Not sure, can't tell, due to issues noted earlier around lack of rich data, direct quotes or details of coding and thematic analysis.

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- +Some of the checklist criteria have been fulfilled, where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter

2. **ID 20475311: Barnes (2012)**

Barnes Maria, Wiles Nicola, Morrison Jill, Kessler David, Williams Chris, Kuyken Willem, Lewis Glyn, and Turner Katrina. 2012. "Exploring patients' reasons for declining contact in a cognitive behavioural therapy randomised controlled trial in primary care". *British Journal of General Practice* 62(598).

Abstract: Background: The difficulties of recruiting individuals into mental health trials are well documented. Few studies have collected information from those declining to take part in research, in order to understand the reasons behind this decision. Aim: To explore patients' reasons for declining to be contacted about a study of the effectiveness of cognitive behavioural therapy as a treatment for depression. Design and setting: Questionnaire and telephone interview in general practices in England and Scotland. Method: Patients completed a short questionnaire about their reasons for not taking part in research. Semi-structured telephone interviews were conducted with a purposive sample to further explore reasons for declining. Results: Of 4552 patients responding to an initial invitation to participate in research involving a talking therapy, 1642 (36%) declined contact. The most commonly selected reasons for declining were that patients did not want to take part in a research study (n = 951) and/or did not want to have a talking therapy (n = 688) (more than one response was possible). Of the decliners, 451 patients agreed to an interview about why they declined. Telephone interviews were completed with 25 patients. Qualitative analysis of the interview data indicated four main themes regarding reasons for non-participation: previous counselling experiences, negative feelings about the therapeutic encounter, perceived ineligibility, and misunderstandings about the research. Conclusion: Collecting information about those who decline to take part in research provides information on the acceptability of the treatment being studied. It can also highlight concerns and misconceptions about the intervention and research, which can be addressed by researchers or recruiting GPs. This may improve recruitment to studies and thus ultimately increase the evidence base.

Theoretical approach

1. Is a qualitative approach appropriate?
   - Appropriate
2. Is the study clear in what it seeks to do?

- Clear
  Context well decscribed. Linked to RCT - sample derived from non-participants, and reasons to decline are the main focus for the research.

Study design

3. How defensible/rigorous is the research design/methodology?
   - Defensible
     Brief questionnaire and in-depth interviews. Time limit to reduce recall bias. Purposive sample with maximun variation approach. Data saturation reached at 25 interviews.

Data collection

4. How well was the data collection carried out?
   - Appropriately
     Topic guide produced; question areas outlined, audio-recorded with consent, and transcribed.

Trustworthiness

5. Is the role of the researcher clearly described?
   - Not described
6. Is the context clearly described?
   - Clear
     Context relating to trial well described
7. Were the methods reliable?
   - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
   - Rigorous
     Descriptive statistics used; free text thematically coded.
9. Is the data 'rich'?
   - Rich

10. Is the analysis reliable?
    - Reliable
      Transcripts read and re-read by two researchers; themes and content discussed by two researchers until consensus was reached.
11. Are the findings convincing?
    - Convincing
      Clearly organised and presented, with themed headings and direct quotes. Contextual information provided with quotes. Strengths and limitations discussed.
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

3. **ID 20475312: Bendelin (2011)**

Bendelin N, Hesser H, Dahl J, Carlbring P, Nelson K Z, and Andersson G. 2011. "Experiences of guided Internet-based cognitive-behavioural treatment for depression: a qualitative study". *BMC psychiatry* 11:107.

Abstract: BACKGROUND: Internet-based self-help treatment with minimal therapist contact has

been shown to have an effect in treating various conditions. The objective of this study was to explore participants' views of Internet administrated guided self-help treatment for depression. METHODS: In-depth interviews were conducted with 12 strategically selected participants and qualitative methods with components of both thematic analysis and grounded theory were used in the analyses. RESULTS: Three distinct change processes relating to how participants worked with the treatment material emerged which were categorized as (a) Readers, (b) Strivers, and (c) Doers. These processes dealt with attitudes towards treatment, views on motivational aspects of the treatment, and perceptions of consequences of the treatment. CONCLUSIONS: We conclude that the findings correspond with existing theoretical models of face-to-face psychotherapy within qualitative process research. Persons who take responsibility for the treatment and also attribute success to themselves appear to benefit more. Motivation is a crucial aspect of guided self-help in the treatment of depression.

Theoretical approach

1. Is a qualitative approach appropriate?
    - Appropriate
2. Is the study clear in what it seeks to do?
    - Clear

Study design

3. How defensible/rigorous is the research design/methodology?
    - Defensible
      Purposive sampling, maximum variation strategy, charactistics provided.

Data collection

4. How well was the data collection carried out?
    - Appropriately
      Interviews held face-to-face, audio-taped and transcribed. Interview based on client change interview, and details provided.

Trustworthiness

5. Is the role of the researcher clearly described?
    - Clearly described
6. Is the context clearly described?
    - Clear
7. Were the methods reliable?
    - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
    - Rigorous
9. Is the data 'rich'?
    - Rich
      Data is rich although only a sample of one quote from each question is provided.
10. Is the analysis reliable?
    - Reliable
11. Are the findings convincing?
    - Convincing
      Findings are convincing but need more direct quotes, rather than just one for each question.
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

4. **ID 20475313: Bjork (2014)**

Bjork Anna-Bell, Sjostrom Malin, Johansson Eva E, Samuelsson Eva, and Umefjord Goran. 2014. "Women's Experiences of Internet- Based or Postal Treatment for Stress Urinary Incontinence". *Qualitative Health Research* 24(4):484-493.
Abstract: Stress urinary incontinence is common and sometimes embarrassing. New, simple, and easily accessible treatments are needed. We telephone interviewed 21 women who participated in a randomized controlled study comparing two treatment programs based on instructions for pelvic floor muscle training. One program was Internet-based and included email support by a urotherapist; the other was sent by post. There was no face-to-face contact in either program. Our main aim was to explore the women's experiences of the Internet-based treatment. Grounded theory analysis revealed three categories: hidden but present, at a distance but close, and by myself but not alone. These were incorporated in a core category: acknowledged but not exposed. The leakage was often a well-hidden secret, but the study treatments lowered the barrier for seeking care. In the Internet group, a supportive patient-provider relationship developed despite the lack of face-to-face contact. Internet-based treatment programs can increase access to care and empower women.

Theoretical approach

1. Is a qualitative approach appropriate?
   - Appropriate
     Relevant methods, postmodernist feminist perspective noted.
2. Is the study clear in what it seeks to do?
   - Clear
     Explore experiences of internet-based treatment.

Study design

3. How defensible/rigorous is the research design/methodology?
   - Defensible
     Appropriate design, sem-structured telephone interviews

Data collection

4. How well was the data collection carried out?
   - Appropriately
     Semi-structured interviews, sampling via RCT participation. Interview guide produced. One researcher conducted all interviews. Data collection, transcription and preliminary analysis conducted simultaneously.

Trustworthiness

5. Is the role of the researcher clearly described?
   - Not described
     Role of researcher clear but not clear about relationship with RCT study researchers.
6. Is the context clearly described?
   - Clear
7. Were the methods reliable?
   - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
   - Rigorous
     Constant comparison, and discussion. External groups of researchers used to check analysis.
9. Is the data 'rich'?
   - Rich
10. Is the analysis reliable?
    - Reliable
11. Are the findings convincing?
    - Convincing

12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

5. ID 20475315: Bossen (2013)

Bossen D, Buskermolen M, Veenhof C, de Bakker , D , and Dekker J. 2013. "Adherence to a web-based physical activity intervention for patients with knee and/or hip osteoarthritis: a mixed method study". *Journal of Medical Internet Research* 15: e223.

Abstract: BACKGROUND: Web-based interventions show promise in promoting a healthy lifestyle, but their effectiveness is hampered by high rates of nonusage. Predictors and reasons for (non)usage are not well known. Identifying which factors are related to usage contributes to the recognition of subgroups who benefit most from Web-based interventions and to the development of new strategies to increase usage. OBJECTIVE: The aim of this mixed methods study was to explore patient, intervention, and study characteristics that facilitate or impede usage of a Web-based physical activity intervention for patients with knee and/or hip osteoarthritis. METHODS: This study is part of a randomized controlled trial that investigated the effects of Web-based physical activity intervention. A total of 199 participants between 50-75 years of age with knee and/or hip osteoarthritis were randomly assigned to a Web-based intervention (n=100) or a waiting list (n=99). This mixed methods study used only data from the individuals allocated to the intervention group. Patients were defined as users if they completed at least 6 out of 9 modules. Logistic regression analyses with a stepwise backward selection procedure were executed to build a multivariate prediction usage model. For the qualitative part, semistructured interviews were conducted. Both inductive and deductive analyses were used to identify patterns in reported reasons for nonusage. RESULTS: Of the 100 participants who received a password and username, 46 completed 6 modules or more. Multivariate regression analyses revealed that higher age (OR 0.94, P=.08) and the presence of a comorbidity (OR 0.33, P=.02) predicted nonusage. The sensitivity analysis indicated that the model was robust to changes in the usage parameter. Results from the interviews showed that a lack of personal guidance, insufficient motivation, presence of physical problems, and low mood were reasons for nonusage. In addition, the absence of human involvement was viewed as a disadvantage and it negatively impacted program usage. Factors that influenced usage positively were trust in the program, its reliability, functionality of the intervention, social support from family or friends, and commitment to the research team. CONCLUSIONS: In this mixed methods study, we found patient, intervention, and study factors that were important in the usage and nonusage of a Web-based PA intervention for patients with knee and/or hip osteoarthritis. Although the self-guided components offer several advantages, particularly in relation to costs, reach, and access, we found that older patients and participants with a comorbid condition need a more personal approach. For these groups the integration of Web-based interventions in a health care environment seems to be promising.

Theoretical approach

1. Is a qualitative approach appropriate?
    - Appropriate
      Part of mixed methods study
2. Is the study clear in what it seeks to do?
    - Clear

Study design

3. How defensible/rigorous is the research design/methodology?
    - Defensible
      Sampling framework described, stratified purposive sampling procedure.

Data collection

4. How well was the data collection carried out?
    - Appropriately
      Face-to-face interview, in respondents homes. Conducted by one researcher. Audio-recorded and transcribed. Open-question guide used -provided as appendix

Trustworthiness

5. Is the role of the researcher clearly described?
    - Not described
6. Is the context clearly described?
    - Clear
      Context described as part of wider trial.
7. Were the methods reliable?
    - Reliable
      Deductive and inductive content analysis. Template using Eysenbach's Law of Attrition. Grounded theory, text analysed and coded. Random sample of five interviews analysed by second researcher. Codes compared and disagreements resolved.

Analysis

8. Is the data analysis sufficiently rigorous?
    - Rigorous
      Deductive and inductive content analysis. Template using Eysenbach's Law of Attrition. Grounded theory, text analysed and coded. Random sample of five interviews analysed by second researcher. Codes compared and disagreements resolved.
9. Is the data 'rich'?
    - Rich
      Additional quotes provided in appendix
10. Is the analysis reliable?
    - Reliable
11. Are the findings convincing?
    - Convincing
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

6. **ID 20475329: Donkin (2012)**

Donkin Liesje, and Glozier Nick. 2012. "Motivators and Motivations to Persist with Online Psychological Interventions: A Qualitative Study of Treatment Completers". *Journal of Medical Internet Research* 14(3):262-273.

Abstract: Background: Many users of Internet interventions do not persist with the full treatment program. As persistence may influence outcomes of such interventions, being able to maximize persistence is vital. However, while studies have begun to explore the predictors of dropout in Internet interventions, few have explored reasons why users persist with the programs, which

may not just be the converse of the reasons for dropout. Objective: To answer the question of what influences persistence with online interventions. Methods: We interviewed participants in the Cardiovascular Risk E-couch Depression Outcome (CREDO), a trial evaluating the efficacy of an eHealth intervention (e-couch) in treating depressive symptoms in those with comorbid depression and cardiovascular risk factors. Interviews were semi-structured in nature and were analyzed using a grounded theory approach. Interview numbers were curtailed (n = 12) after theoretical saturation. Results: All participants reported substantial barriers to completing the program including time constraints, competing priorities, anxiety about spending time on the computer, and perception of limited worth of the intervention. Participants who persisted with the trial reported intrinsic motivations such as personal values about task completion and sense of control, and recognized external motivators that aided the development of habits and identified personal benefits attributable to the program. Conclusions: Online interventions may benefit from content that enhances the intrinsic motivations such as a having sense of control and being able to identify with the program, and by increasing the relative value of the program in order to enhance persistence. Persistence within a trial setting appears modifiable through explicit messages regarding supporting others. In terms of motivators, the use of a hook to engage participants who are starting the intervention due to curiosity and the use of reminder systems to prompt participants may also improve persistence. The worth of such additions should be evaluated using adherence and outcomes metrics.

Theoretical approach

1. Is a qualitative approach appropriate?
    - Appropriate
2. Is the study clear in what it seeks to do?
    - Clear
      What influences persistence, and to develop a proposed model to aid programme development.

Study design

3. How defensible/rigorous is the research design/methodology?
    - Not sure
      Use randomised approach to select participants from the main trial, no details of why this sampling approach was taken though, or discussion

Data collection

4. How well was the data collection carried out?
    - Appropriately
      Data collection via telephone and face-to-face interviews. Audio-recorded and transcribed following consent (did consent come after interview? - not clear). No mention of where and how data to be stored. Hand written field notes also used

Trustworthiness

5. Is the role of the researcher clearly described?
    - Unclear
      Although discussed in limitations, not clear in description of study methods and context.
6. Is the context clearly described?
    - Clear
      Context is sub-study of trial, but no details about relationship of researcher to trial. Interviews held at location of preference for participants.
7. Were the methods reliable?
    - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
    - Rigorous
      Interviewer transcribed and analysed, then analyised by lead trial researcher. Grounded theory approach taken. 'Focused' coding undertaken, and theoretical coding. Conceptual memo's written from focused codes.
9. Is the data 'rich'?
    - Rich
10. Is the analysis reliable?

- Reliable
  Comparison and analysis from interviewer and lead researcher. Consistent provision of direct quotes. No mention of method for discussing disagreement or reaching consensus.

11. Are the findings convincing?
    - Convincing
      Findings are convincing, and some limitations discussed, including lack of expected findings.
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

7. **ID 20475339: Gerhards (2011)**

Gerhards S A. H, Abma T A, Arntz A, De Graaf , L E, Evers S M. A. A, Huibers M J. H, and Widdershoven G A. M. 2011. "Improving adherence and effectiveness of computerised cognitive behavioural therapy without support for depression: A qualitative study on patient experiences". *Journal of Affective Disorders* 129:117-125.

Abstract: Background: Several studies have evaluated the efficacy and effectiveness of computerized cognitive behavioural therapy (CCBT) for depression, but research on the patient perspective is limited. Aims: To gain knowledge on patient experiences with the online self-help CCBT program Colour Your Life (CYL) for depression, and find explanations for the low treatment adherence and effectiveness. Method: Qualitative data were collected through semi-structured interviews with 18 patients. Interviewees were selected from a CCBT trial. An inductive, content analysis of the interviews was performed. Results: The main theme throughout the interviews concerns barriers and motivators experienced with CCBT. The most important barriers included experiences of a lack of identification with and applicability of CCBT-CYL, lack of support to adhere with the program or to gain deeper understanding, and inadequate computer/Internet skills, equipment, or location. Confusion between CCBT and Internet questionnaires resulted in no CCBT uptake of some study participants. Motivators included experiencing self-identification and improvement through CCBT-CYL, participating in a scientific study, and the freedom and anonymity associated with online computer self-help. The addition of support to CCBT was suggested as an improvement towards adherence and the course content. Conclusion: The CCBT program CYL in its current form does not work for a large group of people with depressive symptoms. More tailoring, the provision of support (professional or lay) and good computer conditions could improve CCBT.

Theoretical approach

1. Is a qualitative approach appropriate?
   - Appropriate
2. Is the study clear in what it seeks to do?
   - Mixed

Study design

3. How defensible/rigorous is the research design/methodology?
   - Defensible
     Semi-structured interviews, audio-taped and transcribed. Inductive content analysis, using grounded theory. Two researchers involved in analysis

Data collection

4. How well was the data collection carried out?

- Appropriately
  Audio-recorded and transcribed, no details of how data stored.

Trustworthiness

5. Is the role of the researcher clearly described?
   - Not described
6. Is the context clearly described?
   - Not sure
7. Were the methods reliable?
   - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
   - Not sure/not reported
     Not enough detail provided to be sure
9. Is the data 'rich'?
   - Not sure/not reported
10. Is the analysis reliable?
    - Reliable
      Transcripts validated by participants.
11. Are the findings convincing?
    - Not sure
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate
      Although strengths and limitations not discussed

Ethics

14. How clear and coherent is the reporting of ethics?
    - Not sure/not reported

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- + Some of the checklist criteria have been fulfilled, where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter

8. **ID 20475355: Johansson (2015)**

Johansson O, Michel T, Andersson G, and Paxling B. 2015. "Experiences of non-adherence to Internet-delivered cognitive behavior therapy: A qualitative study". *Internet Interventions* 2:137-142.

Abstract: Many trials on Internet-delivered psychological treatments have had problems with nonadherence, but not much is known about the subjective reasons for non-adhering. The aim of this study was to explore participants' experiences of non-adherence to Internet-delivered psychological treatment. Grounded theory was used to analyze data from seven in-depth interviews with persons who had non-adhered to a study on Internet-delivered cognitive behavioral therapy for generalized anxiety disorder. The process of non-adherence is described as an interaction between patient factors and treatment factors. A working model theory was generated to illustrate the experience of nonadherence. The model describes a process where treatment features such as workload, text-content complexity and treatment process don't match personal prerequisites regarding daily routines, perceived language skills and treatment expectations respectively, resulting in the decision to nonadhere. Negative effects were also stated as a reason for non-adherence. Several common strategies used for increasing adherence to Internet-delivered therapy in general are by these non-completers regarded as factors directly related to their reason for non-adherence.

Theoretical approach

1. Is a qualitative approach appropriate?
   - Appropriate
     Participant experience - to generate theoretical working model for adherence

2. Is the study clear in what it seeks to do?
    - Clear

Study design

3. How defensible/rigorous is the research design/methodology?
    - Defensible
      Semi-structured interview design, using grounded theory

Data collection

4. How well was the data collection carried out?
    - Appropriately
      Semi-structured interviews, audio-recorded and transcribed. Sampling strategy not very clearly described, but is in context of RCT.

Trustworthiness

5. Is the role of the researcher clearly described?
    - Clearly described
      Information on role of researcher provided, and also in limitations section
6. Is the context clearly described?
    - Clear
7. Were the methods reliable?
    - Reliable
      Method reliable in context of RCT study.

Analysis

8. Is the data analysis sufficiently rigorous?
    - Rigorous
      Grounded theory and theoretical sampling used. All authors involved in forming concepts.
9. Is the data 'rich'?
    - Rich
10. Is the analysis reliable?
    - Not sure/not reported
      Concepts checked by all authors but no details on how agreement reached. Some information in limitations section.
11. Are the findings convincing?
    - Convincing
12. Are the findings relevant to the aims of the study?
    - Relevant

13. Conclusions
    - Adequate

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate
      Limitations discussed.

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

9. **ID 20475373: Morgan (2011)**

Morgan P J, Warren J M, Lubans D R, Collins C E, and Callister R. 2011. "Engaging men in weight loss: Experiences of men who participated in the male only SHED-IT pilot study". *Obesity Research & Clinical Practice* 5:e169-266.

Abstract: SUMMARY: Recruiting men to weight loss programs is notoriously difficult and little is known about the experiences of men who participate in weight loss programs. The aims of this paper were to report the perceptions and experiences of men who enrolled in the SHED-IT (Self-Help, Exercise, Diet and Information Technology) randomized controlled trial in the context of (1) what attracted them to the program, (2) their satisfaction with the program and its components,

and (3) their suggestions for improvements to the program. The SHED-IT program exclusively targeted men and was developed to appeal to men. Individual semi-structured interviews were conducted with 18 overweight/obese (BMI between 25 and 37 kg/m(2)) men aged 18-60 years who were employed or enrolled at the University of Newcastle and who had been enrolled to the SHED-IT trial and randomly allocated to receive either the Internet intervention or basic weight-loss Information Only. Significant weight loss was achieved by both groups. A thematic analysis was undertaken applying the constant comparison method. Results indicated that lack of knowledge was a major weight loss barrier and men were attracted to a program that did not require extensive time commitments, was tailored for men and allowed inclusion of 'treat' food and drinks. Men were satisfied with both programs and valued the education about energy balance and the humour used to deliver simple messages. More face-to-face contact was a common suggestion for improvement. Our findings will inform future weight loss interventions for men and assist researchers and practitioners to engage men in weight loss.: A 2011 Asian Oceanian Association for the Study of Obesity.

Theoretical approach

1. Is a qualitative approach appropriate?
    - Appropriate
2. Is the study clear in what it seeks to do?
    - Clear

Study design

3. How defensible/rigorous is the research design/methodology?
    - Defensible
      Study constructed in context of follow-up to RCT.

Data collection

4. How well was the data collection carried out?
    - Appropriately
      Sample taken from variety of participants with different trial results, then selected at random. Semi-structured in-depth interviews, audio-recorded and transcribed.

Trustworthiness

5. Is the role of the researcher clearly described?
    - Clearly described
6. Is the context clearly described?
    - Clear
7. Were the methods reliable?
    - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
    - Rigorous
      More than one reseacher involved in interviews, and data analysed through thematic analysis with constant comparison. Participant characteristics analysed. Data discussed and themes revised, to achieve consensus.
9. Is the data 'rich'?
    - Rich
10. Is the analysis reliable?
    - Reliable
11. Are the findings convincing?
    - Convincing
      Limitations described
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate

Ethics

14. How clear and coherent is the reporting of ethics?
    - Not sure/not reported
      No ethics statement provided - could be provided under main trial ethics?

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

10. **ID 20475375: Nicholas (2010)**

Nicholas Jennifer, Proudfoot Judith, Parker Gordon, Gillis Inika, Burckhardt Rowan, Manicavasagar Vijaya, and Smith Meg. 2010. "The ins and outs of an online bipolar education program: a study of program attrition". *Journal of Medical Internet Research* 12:e57.
Abstract: BACKGROUND: The science of eHealth interventions is rapidly evolving. However, despite positive outcomes, evaluations of eHealth applications have thus far failed to explain the high attrition rates that are associated with some eHealth programs. Patient adherence remains an issue, and the science of attrition is still in its infancy. To our knowledge, there has been no in-depth qualitative study aimed at identifying the reasons for nonadherence to-and attrition from-online interventions. OBJECTIVE: This paper explores the predictors of attrition and participant-reported reasons for nonadherence to an online psycho-education program for people newly diagnosed with a bipolar disorder. METHODS: As part of an ongoing randomized controlled trial (RCT) evaluating an online psycho-education program for people newly diagnosed with a bipolar disorder, we undertook an in-depth qualitative study to identify participants' reasons for nonadherence to, and attrition from, the online intervention as well as a quantitative study investigating predictors of attrition. Within the RCT, 370 participants were randomly allocated to 1 of 2 active interventions or an attention control condition. Descriptive analyses and chi-square tests were used to explore the completion rates of 358 participants, and standard regression analysis was used to identify predictors of attrition. The data from interviews with a subsample of 39 participants who did not complete the online program were analyzed using "thematic analysis" to identify patterns in reported reasons for attrition. RESULTS: Overall, 26.5% of the sample did not complete their assigned intervention. Standard multiple regression analysis revealed that young age (P= .004), male gender (P= .001), and clinical recruitment setting (P= .001) were significant predictors of attrition (F(7,330)= 8.08, P< .001). Thematic analysis of interview data from the noncompleter subsample revealed that difficulties associated with the acute phases of bipolar disorder, not wanting to think about one's illness, and program factors such as the information being too general and not personally tailored were the major reasons for nonadherence. CONCLUSIONS: The dropout rate was equivalent to other Internet interventions and to face-to-face therapy. Findings from our qualitative study provide participant-reported reasons for discontinuing the online intervention, which, in conjunction with the quantitative investigations about predictors, add to understanding about Internet interventions. However, further research is needed to determine whether there are systematic differences between those who complete and those who do not complete eHealth interventions. Ultimately, this may lead to the identification of population subgroups that most benefit from eHealth interventions and to informing the development of strategies to improve adherence.

Theoretical approach

1. Is a qualitative approach appropriate?
   - Appropriate
2. Is the study clear in what it seeks to do?
   - Clear

   Identify factors related to non-adherence, and understand reasons for non-completion

Study design

3. How defensible/rigorous is the research design/methodology?
   - Defensible

   Built in to other measures of adherence through trial. Sampling from sub-set of trial participants.

Data collection

4. How well was the data collection carried out?

- Not sure/inadequately reported
  Some information provided about interview methods. Data not audio-recorded but transcribed in real time. No details about storage. Interview schedule developed

Trustworthiness

5. Is the role of the researcher clearly described?
   - Unclear
6. Is the context clearly described?
   - Clear
7. Were the methods reliable?
   - Not sure

Analysis

8. Is the data analysis sufficiently rigorous?
   - Not sure/not reported
     Thematic analysis used. Essentialist or realist approach used - no specific rationale provided for this choice. Two researchers involved in analysis, issues resolved by discussion. Not reported in depth
9. Is the data 'rich'?
   - Rich
     Rich data, but not large amount of description or direct quotes
10. Is the analysis reliable?
    - Not sure/not reported
11. Are the findings convincing?
    - Not sure
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate
      Not a huge amount of detail regarding limitations

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- + Some of the checklist criteria have been fulfilled, where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter

11. **ID 20475388: Sanchez-Ortiz (2011)**

Sanchez-Ortiz V C, House J, Munro C, Treasure J, Startup H, and Williams C. 2011. "'A computer isn't gonna judge you': A qualitative study of users' views of an internet-based cognitive behavioural guided self-care treatment package for bulimia nervosa and related disorders". *Eating and weight disorders* 16:e93-e101.

Theoretical approach

1. Is a qualitative approach appropriate?
   - Appropriate
2. Is the study clear in what it seeks to do?
   - Clear

Study design

3. How defensible/rigorous is the research design/methodology?
   - Defensible
     Semi-structured interviews, face-to-face or telephone, plus use of questionnaire data. Toic guide produced. Data audio-recorded and transcribed. Thematic analysis using two researchers. Triangulation using interview data and questionnaire data.

Data collection

4. How well was the data collection carried out?
    - Appropriately

Trustworthiness

5. Is the role of the researcher clearly described?
    - Not described
6. Is the context clearly described?
    - Clear
7. Were the methods reliable?
    - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
    - Rigorous
      Two researchers independently coded transcripts, grouped into descriptive themes, discussed and created a coding framework. No details re process for reconciling disagreements. Quotes chosen to illustrate themes.
9. Is the data 'rich'?
    - Rich
      Direct quotes provided for themes.
10. Is the analysis reliable?
    - Reliable
11. Are the findings convincing?
    - Convincing
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate
      Strengths and limitations discussed

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

12. ID 20475391: Short (2014)

Short C E, Vandelanotte C, Dixon M W, Rosenkranz R, Caperchione C, Hooker C, Karunanithi M, Kolt G S, Maeder A, Ding H, Taylor P, and Duncan M J. 2014. "Examining participant engagement in an information technology-based physical activity and nutrition intervention for men: the manup randomized controlled trial". *JMIR Research Protocols* 3:e2.

Abstract: BACKGROUND: Males experience a shorter life expectancy and higher rates of chronic diseases compared to their female counterparts. To improve health outcomes among males, interventions specifically developed for males that target their health behaviors are needed. Information technology (IT)-based interventions may be a promising intervention approach in this population group, however, little is known about how to maximize engagement and retention in Web-based programs. OBJECTIVE: The current study sought to explore attributes hypothesized to influence user engagement among a subsample of participants from the ManUp study, a randomized controlled trial testing the efficacy of an interactive Web-based intervention for promoting physical activity and nutrition among middle-aged males. METHODS: Semistructured interviews were conducted and audiotaped with 20 of the ManUp participants. Interview questions were based on a conceptual model of engagement and centered on why participants took part in the study, what they liked and did not like about the intervention they received, and how they think the intervention could be improved. Interview recordings were transcribed and coded into themes. RESULTS: There were five themes that were identified in the study. These themes were: (1) users' motives, (2) users' desired outcomes, (3) users' positive

experiences, (4) users' negative emotions, and (5) attributes desired by user. CONCLUSIONS: There is little research in the field that has explored user experiences in human-computer interactions and how such experiences may relate to engagement, especially among males. Although not conclusive, the current study provides some insight into what personal attributes of middle-aged males (such as their key motives and goals for participating) and attributes of the intervention materials (such as usability, control, and interactivity) may impact on user engagement in this group. These findings will be helpful for informing the design and implementation of future health behavior interventions for males.

Theoretical approach

1. Is a qualitative approach appropriate?
    - Appropriate
2. Is the study clear in what it seeks to do?
    - Clear

Study design

3. How defensible/rigorous is the research design/methodology?
    - Defensible
      Qualitative sub-study of RCT. Semi-structured interviews. Details re sampling strategy and it's iteration. Interviews conducted by telephone.

Data collection

4. How well was the data collection carried out?
    - Appropriately
      Training interviews undertaken beforehand, and discussion guide produced. Interviews very short ie 10 mins. Audio-taped and also written notes taken. Interview questions provided.

Trustworthiness

5. Is the role of the researcher clearly described?
    - Clearly described
6. Is the context clearly described?
    - Clear
7. Were the methods reliable?
    - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
    - Rigorous
      Two researchers coded independently, disagreements discussed and consensus reached. Participant characteristics provided. Thematic analysis conducted
9. Is the data 'rich'?
    - Rich
      Themes presented, and direct quotes provided.
10. Is the analysis reliable?
    - Reliable
      Undertaken by two researchers
11. Are the findings convincing?
    - Convincing
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate
      Strengths and limitations discussed

Ethics

14. How clear and coherent is the reporting of ethics?
    - Not sure/not reported

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

13. **ID 20475398: Todkill (2013)**

Todkill D, and Powell J. 2013. "Participant experiences of an internet-based intervention and randomised control trial: interview study". *BMC public health* 13:1017.
Abstract: There are an increasing number of interventions being delivered online, and an expanding body of research to assess the effectiveness of such interventions. Yet, little is known about the motivations for participating in online research. Furthermore, internet interventions and online research studies are characterised by poor adherence and high attrition rates. This study aimed to explore participant motivations for taking part in an online trial of an internet intervention and the reasons for continuing. Semi-structured telephone interviews were conducted with twenty members of the intervention arm of an internet-based randomised control trial evaluating an online cognitive behavioural tool to improve mental wellbeing. The qualitative interviews were analysed using the Framework Approach to identify themes and subthemes, through familiarization with the data, identifying a thematic framework, charting, indexing, mapping and interpreting the data. A number of key themes emerged. Trusted brands were key to participants feeling secure in engaging with the trial due to the association with institutions such as the UK National Health Service and the lead University conducting the research. Participants had a number of motivations for signing up with the study; altruism, low mood and as a replacement for a physical health professional. Participants felt the need for the language used in the intervention to be tailored to them as individuals. The majority of those interviewed also described multiple benefits from the intervention, which could have been a reason for them to persist. The nascent field of research on internet delivered healthcare needs to take account of participant views, as have been identified in this trial and future studies would benefit from applying its findings.

Theoretical approach

1. Is a qualitative approach appropriate?
   - Appropriate
2. Is the study clear in what it seeks to do?
   - Clear

Study design

3. How defensible/rigorous is the research design/methodology?
   - Defensible
     Semi-structured interview, and sampling from RCT. Stratification blinded to participants outcome. Purposive sample

Data collection

4. How well was the data collection carried out?
   - Appropriately
     Semi-structured interviews, two researchers. Audio-recorded and transcribed. Interview guide adjusted during process to reflect emergent findings.

Trustworthiness

5. Is the role of the researcher clearly described?
   - Not described
6. Is the context clearly described?
   - Clear
7. Were the methods reliable?
   - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
   - Rigorous
     Two researchers coded independently, and then discussed and agreed thematic codes, through axial coding.
9. Is the data 'rich'?
   - Rich
10. Is the analysis reliable?

- Reliable

11. Are the findings convincing?
    - Convincing
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate
      Strengths and limitations discussed

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

14. **ID 20475399: Tonkin-Crine (2013)**

Tonkin-Crine S, Bishop F L, Ellis M, Moss-Morris R, and Everitt H. 2013. "Exploring patients' views of a cognitive behavioral therapy-based website for the self-management of irritable bowel syndrome symptoms". *Journal of medical Internet research* 15:e190.

Abstract: BACKGROUND: Cognitive behavioral therapy (CBT) has been shown to have positive effects on the management of irritable bowel syndrome (IBS) symptoms. A factorial pilot randomized placebo-controlled trial (called MIBS) tested the potential effectiveness of a self-management CBT-based website alongside two medications: methylcellulose and mebeverine, and a placebo. The results showed no significant differences in quality of life or symptom severity measures, but enablement and participant's global assessment of relief was higher in the website groups. OBJECTIVE: To conduct a qualitative study nested within this trial, in order to explore patients' views and experiences of using the CBT-based website to facilitate self-management of IBS. METHODS: Semistructured interviews were carried out with patients who had used the website with one session of nurse support (n=16) or the website alone (n=15) while participating in the MIBS trial. An inductive thematic analysis was conducted. RESULTS: We identified three types of engagement with the CBT-based website. One group of participants, mostly in the website-only condition, had limited or no engagement with the website. One group engaged with the content and advice on practical lifestyle changes. The final group of participants engaged with the content and advice on psychological aspects related to IBS. Similarities and differences between these three groups are explored. CONCLUSIONS: Teaching self-management techniques through a Web intervention was received positively by most of the participants. Concepts linked to cognitive aspects of CBT appeared to be harder for participants to engage with. Participants who received nurse support rated the cognitive aspects more positively, suggesting that some therapy support alongside the website should be considered. However, the Web format was preferred by some who favored anonymity as well as those who appreciated the accessibility and ease of use of this type of management. Suggestions on how to encourage engagement with Web interventions are discussed.

Theoretical approach

1. Is a qualitative approach appropriate?
    - Appropriate
2. Is the study clear in what it seeks to do?
    - Clear
      Study nested in RCT, to explore acceptability, but focused on theme of website use for trial

Study design

3. How defensible/rigorous is the research design/methodology?
    - Defensible
      Sampling from main trial participants, sampling approach described. Open-

endeed, telephone interviews, conducted by two researchers. Thematic analysis undertaken. Nvivo used for coding and analysis.

Data collection

4. How well was the data collection carried out?
   - Appropriately
     Two interviewers, data audio-recorded and transcribed.

Trustworthiness

5. Is the role of the researcher clearly described?
   - Clearly described
     Researchers independent from the trial team
6. Is the context clearly described?
   - Clear
7. Were the methods reliable?
   - Reliable

Analysis

8. Is the data analysis sufficiently rigorous?
   - Rigorous
     Two researchers took inductive approach to analysis, using grounded theory, transcripts read and re-read, initial codes applied and then refined and expanded. Compared and discussed. Initial themes read and checked by two other researchers from the trial team. Disagreements identified and discussed.
9. Is the data 'rich'?
   - Rich
10. Is the analysis reliable?
    - Reliable
11. Are the findings convincing?
    - Convincing
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate
      Limitations discussed

Ethics

14. How clear and coherent is the reporting of ethics?
    - Not sure/not reported

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

15. **ID 20475410: Wood (2011)**

Wood F, Kowalczuk J, Elwyn G, Mitchell C, and Gallacher J. 2011. "Achieving online consent to participation in large-scale gene-environment studies: a tangible destination". *Journal of Medical Ethics* 37:487-92.

Abstract: BACKGROUND: Population based genetics studies are dependent on large numbers of individuals in the pursuit of small effect sizes. Recruiting and consenting a large number of participants is both costly and time consuming. We explored whether an online consent process for large-scale genetics studies is acceptable for prospective participants using an example online genetics study. METHODS: We conducted semi-structured interviews with 42 members of the public stratified by age group, gender and newspaper readership (a measure of social status). Respondents were asked to use a website designed to recruit for a large-scale genetic study. After using the website a semi-structured interview was conducted to explore opinions and any issues they would have. Responses were analysed using thematic content analysis. RESULTS: The majority of respondents said they would take part in the research (32/42). Those who said they would decline to participate saw fewer benefits from the research, wanted more information and expressed a greater number of concerns about the study. Younger respondents had

concerns over time commitment. Middle aged respondents were concerned about privacy and security. Older respondents were more altruistic in their motivation to participate. Common themes included trust in the authenticity of the website, security of personal data, curiosity about their own genetic profile, operational concerns and a desire for more information about the research. CONCLUSIONS: Online consent to large-scale genetic studies is likely to be acceptable to the public. The online consent process must establish trust quickly and effectively by asserting authenticity and credentials, and provide access to a range of information to suit different information preferences.

Theoretical approach

1. Is a qualitative approach appropriate?
    - Appropriate
      Is online consent acceptable, and what barriers are present
2. Is the study clear in what it seeks to do?
    - Clear

Study design

3. How defensible/rigorous is the research design/methodology?
    - Defensible
      Sampling approach described, qualitative telephone interviews, with semi-structured interview schedule, quantitative and qualitative data collected

Data collection

4. How well was the data collection carried out?
    - Appropriately
      Telephone interviews, following provision of sample recruitment adverts. Participants observed during work through examples, and then asked questions which were audio-recorded and transcribed. Hand written notes taken and answers and observations recorded on a structured response form.

Trustworthiness

5. Is the role of the researcher clearly described?
    - Not described
6. Is the context clearly described?
    - Clear
7. Were the methods reliable?
    - Reliable
      Mixed methods, quantitative, observation and qualitative interviews

Analysis

8. Is the data analysis sufficiently rigorous?
    - Not sure/not reported
      Limited amount of information provided about data analysis. One researcher coded questions initially into a thematic framework, analysis reviewed by second researcher, and queries discussed.
9. Is the data 'rich'?
    - Rich
10. Is the analysis reliable?
    - Reliable
11. Are the findings convincing?
    - Convincing
12. Are the findings relevant to the aims of the study?
    - Relevant
13. Conclusions
    - Adequate
      Strengths and weaknesses discussed

Ethics

14. How clear and coherent is the reporting of ethics?
    - Appropriate

Overall assessment

As far as can be ascertained from the paper, how well was the study conducted? (see guidance notes)

- ++ All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

APPENDIX 5B - DATA EXTRACTED FROM INCLUDED STUDIES

1	Direct quotes: primary research	Themes	Authors findings: primary research
1	"I think I actually stopped going [to the face-to-face therapist] because well, you could say I was a bit caught up with the emotional type of you know, guff that they go on with in therapy and some of the questions that he asked me I kind of thought, you know, well, what does that have to do with anything, you know it was more looking at relationships and all that. I just wanted answers and I think the website gave me that". *(Patient)*	'Consuming the psychological'	'In effect Jill was searching for a better therapeutic product to consume which provided the kind of treatment, or ''answers'' she felt she required'.
1	One participant used the website ''just to read the information, because it would make you realize that what you were experiencing is quite normal and that you weren't losing your mind.'' *(Patient)*	'Consuming the psychological'	'Many of the participants were grateful to think of their panic attacks through a physiological framework instead of one which relies on their exploration of past memories, through which they sometimes felt blamed or stigmatized for having panic disorder'.
1	"I felt like I was dealing with the mental you know the mind side of it by doing this, the physical side with the chiropractor. And the kinesiology was tapping back into, perhaps the root of the problem, and try and work out those points in my life that created that fear…so. I was taking care of how it began, the physical side and the computer side was the today and focusing and all that stuff. So yeah, covering all aspects of what needed to be done for a cure". *(Patient)*	'Consuming the psychological'	'Robyn understood her participation in the online trial as simply another way to draw from and engage with a particular kind of expertise and another service to consume as necessary. The participants often understood their participation in the trials as just one more way that they could exercise their choice, or even their right, to seek out appropriate expert assistance'.
1	"The way I conceptualise Internet-based treatment per se is that it is just an additional option that a therapist could provide. So it's like, the majority of time you probably see clients face-to face… but you could also say [to them], 'there is this other type of delivery format, Internet-based therapy, here are the advantages and disadvantages'. So it's really just giving the consumer more choice". *(Res)*	'Consuming the psychological'	'Some of the researchers understood free Internet-based treatments as a way to offer more choice to the consumer.'
1	"Julia, a therapist, said ''…. it's very much up to them, it's like they have the power to turn us on, they have the power to make contact, it's up to them because they know it is very much [on] their own time, it's like going to the gym.'' *(Researcher)*	'Choosing not to participate and feeling guilty'	'Exercising is commonly regarded as an activity that should be done, like a chore, and it has been linked to consumerism and the increasing impetus for self-improvement'
1	''cheat …….magic pill … system, method [or] whatever is gonna fix you, right now today because you've had enough, your ability to discipline yourself in that manner is gone.' *(Patient)*	'Choosing not to participate and feeling guilty'	'Anne wanted not to be understood as simply a consumer, but as a client, a patient even, a person needing help from an expert'.

1	" …maybe [I] would have spent more time, I was always racing around with the kids. I have three kids and all that, but um, maybe spending a bit more time really sitting down and read, like I'd read it and I'd think, 'oh, geez no, I've got something else I've gotta be doing.' And I should have spent more time sitting there, and think 'well, that can wait, this is mine and I'll give it 20 min,30 min, half and hour, this is my half hour to do this.' Cause I always seem to be in a hurry. Better hurry up and do this cause something else is, you know, yeah, probably having more time". *(Patient)*	'Choosing not to participate and feeling guilty'	'When the participants completed the trial and reflected on their level of engagement during the interviews, most of them said that ir they were to participate in the trial all over again that they would ''try harder.'' They felt guilty for their lack of commitment to their obligations to the trial. In this way, the objectifying gaze to which the participants were subjected was also their own. They judged themselves for not managing their participation exactly as the program suggested'.
1	''I would be more prompt with my responses, I would really get into [it], I would get stuck into [it], I would read everything, I would do all of the assignments, I would do it properly.'' *(Patient)*	'Choosing not to participate and feeling guilty'	'The participants internalised their obligation to engage with the trial but some simultaneously felt as if they never did enough, even though they saw improvement in their lives. Ultimately, participants engaged with the program as much as they needed to and, as health consumers, they were able to choose for themselves to what extent they participated. Sometimes, however, their reluctance to engage related to their lack of understandings of the trials'.
1	''I mean I was just doing the program, I guess the fact that it is a trial indicates that you can improve it or yeah, I wasn't at all critical or analytical of the way it was done..'' *(Patient)*	'It's there when I need it'	'few of them conceptualised their involvement as participation in research. Instead, almost all of them understood their participation as a convenient way for them to get treatment, for which most of them were desperate. In the interviews, participants reflected on the term ''trial,'' explaining how they understood a trial to work and the reasons one would undertake such a project'
1	''…. teach the doctors that haven't actually had a panic attack what it's like to have a panic attack..'' *(Patient)*	'It's there when I need it'	'Not only did Sue misunderstand the purpose of the trial ..'
1	''No not really. It was more like answering [quizzes in magazines], you know like in the T.V. Week and Women's Day..'' *(Patient)*	'It's there when I need it'	'despite signing an informed consent form, when asked, she did not really feel that she was even participating in one'
1		'It's there when I need it'	'Despite the fact of the treatment taking the form of a trial, implying that its effects relative to standard treatment were unknown and unproven, the participants approached the trials as something to consume. The fact that the trial existed almost entirely online (with the exception of the assessments) may play a role in such understandings'.
1	''.. if they had a [face-to-face] appointment there was at least somewhere they needed to go to do stuff. [but instead] they have to organise it amongst the chaos of their world to dedicate it time and for some of them it struck me that that was too difficult to do.'' *(Researcher)*	'It's there when I need it'	'they interpreted this as a kind of lackadaisical attitude from the online participants. The trialists could have, instead, considered that the participants just referred to and used the information as treatment when they needed it'.
1	''the. ..[participants] think, 'it's there when I need it' kind of thing.'' *(Researcher)*	'It's there when I need it'	We argue that participants' attitudes did not reflect a straightforward laziness which could be explained as simply a part

			of the participants' personalities, as the researchers sometimes implied. Rather, they reflect a common perception, which some of the participants referred to, of the infinite and timeless nature of the Internet. The Internet, then, can be seen as offering a particular kind of product, one that was found to be a preferred treatment choice in some ways, and one that offered participants increasing levels of responsibility for their involvement in the trial and their efforts to overcome their panic'.
3	Q 1 '...you got some information about a few things, statements, that you recognized and was relevant to you...I guess it (the treatment program) gave me something...The material you read, it made you, it started something. Something new' (Participant 8).	'Working process; readers'	Read Eye-opener Sporadic work Giving up/avoid
3	Q 2 'I think I've realized that I'm kind of, I realized that I'm kind of lazy, by nature, one likes to take shortcuts, and perhaps not do the things you really ought to do. It might feel difficult or you can easily put these must-remember thoughts aside. I have realized that it's really easy to do that. If you got an assignment that made it clear that one should do so and so, then it might feel difficult, it was interesting though...but still, it felt difficult'(Participant 8).	'Working process; readers'	Read Eye-opener Sporadic work Giving up/avoid
3	Q 3 'Yes, I got rid of that thing (laughter). Well not really, I stopped doing all those assignments....it was kind of a relief when it was over' (Participant 4).	'Working process; readers'	Read Eye-opener Sporadic work Giving up/avoid
3	Q 4 '...you tried to register what you did at every moment. What you thought and how you felt. And I tried to do it regularly during the day, both at work and home.... When you write it down, it forces you to put your thoughts into words. And there's something positive about that, when you write it down, it's almost like doing it, and then you can go back and look at it' (Participant 2).	'Working process; strivers'	Interpreting Ambivalent regarding practice Uncertain Trying to redefine
3	Q 5 'I sometimes thought it was hard, that it was tough...I suppose, if it was a good day I got it (treatment assignments) done (laughter)' (Participant 12).	'Working process; strivers'	Interpreting Ambivalent regarding practice Uncertain Trying to redefine
3	Q 6 'When you had read something, for example the night before, then you tried to practice it the following day, and you put effort into it. For example every little action that you did, you try to think why am I doing this...And it was a lot of work, until you could practice it on a more unconscious level' (Participant 9).	'Working process; doers'	Methodical work Emotional insights Apply/practice Redefine barriers

3	Q 7 'I sometimes feel it would be good for me to do the week (with behavioural activation) again' (Participant 10).	Working process; doers'	Methodical work Emotional insights Apply/practice Redefine barriers
3	Q 8 'Yes, I guess it was that week (with behavioural activation), after all, I think, because it was tough, and it was noticeable, made me so aware...' (Participant 10).	Working process; doers'	Methodical work Emotional insights Apply/practice Redefine barriers
3	Q 9 'Yes, it's important for me that I'm able to show someone what I've accomplished, and get some kind of response, someone who expresses his or her opinion. I guess, you get some kind of assurance or something like that. That's not what happened here' (Participant8).	'Motivation: readers'	Lack of support Not seen No response
3	Q 10 'I felt guilty because I didn't do all the assignments (laughter). Yes, it became an extra burden, so I felt like, this is not what I really need' (Participant 4).	'Motivation: readers'	Lack of support Not seen No response
3	Q 11 'Put simple, I couldn't find time for it (the treatment program)' (Participant 4).	'Motivation: readers'	Lack of support Not seen No response
3	Q 12 '...someone to talk to, I think that would have motivated me' (Participant 12).	'Motivation: strivers'	Missing conversation High demands Need of more support
3	Q 13 'I felt like I couldn't control it, it became something of a burden that was added to me, you could say that it created anxiety, one more thing that I couldn't do or complete, that I promised to do' (Participant 2).	'Motivation: strivers'	Missing conversation High demands Need of more support
3	Q 14 'Of course, much of what I did, I did because I promised to do it (the treatment program) and then I felt like I had to do it' (Participant 2).	'Motivation: strivers'	Missing conversation High demands Need of more support
3	Q 15 'I think it was important for my self-esteem. To feel that I did it on my own, like I was able to do things' (Participant 6).	'Motivation: doers'	Self-reinforcement Optimal support Autonomy Security
3	Q 16 '... if you needed to consult someone about something there was someone there. If I needed, I could choose to take contact' (Participant 5).	Motivation: doers'	Self-reinforcement Optimal support Autonomy Security
3	Q 17 'You felt like, I feel fine now, why should I continue (with the treatment)' (Participant 9).	Motivation: doers'	Self-reinforcement Optimal support Autonomy

			Security
3	Q 18 'The expectations were probably higher than the outcome' (Participant 8).	'Attitudes towards treatment: readers'	Not suited for me Ambivalence
3	Q 19 'Although it wasn't what I expected, or whished for, but that had a lot to do with me....I still believe it's a concept that works' (Participant 4).	'Attitudes towards treatment: readers'	Not suited for me Ambivalence
3	Q 20 'Some part of me was all the time scared like, to work with it, I don't know...I don't think it was the material that frightened me...What if it goes out of control?' (Participant 7).	'Attitudes towards treatment: strivers'	Avoidance Skepticism/fear
3	Q 21 'I don't believe in going to a "shrink", like the Americans do, right, I don't believe in that. But...if you feel bad, and if I'd find myself in some kind of crisis or something, right. Then I believe, or I know, that this is a good model to help you through a crisis. When a depression appears I know that this is a good model' (Participant 1).	'Attitudes towards treatment: doers'	Works Faith in program
3	Q 22 'I sometimes find it difficult to sit down and talk to someone, who'd try to understand me, and this way I got to work with myself...in a completely different way' (Participant 5).	'Attitudes towards treatment: doers'	Works Faith in program
3	Q 23 '...perhaps, it has affected me, without my knowledge. But, I can't think on any specific part, that I'm thinking about, that I'm using' (Participant 4).	'Consequences of treatment: readers'	Disappointed/shameful Lonely Lack of reinforcement Awareness of needs
3	Q 24 'I gave up after a while and I guess I thought: There's no purpose of me sitting here doing this, it's not going to make a difference anyway' (Participant 11).	'Consequences of treatment: readers'	Disappointed/shameful Lonely Lack of reinforcement Awareness of needs
3	Q 25 '..And in that way I've become more aware of how strange I sometimes think and how that affects my mood and I've become better on thinking other thoughts' (Participant 12).	'Consequences of treatment: strivers'	Ambivalence Dependence Needed more help Gained insights
3	Q 26 'Actually, the treatment program could have made a larger impact than it did, but I guess that's because I was too scared to work with it, I didn't use the material enough...' (Participant 7).	'Consequences of treatment: strivers'	Ambivalence Dependence Needed more help Gained insights
3	Q 27 'Perhaps I should look at it (the treatment material) some more... At least it's not uninteresting, it's educational....I kind of see it as a	'Consequences of treatment: strivers'	Ambivalence Dependence Needed more help

	course, a course that you should look at some more, because when you think of it, it wasn't that bad' (Participant 7).		Gained insights
3	Q 28 'It feels like I've regained the ability to take control of my life' (Participant 10). 'It (the treatment program) has meant a great, great deal to me in several different ways. Personally I feel a lot better, and then also, at work too, I work in, as a nurse ... So I used it both in my work and on my self' (Participant 1).	'Consequences of treatment: doers'	Emotional insights Generalization Model of treatment Acceptance
3	Q 29 'I don't feel that it's overwhelming, it's much and it's though, but you always know that you're going to get through it' (Participant 9).	'Consequences of treatment: doers'	Emotional insights Generalization Model of treatment Acceptance
3	Q 30 'That's why I now look at depression and feeling down as a natural thing, which happens to people...' (Participant 9).	'Consequences of treatment: doers'	Emotional insights Generalization Model of treatment Acceptance
4	"Well, it does affect me, even though I haven't exactly suffered, it affects me" (I).	'Hidden but Present'	'Most women did not define their incontinence as a major health problem'
4	"Yes. You can talk about almost anything else I think, all kinds of matters considering your genitals and . . . but not this, this I think is very taboo" (I).	'Hidden but Present'	'Still, living with an ever-present concern of leaking urine was described as a private and usually well-hidden secret that might result in awkwardness and embarrassment. Most of the women described their incontinence as shameful, and something they disclosed to no one or to very few other people'
4	"Well, I haven't explicitly looked for it, but since I was there I asked them and told them about my problems, but they didn't think there was much to be concerned about" (I).	'Hidden but Present'	'Having sought care on previous occasions, some women felt they had not been taken seriously or had even been ignored. On mentioning their incontinence, they had experienced a dismissive and sometimes embarrassed attitude from health care providers'
4	I saw it in a newspaper and thought it was a good idea, because I didn't have the kind of trouble where I would have sought help from the ordinary health care providers. I didn't think I had that much of a problem. (I)	'Hidden but Present'	'The women perceived the treatments as a possibility to do something about the leakage on their own. They also saw the treatments as timesparing and easily accessible, which was appealing'
4	One could say, had she been sitting in front of me like anybody else, then I would not have asked in the same way. . . . Yes, I thought so. It felt natural in a way, I did not feel as exposed and vulnerable. (I)	'At a distance but Close'	'Most women in the Internet group experienced the establishment of a relationship with the urotherapist. They described the relationship as both personal and distant, and said that it gave them a sense of being acknowledged and supported without being exposed. They mentioned many factors as important for the development of the relationship, including the fact that someone seemed genuinely interested in their concerns, gave them praise

			when they were doing well, and supported them when their motivation was low'
4	I mean, I think I developed a close relationship with her anyway. I mean, just because I could ask about things more directly than I normally would. And you got an answer the next day, she didn't try to escape. She was there, it was a comfort to have her there. And I knew that if I needed to ask about something, I could email her. (I)	'At a distance but Close'	'The lack of face-to-face contact had both positive and negative consequences. Some women experienced the relationship as more harmless and less potentially judgmental, compared to a face-to-face relationship, and this made them feel freer to talk openly about the leakage'
4	No, and that's why it felt good on the 'net [Internet]: You're an anonymous person. Because I would think, I've been thinking about this for quite a while and thought that it's a bit hard to go to a health care center or doctor with these problems. So, I think I thought that this anonymity was comfortable.	'At a distance but Close'	'The lack of face-to-face contact had both positive and negative consequences. Some women experienced the relationship as more harmless and less potentially judgmental, compared to a face-to-face relationship, and this made them feel freer to talk openly about the leakage'
4	It is easier to cheat, what should I say, if you don't have a physical meeting. It gets more distant and it can be easier to skip, if you don't feel really engaged, because it becomes a more impersonal contact that hasn't got the same weight.	'At a distance but Close'	'Some aspects of the relationship were lost or became more superficial without face-to-face contact. For example, small shifts in facial expressions, body language, or intonation were missed, and for some women this led to an experience of a less-close patient–provider relationship. As a consequence, these women also felt less motivation to do PFMT'
4	Sometimes it can be tough to have a contact, get to the contact, sit face to face, and go there every week. It feels demanding and it takes too much time, so that was really positive. Sometimes it is good, though, to have someone to look you straight in the eyes and tell you what to do. It is easier to take it seriously. But I thought that the contact over the Internet worked really well. (I)	'At a distance but Close'	'A few women said that it was more difficult to explain complex situations and feelings in written text than face to face. One woman expressed the ambivalence like this'
4	Yes, toward the end there was a negative pressure. But it wasn't because of the emails I got, but because I felt that I should have done more, and this was important for me. And then I felt guilty about it and chose not to answer, because I felt that, no, I have to do the exercises properly now for a week before I can answer. (I)	'At a distance but Close'	'some women experienced this as stressful. Many women also mentioned a sense of guilt because of the inconsistency between their own goals for the training and their actual achievements. These women placed high demands on themselves, and wanted to do the right thing to meet the expectations they perceived from the urotherapist'
4	"It is in my own interest to do this, but it still feels like I need to have someone to keep an eye on me so that I do the training" (I).	'At a distance but Close'	'Conversely, many women said they needed the reminders to maintain their motivation for training'
4	It is so boring to do. I really felt motivated when I joined. I figured it was now or never, but then three weeks go by, and then you've lost your motivation. You don't talk about it with anyone. It's not like when you've been out jogging five kilometers and brag about it; this is something you're quite alone with. (P)	'At a distance but Close'	'The women in the postal group expressed a lack of communication and support. They wanted someone they could tell about their progress, and they wanted help with motivation and reminders to do PFMT. They found it difficult to retain

			motivation over a long period without support. One woman described the PFMT as follows'
4	"It felt like, like I was, the participation in a study like this, like my contribution was important, and all of these questionnaires, it felt important to do. And I think that my motivation to do this also increased" (P).	'At a distance but Close'	'Women in the postal group talked less about guilt and negative pressure than women in the Internet group, and more often described their participation and contribution with purely positive words. They also expressed a sense of loyalty toward the research team, and took responsibility for their participation in the study. It is likely that this also helped them maintain their motivation for training'
4	"And when you know how, then it is easier to do it" (I).	'By Myself but Not Alone'	'One effect of the Internet-based treatment, and to some extent also of the postal treatment, was an increased awareness of how to handle the incontinence. The majority of the women felt empowered by the treatments'
4	"I think it was good that you included those things, because then you gained awareness. At first I thought, I don't do any of those things, but then I thought again and oh, yes, actually I do" (I).	'By Myself but Not Alone'	'Some of the women said that this part was helpful, and a few clearly expressed that it helped them avoid negative patterns'
4	"Even though it hasn't happened that much during the study time, I got a little bit better. I have gained a tool to use when I get time and decide to do this" (I).	'By Myself but Not Alone'	'For some women, the treatment did not improve the leakage; however, most of these women expressed a positive experience of the treatment because they had gained new knowledge, increased their awareness, and received tools to work with in the future'
4	Yes, I have noticed that since I said that I joined this study, both at work and among friends, that people have said, "No, so should I. That's exactly the way it is." Well, I didn't know it was that common a thing, I had thought it was mostly just me. (P)	'By Myself but Not Alone'	'Participation in a study in which incontinence was openly discussed also helped to break down some of the shame barriers. One woman described how she was now brave enough to bring the topic up'
4		'Acknowledged but Not Exposed'	'During the analytical process, a core category emerged that described the results in all three categories: acknowledged but not exposed. This core category included a number of aspects, as follows. A woman living with a condition she perceives as embarrassing might feel alone and exposed. Many of the women wished that SUI would be more recognized and openly talked about instead of being a well-hidden secret. Some of the women were afraid of exposing themselves, and this led them to adapt their daily activities and sometimes deterred them from seeking health care. Participation in a treatment program made the women feel acknowledged and supported, and it helped them to retain control and gave them a feeling of less exposure. The women were empowered by the treatment programs; the discovery that they were not alone made them see themselves as

			part of a group, and this new knowledge helped them feel less exposed in their everyday lives'
5	"A while after registration I began to suffer from tendinitis in my right foot. During the first module the foot was so painful that I decided to quit" [woman, knee and hip OA, non-completer].	'Patient characteristics 'Comorbidity'	'Another reason for discontinuation was the presence of an additional health problems, other than OA. Due to pain and/or other (medical) treatments, it was difficult for interviewees to continue their involvement in the Join2move program'.
5	"In the year that I registered, I was diagnosed with prostate cancer. I have had surgery and received radiotherapy treatments for several months. Therefore using the Join2Move program was too hard for me" [man, knee OA, non-completer].	'Patient characteristics' 'Comorbidity'	'Another reason for discontinuation was the presence of an additional health problems, other than OA. Due to pain and/or other (medical) treatments, it was difficult for interviewees to continue their involvement in the Join2move program'.
5	"I had a bad year and I was not at ease with myself. I was not in the right mood to exercise. It was all too much" [woman, hip OA, non-completer]	'Patient characteristics 'Well-being'	'Interviewees reported that a low mood interfered with their ability to perform modules'
5	"My husband and friends joined me regularly because I told them about the program. This motivated me to continue". [woman, knee OA, completer]	'Patient characteristics 'Social support'	'Patients who felt themselves responsible for their own progress were most likely to use the program. These individuals perceived the program as something that needed to be done, rather than appreciation or enjoyment. Furthermore, those who emphasized the importance of their partner, family, or friends in maintaining the Join2move program were mostly adherent'.
5	"I have a full time job and walk around the office all day. So for me it was not necessary to walk the extra miles for the Join2Move program"[man, knee OA, non-completer]	'Patient characteristics 'Already physically active'	'In addition, participants who regarded themselves as already physically active found it less necessary to participate'.
5	"This kind of program does not work for me. I find it difficult to stay motivated all the time. At the beginning I was motivated but then it went downhill quickly. I got lazy and other activities became more important". [man, knee OA, non-completer]	'Patient characteristics 'Lack of motivation'	'Lack of self-discipline was another identified reason for nonusage'.
5	" Although it was a virtual person, I made an agreement and if I make an agreement I stick to it" [man, hip OA, completer]	'Patient characteristics 'Sense of duty'	
5	"Join2move is based on an evidence based theory. This persuaded me to participate and continue with the program". [man, knee OA, user].	'Intervention characteristics 'Trust and reliability'	'The values "trust" and "reliability" were important in the decision to engage the Join2move program'
5	"The content and feedback of the system was put together well. This made me feel confident that I was in good hands". [man, knee OA, user].	'Intervention characteristics 'Trust and reliability'	

5	“The language used in the program was easy to understand and appealing”. [man, knee OA, non-user].”	‘Intervention characteristic ‘Usability and complexity’	
5	“Although it was quite simplistic, the structure of the program was an effective and appropriate way to increase my physical activity level” [man, knee OA, user].	‘Intervention characteristic ‘Usability and complexity’	
5	“The internet aspect of the program was very convenient. It was not necessary to go out for a weekly appointment. That saved me a lot of time” [woman, hip OA, completer.]	‘Intervention characteristic ‘Advantages and disadvantages	‘patients consistently reported that the Web-based character of the intervention was an advantage compared with face-to-face treatments. The flexibility of being able to complete modules at one’s own pace without time or travel restrictions was cited as an advantage’
5	“Although it was possible to fill out an evaluation form about pain and performance, sometimes I just needed a personal chat to talk about my progress” [man, knee OA, non-completer].	‘Intervention characteristic ‘Advantages and disadvantages’	‘Some participants had a strong need for personal guidance’
5	“I expected a package of specific exercises instead of performing ‘all day activities” [woman, knee OA, non-completer].	‘Intervention characteristic ‘Expectations about the program’	‘gradually increasing a self-selected activity was not always compatible with expectations’
5	“Because I was allocated to the intervention group, I wanted to finish the entire program. Maybe a little old fashioned but I found it inappropriate to stop halfway. [woman, knee OA, completer]	‘Study characteristic ‘Commitment to the researchers’	‘Study-related factors were also cited as reasons for remaining or not remaining engaged in the program. Some participants felt under obligation to continue. They described a feeling of commitment to the organizers of the study’
5	“The questionnaires included too many questions and some questions were hard to answer. Eventually I didn’t want to make the effort anymore, so I decided to quit the program.” [woman, knee OA, non-completer].	‘Study characteristics ‘Questionnaire	‘Some participants perceived the questionnaires used as being too long or too difficult. The questionnaire consisted of 17 pages with a total of 171 items. Participants not only lost interest in completing the questionnaires but were also less motivated to continue with the program’
6	“It was good, but I did especially appreciate the reminder because sometimes it came through at a busy time, um, I didn’t mean to forget about it but it happens. And I was thankful for the reminder”. [Interviewee #11]	‘Barriers’ ‘Personal Factors that Decreased Intrinsic Motivation to Participate’ ‘Forgetfulness or a Lack of Awareness That the Program	‘The competing demands for time and need to prioritize also appeared to result in many participants “forgetting” to complete their module and associated activities on a weekly basis. Many participants alluded to relying on weekly reminders that a module had opened, rather than initiating seeking out the new module themselves. Forgetfulness appeared to be particularly prevalent when the participants postponed completing a module until a later time. Many stated that they would put the module off, intending to complete it when they would be able to focus on the intervention

		Needs to be Completed'	without competing demands, but often forgot to return to it. They often forgot when other demands on their time arose or when they lacked regular computer time, resulting in a lack of visible reminders that the program was open'.
6	"...I get anxious, and then I begin to think to myself that "I've got to do this" and "I've got to do that," and "I can't do my [program] now, I'll do it later," and really there is nothing that can't wait. Nothing at all. I have a set routine. I'm retired. But I get myself into such a state of anxiety that I can't relax and do my [program]. So I leave it and go and do my silly little things such as taking my dog for a walk and doing my shopping. All sorts of, you know, mundane things that are not important, well they are important, but I could give myself the time to relax and do it..." [Interviewee #1]	Barriers' 'Personal Factors that Decreased Intrinsic Motivation to Participate' 'Mood/Anxiety'	'Mood and anxiety were also often cited as barriers to engagement. When anxiety was high, participants found it difficult to find the time or concentrate on the program. When mood was low, participants lacked motivation to complete the program, often feeling overwhelmed by its demands. This resulted in participants focusing on other more manageable tasks, which allowed them to feel that they had completed at least some tasks throughout the day. Tasks of daily living were often prioritized ahead of the program, even when participants believed that they would benefit from taking the time to complete the program and objectively had the time'.
6	"I found the questions strange. The question that said "Do you do what your doctor tells you?," I'm going "I'm not 4,...how am I going to respond to this?" And in the end I throw my arms in despair and go "Urgh! I don't know, I don't know the answer!" and put it in the appropriate box...I found that when I clicked on the "Do I take x, y, z medicine" and put "Yes" and the window came up and gave me space to write in it. I want more of those windows". [Interviewee #4]	'Barriers' 'Factors That Reduced Engagement With the Program' 'Program Seen to be a Poor Fit to the Individual'	'Several participants reported frustration with the program's lack of personalization. This was particularly reinforced by frustration with the standardized questionnaires embedded in the program and trial. Participants frequently cited that the answers were unlikely to reflect their true state, as they did not believe that they fit within the categories provided. This resulted in them feeling frustrated and wanting to stop completing the questionnaires. Many indicated that the capacity to provide additional information in terms of a free-text box would be beneficial and would enhance their desire to persist with the program'.
6		'Barriers' 'Factors That Reduced Engagement With the Program' 'Program Seen to be a Poor Fit to the Individual'	Other participants were concerned that their answers were being misinterpreted, which may have influenced their answers and therefore the time taken to answer the questionnaires or complete program activities. This was reflected in the number of emails participants sent, unsolicited, to the project team to contextualize their answers to the questionnaires'.
6	"Because you need a bit of feedback...It's a bit of an empty system, because...you know...you put out a few stories about your thoughts and experiences, but you know...nothing comes back". [Interviewee #1]	'Barriers' 'Factors That Reduced Engagement With the Program'	'The perceived unidirectional relationship between the user and the program also led participants to consider that how they engaged in the program was irrelevant and decreased their motivation to continue. They felt that the computer offered little in terms of support, interaction, and feedback. Participants frequently reported thoughts of giving up on the questionnaires

		'Program Seen to be a Poor Fit to Individual'	and the trial due to feeling that their information would be misrepresented and therefore not useful to the trial team'.
6	"...it's a lot easier to ignore. Um...and truly and if you've made an appointment and you know you have to pay for it, you're going to turn up". [Interviewee#1]	'Barriers' 'Factors That Reduced Engagement With the Program' 'Program Seen to be a Poor Fit to the Individual'	'Although some participants reported that this unidirectional nature of the relationship was beneficial, for others, it reduced any obligation to log on to the system and use it. The sense of accountability was decreased, as there was no feedback or cost of engaging with the program. A lack of perception of the program being a therapeutic relationship and of someone relying on their attendance meant that several participants felt that they were able to put off completing the program. The freely available nature of the program, without cost, waiting lists, or time restrictions, meant that participants placed less value on completing the program when it was opened to them'.
6	"...think I was a bit of a difficult ah...participant, because I know a lot about uh...um...emotional therapies. And...and...a lot about the theories, so...um... it was uh...it was a bit tedious to go through each of the programs and the theories and then the examples for me..." [Interviewee #1] "...a lot of the stuff we did online was not new...and that frustrated me". [Interviewee #2] "Yeah, and the other thing you know, it's long-winded. I can, sure there are some people, but for people who have, maybe, who have been to university, who have a certain level of understanding of these problems or a certain level of education um, it was too simplistic for me". [Interviewee #10]	'Barriers' 'Factors That Reduced Engagement With the Program' Failure to Learn Anything New'	'Participants who felt they were not learning anything reported lower levels of motivation to persist with the program. Some had had previous psychological treatment for depression and felt that the program did not offer them anything substantially different'.

6	"Um...ah...because you have no feedback, they're like chalk and cheese really. Well, yes...it was educative, but I didn't feel like it was a therapy session..." [Interviewee #1]	'Barriers' 'Factors That Reduced Engagement With the Program' Lack of Perception of the Program as a Therapeutic Relationship'	Previous therapy experiences also meant that some had different expectations of the therapeutic relationship. The program therefore offered reminders and information, but not therapy as such. This meant that participants struggled to engage in the computer intervention and to see it as therapy. Those participants who perceived little personal benefit from the program reported persisting due to the perception of obligation to the researcher or the belief that their input would help the wider community. They appeared to hold values around completion and contributing to society that allowed them to continue to persist with the program'.
6		'Motivating Factors That Enhanced Persistence & Adherence to the Program'	'Participants reported several strategies and motivations that allowed them to complete the program on a (semi)regular basis. These strategies were rarely linked to a specific intervention barrier but were rather seen as intrinsic traits or behaviors that allowed them to continue engaging with the program'.
6	"...if I thought to myself this is useless I'm not getting anywhere. I possibly wouldn't finish it...I think that it was very, very interesting. There was a heck of a lot to learn from it, there was a lot I found, the reading, everything, I found I quite...I enjoyed it. There you go". [Interviewee #3]	'Motivating Factors That Enhanced Persistence and Adherence to the Program' 'Noticing an improvement'	'The perception of receiving a benefit from the program was considered to be the primary reason many participants persisted with the intervention. Participants reported experiencing benefits of the program beyond a sense of accomplishment and looking forward to completing the next part of the program. These participants frequently spoke about the benefits of the program and how they were implementing changes from the program into their daily lives'.
6	"I felt satisfied at the end of it. That I'd done it, it was interesting and it was...I suppose it reinforced what I probably should be doing myself. It was easy to do and pleasant, and yeah I felt good about doing it..." [Interviewee #5]	'Motivating Factors That Enhanced Persistence & Adherence to the Program' 'Noticing an improvement'	'Participants who saw personal value often used the language of the program. They were able to recall tasks they completed, appeared to have a better recall of the program, and continued to refer back to the program after they had completed it. They reported an overall sense of satisfaction that carried through each module and they appeared engaged in the program as a whole'.
6	"...you could sit there and just actually take your time to do it. You know you could really think. Whereas when you're talking to somebody and you've got an hour or three-quarters of an hour or something, you	'Motivating Factors That	'Several participants reported that they had dropped out of previous face-to-face therapeutic relationships due to the nature of the interactions. They reported feeling as though the therapist

	really kind of you know...so time to me is the important thing". [Interviewee #3]	Enhanced Persistence & Adherence to the Program' 'Feeling in control'	had been restrained by the amount of time available and that they were rushed by the time allocated to individual sessions. This resulted in their feeling unimportant and merely a patient rather than a person, and that their agenda was not as important as the agenda of the therapist'.
6	"I think when I reflect on therapy you've got the lead up, going to [laughs] therapy, the anxiety beforehand, you know. You're going into the therapist's room, you're in someone else's domain, but it's like being in front of a stranger, you know, you're in front of a stranger and you feel you have to perform a little bit. [Laughs] whereas if you're by yourself, controlling it yourself, I think you can be more reflective about yourself". [Interviewee #11]	'Motivating Factors That Enhanced Persistence and Adherence to the Program' 'Feeling in control'	'Being able to dictate the pace in the online intervention meant that they felt they got more benefit from it. The ability to choose which activities to complete and what areas to focus on for the activities resulted in many feeling as though their agendas were catered for in the program rather than that of the therapist. Due to this, they felt that they could be more honest with the program, and this led to greater reflection'.
6		'Motivating Factors That Enhanced Persistence and Adherence to the Program' 'Feeling in control'	'Many participants reported returning to the intervention several times. This allowed them to reflect on what they had learned. This appeared to facilitate the program being incorporated into everyday life. Those who returned to the program several times were more likely to find the program material novel and interesting. Several of these users often frequently returned to other trusted websites when they needed information. These participants appeared to view the program as a useful tool for themselves, rather than a research project where their contribution would be more valuable to others instead of themselves'
6	"I remember doing a long one and thinking, "Oh yeah! I missed one! I can go in and do that one again". It always good because you know you can go in and do it again. That's the first time I actually left the memory one and come back and do it again and I'm going "I'll do that later" [Interviewee #4]	'Motivating Factors That Enhanced Persistence & Adherence to the Program' 'Feeling in control'	'The ability to be flexible in the completion of the program also meant that participants were able to overcome time-related barriers, allowing them to complete modules in sections, when time allowed. Sometimes this appeared to be prompted by reminders that were part of the program'.
6		'Motivating Factors That Enhanced Persistence & Adherence to the Program' 'Feeling in control'	'The perception of flexibility and control of the program appeared to enhance engagement in the program and therefore improved motivation to persist with the trial'.
6	"...because I had committed to doing something and so I did it". [Interviewee #2]	'Motivating Factors That Enhanced Persistence &	'Many participants cited value in completing what they had started as a reason to continue the program despite being frustrated with it. The participants often contextualized these values as being a learning of their generation, with many indicating that these values

		Adherence to the Program' 'Sense of Duty to Oneself'	had developed as they had grown up and had persisted into adulthood'.
6	"Sheer determination to see what's this one going to be about, curiosity perhaps and it was determination. I feel you know if a job's worth doing you do it as good as you can. There's no point in giving up in the middle of [a] thing you just keep on plodding on". [Interviewee #3]	'Motivating Factors That Enhanced Persistence & Adherence to the Program' 'Sense of Duty to Oneself'	'Due to having these values, they were going to complete the program regardless of how frustrating or tedious it was. They completed it because their sense of what they should and shouldn't do directed them. Holding such values meant that they did not consider stopping the program or dropping out from the study'.
6		'Motivating Factors That Enhanced Persistence and Adherence to the Program' 'Sense of Duty to Oneself'	"On completing the entire program they described a sense of accomplishment coupled with relief, a sense of having done something that was difficult, but that they had overcome their difficulties. These participants placed value in hard work and were often scornful of those who dropped out, implying this was a weakness of character. They placed pride in completion where they saw the task as a chore rather than a personally useful tool or activity'.
6	"I log in to my Internet every morning. I spend an hour or two hours, depending on what I have to do. And...um...and I'll always complete task as they come up. So with my emails, it's the same. I'll answer them on the same day or possibly the next day". [Interviewee#2]	'Motivating Factors That Enhanced Persistence and Adherence to the Program' 'Something That Needs to be Done: Task Completion'	'Participants who integrated the program into their day-to-day routine appeared to be less likely to struggle to be adherent. They did not see the program as an activity to be reflected on, but rather as a task to be completed when it was available. These people did not report the frustrations with the program that those who saw completing the program due to a sense of duty did; rather, they saw it as a task to be done with little emotional connection to it'.
6		'Motivating Factors That Enhanced Persistence and Adherence to the Program' 'Something That Needs to be Done: Task Completion'	'This was more common in participants who logged on to the computer daily and who often referred to themselves in terms that implied a perception of being organized or task driven. Routine was often highly valued and the ability of the program to fit into this allowed it to become routine. These participants saw the program as something that needed to be done, rather than something that they wanted to do or enjoyed doing. They often described it as part of the daily chores or to-do list for that day. The development of habit and the perception of the modules as needing to be done is particularly interesting given that

			participants were able to opt out of the trial at any stage. Instead, they conceptualized the trial as medicine that needs to be taken'.
6	"Well, I mean, you really, you have to keep going. Um, when you start something you got to finish it, unless it drives you crazy. And it didn't drive me crazy. There were some days when I did it and I thought "God how much more of this?," but you made a commitment, so you followed through and you did it. And I mean if you don't finish it how can you help if you're only giving half information how can you help? And as I say the main criteria was perhaps I could help". [Interviewee #9] "I am thinking of the fact that I have committed. Commitment is all I can think of. And I am thinking that the person I have committed to is relying on my support. And um...it would be very unfair to let them down. I know that I am only one of many people, but if everybody would drop out...where would we be"? [Interviewee #2]	'Motivating Factors That Enhanced Persistence and Adherence to the Program' 'Obligation to the Research and the Researchers'	'Many participants used words such as commitment and obligation to describe the things that made them remain engaged in the program. They described feeling a sense of commitment to the researcher or to the research. Many of these participants had been part of research teams in the past and therefore placed heavy emphasis on participating in research projects. Some were also aware of the numbers required to successfully complete a research project and aware of the impact of dropout on research outcomes'.
6	"For instance, with my [other program]. I drop in and I drop out depending on my other commitments because I know that nobody else is involved but myself". [Interviewee #2]	'Motivating Factors That Enhanced Persistence and Adherence to the Program' 'Obligation to the Research and the Researchers'	'When participants had engaged previously in programs that were not obviously linked to research, they were less likely to adhere to the program outline. This research-related engagement appeared to be driven by an obligation to others, rather than an obligation and perception of the benefits that they might have received themselves. Participants reported that when they were completing a program for only themselves, program use was more adhoc, as they believed that they could complete the program at their own pace without affecting others. However, when engaged in research, there was more pressure to complete the program in a timely manner and in its entirety to ensure their contribution was able to benefit others.
6		'Motivating Factors That Enhanced Persistence & Adherence to the Program' 'Obligation to the Research and the Researchers'	'This motivating factor appears to be linked to the completion of research and may not enhance motivation in open access users of freely available online programs. The removal of an obligation to others when there is no research project attached to the program may lead to open access users not completing programs, not obtaining the full benefits of programs, or dismissing online programs as ineffective. Such experiences may also lead to participants dismissing psychological therapies as ineffective for their problem and may actually decrease help seeking'..

7	“I have noticed that there are many ups and downs in the way you feel”. (COMBI05, COM) “It just cleared up a whole lot of things, the course (…) It made me think a bit”. (CCBT03, COM) “I know now how I can keep an eye on my mood”. (CCBT10, NON)	‘Experiences of the course content’	‘An important aspect in the experience with CCBT is to what extent the course is adjusted to the patient's situation. In general, the interviewees experienced the course content positively. The sessions provided them with useful information to create more awareness of the symptoms, and on how their thinking and doing are interrelated with the depression symptoms’.
7	“That [the theory]was the stimulus to carry on, that it was serious enough because you recognize enough things in yourself, and therefore carry on”. (COMBI05, COM) “And then I started to link the examples in the films to myself, and think about how I could make things better. It kept me occupied the whole week and then I noticed that I felt a bit better and that motivated me to follow the next lesson”. (COMBI07, COM)	‘Experiences of the course content’	‘Being able to apply the course to one's own situation was generally experienced positively. As such, experiencing self-identification and improvement through CCBT-CYL, was a motivator towards adherence’
7	“Every week I thought it was exciting: like “what are we going to do now?” (COMBI03, COM)	‘Experiences of the course content’	‘For some users, the CCBT-CYL program created curiosity about the next sessions’
7	“I think that I've probably gained more from the mood diaries than from the whole course up until now. (…) Why is it (…) that I get up in a good mood in the morning and then an hour later I'm suddenly in a bad mood. How come?” (COMBI01, NON) “I just thought: I'm just torturing myself, I've had enough, I don't want this anymore (…). To write this feeling down and then at the end of the day to think about how I felt. It made me even more depressed so I just let it go”. (CCBT03, COM)	‘Experiences of the course content’	‘However, the examples provided in the sessions, the homework assignments and the mood diary are experienced as either positive or negative’. ‘While some interviewees experienced the mood diary as the most essential part of the course for creating awareness, others experienced it as a burden’.
7	“This is distant enough to be used as a mirror, and because it's the same people in the films each time this also gives a feeling of familiarity”. (COMBI06, COM) “Go and find friends. I haven't got any friends (laughs), I don't need any friends. (…) Not for me, the examples were nice. Nice okay, but not for me”. (CCBT02, NON) “The little things that make people depressed, as examples. Making me think “man stop moaning about it and try and get over it”. (CCBT07, COM) “They try to brighten people up with material things. I thought that was a pity, that there was nothing else that could put you in a better mood (…) If I buy something than I only feel better for a moment and then it's gone. Therefore it doesn't really solve the problem. I found that a bit shortsighted” (CCBT10,NON)	‘Experiences of the course content’	‘Many CCBT users had difficulties in translating and applying the homework assignments to their own social situation. The film fragments were partly experienced as good, recognizable examples. However, some CCBT users experienced these examples as incomparable to their own lives, which did not provide appropriate solutions for them personally’.

7	“The most important thing for me was the theory and I did that in my own way, I did something with it (…) and to also fill in a diary and make tasks, that was too much for me”. (COMBI05, COM)	‘Experiences of the course content’	‘Due to negative experiences with some components (eg homework or mood diary), completers did not necessarily use all the components of each course session. These completers tailored the CCBT program to their own situation by selecting only those components experienced as beneficial’.
7	“The problem was that the whole computer course didn't fit in with my problems and my feelings. There were often things that I never had any problem with, then I thought this has nothing to do with me and I don't think that I followed the last lessons if I'm honest. Because I just had the feeling that it didn't help me”. (CCBT05, NOH)	‘Experiences of the course content’	‘But negative experiences could also result in not completing the course’.
7		‘Experiences of the course content’	‘The abovementioned positive and negative aspects of the CCBT content were reported in both groups of CCBT completers and non-completers. However, completers seemed to have more often a positive experience with CCBT, while the inability to identify and apply the course content seemed to occur relatively more among the non-completers. Almost all completers experienced an improvement in their depression symptoms which was partly attributed to CCBT and partly to other aspects (e.g. changes in work, at home). Non-completers who changed to other help did not attribute improvements in symptoms to CCBT. Finally, all non-completers who did not seek other help, reported that they had not experienced a significant improvement’
7	“I'm not that great with the computer. Things kept going wrong in the program or something, I don't know. And then I lost everything in the diary that I had just filled in. I was so frustrated that I just thought: I'm not going to do it anymore”. (CCBT03, COM) “In the first weeks, it was so difficult then. I'm not so handy in (shows with hands typing movements). And that's where it begins”. (CCBT02, NON)	‘Computer aspects’	‘CCBT-CYL requires working on a computer on the Internet. Throughout the interviews, several computer aspects emerged to be important issues for the users including computer/Internet skills and equipment, the location and time of computer/CCBT access, and the reading of an online versus a printed medium’. ‘Not everyone is used to computer work, or has a fast-working computer or Internet connection. Difficulties with computer work were experienced as frustrating, especially when it comes to difficulties in saving homework assignments or mood diaries’.
7	“My computer always stood here on the table (…) It was always within reach. But meanwhile we now have a laptop. (…) I only open my post, and do nothing more on the computer”. (CCBT01, NON) “I often argue with my wife. We have a computer and that's in the living room. Everything that I do she can see and I don't like that. So I could only do that program when she was gone” (CCBT02, NON)	‘Computer aspects’	‘Moreover, an inconvenient computer location could endanger the experienced accessibility and required privacy to follow the course’.

7	“You could make up your own mind when you did something and for how long and what you do. And you're completely free to do whatever you want”. (CCBT03, COM) “The ability to solve it yourself, I think that's a big advantage of such a course. That you can do it in your own way. If you go to the doctor then you have to make an appointment. You go away for a while; if you get a visitor he will hear straightaway where you have gone (…) Whilst with the course, if someone comes in than you push the page away and then later on you just carry on”. (COMBI05, COM) “If I should go to someone else or go somewhere, than I act differently than when I'm alone in my own surroundings. Here I drop my mask. And I only had that when I sat alone behind the computer, this is me, this is how I feel, and I experience it like this”. (CCBT01, NON)	‘Computer aspects’	‘Some interviewees pointed to positive and/or stimulating aspects of doing a therapy in your own time, sitting behind your own home computer. These aspects concerned freedom, enjoying computer work, anonymity and being yourself’.
7	“I liked it that there was a schedule, a rhythm. Also for yourself”. (COMBI05, COM)	‘Computer aspects’	‘Holding on to a regular rhythm was sometimes reported as a motivator towards treatment adherence’
7	“I printed everything. (…) And I notice that I pick it up quicker to glance through it again. Easier than the computer and also easier than that book from the last course”. (CCBT03, COM) “A summary of it all, in a way that you can easily print out. That you have for yourself in any case a sort of checklist of the main points. That is really what I miss”. (COMBI05, COM)	‘Computer aspects’	‘Although the program was experienced as clearly written, many interviewees preferred to also have a printed summary version of the course content which was easier to revive as the online version’.
7	“But the course, you can look back on it, you can look and see what it was like again? What did they say there?” (COMBI04, COM) “They gave examples. Of nice things to do, they gave 25 examples. And I like having that list (…) I want to read: “What must I do?” That really stimulates me”. (CCBT02, NON)	‘Computer aspects’	‘The program enables to retrace the items handled in the previous sessions. Some interviewees experienced this as an advantage’. ‘Thus, for an optimal CCBT usage, it is important that the user possesses the right computer skills and equipment’.
7	“You haven't really got someone or something forcing you (…) I really need that. I either put it off or I just don't look at it (…) Ir you're in a bad mood then you really don't feel like it. Yes, that is motivation. Someone should say to me “you have to do it”. (CCBT04, NOH) “Someone who wants to be treated, should just keep to the rules. If you leave it to the patient themselves than they will look for the easiest way”. (CCBT10, NON)	‘Social aspects’	‘Many interviewees reported a preference or need for some kind of support to complete CCBT successfully. The demand for support took three different forms: the main reason for wanting support was to create sufficient discipline to adhere to CCBT’.
7	“I think that that [personal talks] is not so easy to put off. That I put it off less easily. (…) I think that it is nicer if (…) you can exchange ideas”. (CCBT01, NON) “I need to be with people, I can't just be alone behind my computer screen”.	‘Social aspects’	‘Next to self-discipline, a second reason for wanting support was to have personal contact’.

	(CCBT09, NOH)		
7	“That thing doesn't talk back, (…) I haven't got any contact with it. Whereas when I talk to you, then you react, and then you straightaway reach a much deeper level than with the computer.” (CCBT07, COM) “You can't judge whether or not you're doing good. I find that difficult (…) I think that the most important thing is, that you can just ask a question like am I doing it right. Just a bit of confirmation that is actually the only thing”. (COMBI06, COM)	‘Social aspects’	‘Thirdly, some interviewees preferred feedback or wanted to go more in depth into the course through personal support’.
7		‘Social aspects’	‘Nearly all non-completers who followed at least one CCBT session indicated a preference or need for support. But also some of the completers preferred some kind of support or argued that other CCBT users could need support. A last finding on support was that the group of COM and NOH interviewees differed from the NON interviewees in the experienced support of the social environment. Interviewees from the first group nearly all reported possibilities to discuss their depression symptoms with someone in the near social environment, while nearly all interviewees from the second group did not report this experience. This finding suggests that the near social environment influences depression treatment’.
7	“I just didn't think that it was so bad to get treatment for it: “go to the doctor about this, no need”. (CCBT03, COM)	‘Research aspects’	‘Research aspects had an unintended motivating impact on treatment adherence. During the trial study, several research activities took place: the screening process consisted of an invitation letter, Internet questionnaires and a face-to-face screening. After inclusion, the participant monthly received Internet questionnaires and reminder e-mails. If a participant failed to fill in the questionnaire, he/she was contacted by phone. Although these activities were no part of CCBT, this distinction between research activities and CCBT was often experienced as less strict. Moreover, there might have been a Hawthorne effect of the research activities, since participating in our trial study might have changed the participant's behaviour’. ‘Firstly, some interviewees would not have had treatment or not have been to the GP if not invited for research participation. The interviews showed several reasons for this finding: the interviewee experienced no need to receive a treatment for the symptoms, or did not want to go to a GP or receive medication for the depression symptoms’.

7	“If I take part then I do it wholeheartedly. In the name of science I owe this to them” (COMBI06, COM)	‘Research aspects’	‘In other cases, the interviewee was not aware of the depression symptoms prior to the research participation. One participant also mentioned a lack of time as the reason for not seeking help on her own. Secondly, the fact that CCBT was offered as part of a study was often experienced as stimulating to follow or continue CCBT and/or filling in the questionnaires. This impact varied from routine external discipline to the obligation felt to join the study’.
7	“I thought this is something where experts are busy with, something valuable should come out of it. You mustn't just let that pass, therefore I wanted to just finish the lessons”. (CCBT10, NON)	‘Research aspects’	‘For one interviewee the impact was situated in the belief that CCBT must be good since it is developed by experts as part of a scientific study’.
7	“I thought that the computer program was the questionnaire, and the doctor. So however, I read it I thought computer program and doctor. That was it for me: questionnaire and doctor”. (COMBI02, NOS)	‘Research aspects’	‘Thirdly, the face-to-face screening and the Internet questionnaires were sometimes experienced as part of the treatment. Sometimes, the impact was directly visible: two interviewees confused CCBT with the Internet questionnaires. They thought that the questionnaires were CCBT’.
7	“I found it extremely tiring. You notice that you are not yet over certain things. That there are a lot of things that annoy you unconsciously and annoy you because you haven't done anything with it”. (CCBT01, NON)	‘Research aspects’	‘But most of the time, the impact emerged rather through the experiences participants expressed regarding the questionnaire and the screening. Screening aspects were often experienced as consciousness-raising or confronting with the depression symptoms’.
7	“When you fill in the questions you notice at a certain time that you aren't on the bottom anymore (…) and that helps you at a certain moment to notice that you are climbing out of it”. (COMBI06, COM) “Then you think that they are all the same questions. Apart from the fact that I don't really think about suicide anymore, it is really the same. (…) If I see that it doesn't really make any difference? Not very motivating”. (CCBT01, NON)	‘Research aspects’	‘The monthly questionnaires were experienced as a reflection on the symptoms. This reflection could work both positively or negatively on the participant's feelings’.
7	“As far as I'm concerned they can higher the frequency of the monthly questionnaires. To rub your face once more in the research (…) It would help me to follow the lessons more regularly” (COMBI01, NON)	‘Research aspects’	‘And for some, monthly questionnaires or reminder mails were experienced as helpful towards treatment adherence’.
7		‘Research aspects’	‘The impact of research aspects was identified through interviews with both completers and non-completers. A difference among both groups was that two of the NOS non-completers confused the CCBT course with the Internet questionnaires’.
7		‘Main results’ ‘The interviews pointed out that barriers and motivators experienced within CCBT were related to the course content and to contextual social, computer, and research aspects. The main barriers included: experiencing a lack of	

		identification with and applicability of CCBT-CYL, lack of support to adhere to the program or to gain deeper understanding, and inadequate computer/Internet skills, equipment, or location. However, a positive experience with the CCBT course content and reduction of depression were experienced as motivators to adhere to treatment. The opportunity to do the therapy at your own time, pace and place was also experienced positively by some interviewees. Adding support to CCBT was suggested as an improvement towards adherence and the course content'.	
7		'Research aspects had an unintended impact: research activities were often experienced as consciousness-raising or as stimulating to start or adhere to CCBT or the research. Confusion with the Internet questionnaires resulted in no uptake of CCBT'.	
8		'Working model theory'	'The analysis generated a working model theory consisting of two core categories containing groups of underlying concepts, these concepts emerged as particularly relevant for the participants' decision to non-adhere. The theory indicates that the two core categories needs to be compatible, the experience of non-adherence to Internet delivered therapy can be described as an incompatible relationship between any of the underlying concepts'
8	"…as a student you read so much already. I felt like I couldn't muster more energy or more time to spend by the computer and to read 10 or20 more pages and also answer questions. It felt as if you were inclined to have a very structured life to handle that" (Informant 4).	'Extensive text content of the modules, fixed treatment arrangement and personal life factors'	'The participants' statements regarding non-adhering showed an incompatible relationship between the length of the weekly text modules and factors or conditions in the personal life of the participants, i.e. how well the effort required could be fitted into the daily life of the participants. The content of the treatment was perceived as a tiresome burden because of the length of the text modules and the time consuming effort to complete them in parallel with personal life circumstances'.
8	"…this treatment could have suited me if it would have been more flexible. The fixed format with one week per module, it feels as if you are so easily getting behind schedule" (Informant 1).	'Extensive text content of the modules, fixed treatment arrangement and personal life factors'	'The fixed format consisting of one module each week being sent to the participants was also perceived as inflexible for some participants because of their personal life'.
8		'Extensive text content of the modules, fixed treatment arrangement and personal life factors'	'Some participants referred to the fixed study design as the immediate cause of their non-adherence. One aspect of this was participants' need for time to let the new knowledge sink in between reading parts of the text modules. Requests were made for a more flexible program in terms of time restraints'.

8	“I thought that it was too much to read, and I cannot read anything at all that I need to remember or learn. It goes in here and out there (pointing at the ears)” (Informant 6).	‘High demands on levels of concentration, reading- and writing skills and individual capabilities’	This concept relates to content complexity. The content of the treatment modules was perceived as difficult to understand and process by individuals who considered themselves as having attention problems or limited reading and writing skills’ ‘One critique was that information was difficult to understand because the content was perceived as complex and abstract. In some cases the participants felt unintelligent for their inability to understand’
8	“I did not cope with the exercises. I did them at the start but it gradually became more difficult to complete them (…) particularly the breathing exercises, I got a bit dizzy and it increased my feelings of anxiety” (Informant 3).	‘Side effects and personal psychological vulnerabilities’	‘Some participants viewed the ICBT as a trigger of anxiety symptoms. Other participants felt stressed by the content of the treatment program’. ‘The stress level caused by aspects of the treatment seemed to enhance or trigger participants' existing or prior psychiatric symptoms. This caused some participants to avoid the treatment and its exercises’
8	“I would have liked to have more of a personal contact, it became a little distant everything, to do this on the Internet, because it is so heavy stuff, it's nice to meet a real person when you're working with heavy things like this” (Informant 7).	‘No face to face contact during treatment and perceived need for face to face meetings’	‘Some participants perceived that the therapists did not really care about their personal issues. The therapists were sometimes considered only to have the task of checking that the participants read the text modules and completed their exercises. Some participants told us that they realized that they sought different aspects of having a face to face contact after they started the ICBT. Some participants felt a desire to share their problems in a face to face manner, to get support and being motivated by someone sitting in front of them. Some described a need for a face to face contact when sharing difficult issues such as anxiety and depression’
8		‘No face to face contact during treatment and perceived need for face to face meetings’	‘Some participants changed to other treatment formats after terminating the Internet delivered therapy. Onparticipant explained that she had never prioritized her own personal development and that an individual therapy consisting of face to face meetings was needed to get away from home and focus on the therapy’
8	“I had no idea at all really about what the treatment would be like; I was only interested in doing anything that might help me…” (Informant 2).	‘Limited information before starting the treatment and insufficient awareness or capability to grasp information about the treatment’	‘Before the treatment started the participants received written information about the treatment. They were also encouraged to contact the staff for additional information if needed. The concept “insufficient awareness of the treatment” is based on statements from participants explaining they were offered and recommended to test a treatment but without getting or trying to find sufficient information about it’ ‘Participants explained that they were grateful for being offered the treatment, but not all of them seemed to be fully aware of the outline or the extent of the treatment’.

8		'Limited information before starting the treatment and insufficient awareness or capability to grasp information about the treatment'	Some participants did not remember what kind of information they had received and others had just entered the program out of curiosity. Insufficient awareness of content and outline of the treatment appeared to be an aspect that influenced participants' decision to terminate the treatment'
8		'Working model theory'	'Non-adherence emerged as a complex process made up of two core categories: Perception of the treatment and Patients' situation. The two core categories in turn were influenced by each other, the working model theory, grounded in interview data, visualize and highlight aspects of this complex process. The working model theory can be visualized as two cogwheels, where the underlying categories represent the cogs'
8		Working model theory'	Five incompatible concepts describing the Perception of the treatment and Patients' situation emerged during the research process. It is important to note that an aspect of the treatment only caused problems if certain characteristics of the patient was present and vice versa. For instance the text modules were not necessarily always perceived as difficult, but it turned out to be so if the patients experienced themselves as having a lowered reading or writing capability. These different conditions and characteristics, presented in interplaying pairs, seem to play a role in non-adherence to Internet-delivered therapy.
9	''. . . it was just an information session and that's kind of all I think that you need.'' (Information, 43 yrs, - 12.73%)	'Recruitment and appeal of recruitment materials	'When asked what they found appealing about the SHED-IT recruitment materials, respondents identified the perception that it would be non-intrusive, flexible, and compatible with a busy lifestyle in that it did not require extensive time commitments'.
9	''Well I've been thinking about losing weight for a bit and needed a kick start, but initially I think I saw a beer glass on the advert so I booked straight away" (Information, 29 yrs – 13.81%)	'Recruitment and appeal of recruitment materials'	'The use of comical language in the recruitment materials and portrayal of a beer glass on the recruitment flyer were consistently reported as having made the program appear attractive and may have contributed to the effective communication of the nature of the SHED-IT program'
9	''it's the opposite to those sorts of crash diets. Like they impose on you what you're going to eat, I was thinking oh gee, this sounds really good.'' (Internet, 35 yrs, - 14.7%)	'Recruitment and appeal of recruitment materials'	'The recruitment materials led the respondents to form a perception that the SHED-IT program would facilitate achievable, sustainable change. They described this as a contrast to weight loss programs they had experienced before'

9	‘‘SHED-IT said you can have your beer and lose weight too.’’ (Internet, 35 yrs, − 14.7%)	‘Recruitment and appeal of recruitment materials’	‘Effective communication of the SHED-IT approach, which did not advocate a strict eating plan or being overly regimented, was particularly appealing to those who had attempted previous weight loss programs. In particular, the idea that they could still enjoy ‘treats’, including beer, was very appealing’
9	‘‘So the real blokey thing about it I think when we all got together as men it is easier to have those blokey sorts of jokes and stuff, carry on a bit like that without women being there.’’ (Internet, 35 yrs – 14.7%) ‘‘I think it was the fact that it was specifically targeted at a male only.’’ (Information, 21 yrs, − 16%) ‘‘It didn’t matter to me that it was men only, the program just sounded doable.’’ (Internet, 19 yrs, − 8.2%)	‘Recruitment and appeal of recruitment materials’	‘The idea, clearly stated on the recruitment materials, that SHED-IT was a program specifically for men appealed to some but not all of those who responded to this question’.
9	‘‘I had a health scare recently. . . so I was more inclined to act. I’m not getting any younger.’’ (Internet, 44 yrs, − 9.5%)	‘Recruitment and appeal of recruitment materials’ ‘Motivation’	‘Health and physical appearance featured in respondents’ description of their motivation to respond to the SHED-IT recruitment materials. A number of men reported that a recent confrontation with a weight-related health issue (e.g. high blood pressure) had provided the impetus they needed to respond to recruitment publicity’
9	‘‘Saw myself in the mirror [laughter] from a different angle and went oh that’s a very large stomach I’ve got there. . . and I thought ****, I look like my old man used to [laughter].” (Internet, 50 yrs, − 8.72%)	‘Recruitment and appeal of recruitment materials’ ‘Motivation’	‘Along with a desire to obtain health-related benefits from weight loss, respondents described a desire to ‘regain’ a better appearance’. ‘In general, we observed more young men responding to advertising out of a desire to improved self-image’.
9	‘‘but the energy-in, energy-out equation was really simple and that was the most powerful thing for me” (Information, 43 yrs – 12.73%)	‘Value of the information session and weight loss handbook’	‘The initial information session was well received by participants from both groups. All the respondents who had participated in the Information Only group commented on the value of the information session. In particular, this group of respondents appreciated the clarity and simplicity of the ‘energy in/energy out’ message’.
9	‘‘the first off information session was really enjoyable, it really got the point across and got motivation high up there and made me really want to get involved with it” (Internet, 19 yrs, − 8.2%)	‘Value of the information session and weight loss handbook’	The examples, anecdotes and humour that were used to deliver the key messages were also appreciated. Although fewer of those respondents who had participated in the SHED-IT Internet Group commented directly on the information session (possibly because the use of the study website was the more salient part of their experience of SHEDIT), those who did also described it as informative, relevant and motivating’
9	‘‘I used it early on. . . so that I knew what I was doing was right and sort of stuck closely to it. Once I sortof got my head around keeping an eye on kilojoules and all that sort of thing, I didn’t use it as much.’’ (Information, 21 yrs, − 16%)	‘Value of the information session and	‘Although theWeight Loss Handbook was less popular than the information session, respondents from both groups reported that they had found it useful’

	‘‘it just spelled everything out in black and white, there’s even a maths equation. . . it’s not wishy washy kind of support stuff, it’s just fact and you either accept it or you don’t. . . every couple of weeks I’ll go and review it.’’ (Internet, 19 yrs, − 8.2%)	weight loss handbook’	
9		‘Value of the information session and weight loss handbook’	‘However, some respondents from the Information Only group commented that the handbook lacked information or resources regarding the kilojoule contents of specific foods. This information was provided to participants in the SHED-IT Internet Group via the study website so it was not surprising that they did not make the same observation. The majority of participants from the SHED-IT Internet Group reported that they found the website more useful than the handbook on a continuing basis’
9		‘Program experiences’ ‘Previous weight loss’	Many contrasted their prior experiences with their experience of SHED-IT, noting that the latter experience had enabled them to identify barriers to weight loss. Barriers identified by the respondents included a lack of knowledge about the relationship between energy balance and weight change and a consequent lack of insight into the reasons for their failure to lose weight or keep it off. Other barriers identified by the respondents were a lack of self discipline, tendency to blame external factors for weight gain (which may be a response to a knowledge gap), and a lack of time to exercise’
9		‘Program experiences’ ‘Overall perceptions/levels of satisfaction’	‘Although, several respondents indicated that they would have benefited from more face-to-face contact, it is important to note that most of these men lost weight on the trial. This result suggests that, in contrast programs that have achieved success amongst women [24], a flexible, non-intrusive program that does not require extensive face-to-face commitments such as SHED-IT can facilitate clinically important weight loss in men’
9	‘‘The site was really handy. It was really good to start to learn what you ate and what the kilojoule values were rather than having to constantly sort of have a black book …’’ (Internet, 51 yrs, − 0.94%)	‘Program experiences’ ‘The online program’	‘Most respondents found the Calorie King website an invaluable part of the program, especially during the initial month. Respondents commented that the Calorie King website improved their understandings of the effects of diet and exercise on weight loss because they could gain feedback from the website that was instant and visual. This medium appeared to eclipse the role of the handbook, particularly in educating about foods and for self-monitoring’
9	‘‘I found calculating kJ input everyday was time consuming.’’ (Internet, 21 yrs, − 1.37%)	‘Program experiences’ ‘The online program’	‘However, the use of the website was not viewed as unproblematic. While daily entry of food intake was viewed by most men interviewed as a necessary discipline, they initially found it time-consuming’

9	‘‘it took a bit of time to learn the website, but eventually you get in the knack of it and it just becomes natural. . . and a lot of the time you eat similar meals, you just pull them off the favourites.’’ (Internet, 35, − 14.7%)	‘Program experiences’ ‘The online program’	‘As a result, compliance with the self-monitoring of food intake varied. However, many commented that it became easier with time as repeat meals/foods could easily be inserted’
9	‘‘I found the food diary difficult to use. It presumed that I lived on fast food and supermarket products. May need to be more tailored.’’ (Internet, 48 yrs, - 1.09%)	‘Program experiences’ ‘The online program’	‘One of the most frequent complaints about the Calorie King website was that it catered poorly for those who ate meals which weren’t standard or pre-prepared’
9	‘‘if you had an application that you could download and that would be run at the speed of your own computer that would help. . . but that was a great facility but it was a challenge to use.’’ (Internet, 51 yrs, - 0.83%)	‘Program experiences’ ‘The online program’	‘A few participants had problems getting to a computer on all days or found Internet connection speed unsatisfactory’
9		‘Program experiences’ ‘The online program’	‘The email feedback was reported to be helpful for identifying potential problems by nearly half the men; the main complaint about the feedback was that it was too generic. The forum facility of the website was not utilized by men: most commented that they were not interested in engaging in discussion with other men about their weight loss experience’
9	‘‘Meeting with other people in addition to the website would be useful to keep up motivation. I find self-motivation hard without face-to-face support.’’ (Internet, 48 yrs, − 1.09%) ‘‘I would have liked every second week or once a month because there were lots of messages about weight loss coming in from all different sources. . . you definitely needed some support with it” (Information, 43 yrs, − 12.73%)	‘Suggestions for improvement’	‘One of the most common suggestions for improvements related to increased face-to-face contact in the form of small group meetings or lectures. It was thought that this would give a more ‘human feel’ to the project, facilitate peer support, and help maintain focus and motivation’
9		‘Suggestions for improvement’	‘One respondent from the SHED-IT Internet Group suggested that we spend more time explaining how to use the website in future. It was apparent that men who were more successful perceived fewer barriers to adopting behaviours that promote weight loss and were more satisfied with the program’
10	“The biggest problem I have with my bipolar disorder is consistency; when I’m down I can’t even brush my teeth or get up in the morning. So doing an education program with workbooks was beyond me”. [Female, 18-29 years, BEP group] “A very short while after doing the program I fell into another episode, a depressive episode, and pretty much stopped doing everything, the program included”. [Male, 18-29 years, BEP+IS group]	‘Discontinuation Due to the Illness Itself’	‘Many interviewees reported that, while they were able to complete the modules and workbooks when well, being in an acute phase of the illness interfered with their ability to participate in the program. Those in a depressive phase of the illness found the lack of energy and motivation common to depression a significant hurdle to completing the program’

10	“My highs interrupt my ability to see things through, and I get caught up in my highs”. [Female, 30-39 years, Control group] “I often go walking when having highs because I have to keep moving, so I didn’t want to sit at a computer”. [Male, 40-49 years, BEP+IS group]	‘Discontinuation Due to the Illness Itself’	‘Participants who experienced episodes of mania during the study discussed how they became distracted by their manic symptoms and were unable to complete the online modules’. ‘ Thus, the nature of the illness itself made it difficult for some participants to continue their involvement in the program. This was the most common theme in terms of reasons for discontinuation’.
10	“I found it quite confronting, and reading the information made me feel uncomfortable, thinking that these issues related to me—I preferred the ostrich approach”. [Male, 40-49 years, BEP group] “[I] found it difficult to sit down and do those things. I got into an anxiety and went off to do other things. I didn’t really want to sit down and think about it”. [Female, 50-59 years, BEP+IS group]	‘Did Not Want to Think About Illness’	‘Several participants reported that they found receiving weekly information about their disorder confronting or overwhelming. Many said they did not want to think about their illness and instead wanted to put it out of their minds’
10	“I wasn’t ready to accept the illness. At that stage after diagnosis I wasn’t willing to change my life according to the program”. [Male, 18-29 years, control group]	‘Did Not Want to Think About Illness’	‘Some participants reported that they were not ready to accept their diagnosis of bipolar disorder and so didn’t relate to the program’s information and practical advice. As the wider study was investigating the utility of the program in those newly diagnosed, some expressed the opinion that they may have enrolled in the program too soon after their diagnosis’.
10	“The information in the modules was too general and too limited”. [Male, 18-29 years, BEP group]	‘The Online Program’	‘The online bipolar psycho-education program itself was identified as a reason for discontinuation by a few of the participants who received that intervention. Most commonly, the information was regarded as too basic or simplistic, and those participants reported that they were already aware of a lot of the content before commencing the program’.
10	“I wanted something more about me specifically, as opposed to talking about general issues”. [Male, 40-49 years, BEP group]	‘The Online Program’	‘Other participants said they were dissatisfied with the program because they expected personally tailored information or feedback, which was beyond the scope of the current program’ ‘There were also comments around the layout of the programs and the amount of personal information participants were required to disclose, but these were raised by single participants and therefore, represented a minority opinion’

10	'I was so self-absorbed at the time that I was only interested in the information [rather than in returning workbooks]". [Male, 50-59 years, BEP+IS group]	'Feeling Well'	'Some participants reported ceasing to utilize the program after they gained what they wanted from it or once their mood had stabilized. Other participants indicated that they worked through the modules but did not complete the associated workbooks'
10	"Things really improved for me…I just felt really good and didn't really feel like I had that much to offer in regard to finding out more about it". [Female, 30-39 years, control group]	'Feeling Well'	'It was also reported by some participants that they no longer felt the need to participate in the program once their mood had stabilized and they were feeling well. This response was associated with another issue raised in the interviews, whereby a number of participants stated that they would reaccess the programs' information after the study was completed if/when they were feeling depressed'.
10	"I didn't have the time, and with everything else, it wasn't a priority". [Female, 18-29 years, control group]	'Time Pressures and Competing Demands'	'Time-related factors such as being too busy or life being too hectic were also given as reasons for discontinuation. Such reasons included being busy at work, moving house after signing up for the program, and having more important focuses'
10	"I have issues with procrastination. I suppose laziness is the only reason". [Female, 18-29 years, control group]	'Time Pressures and Competing Demands'	'However, lack of motivation was also a commonly mentioned reason, such as being forgetful or lazy about completing the program'. 'In these cases, the motivational problems were cited as personality characteristics, as distinct from symptoms of the bipolar disorder'.
11	"Through my studies [health-related] I have heard that CBT was very good for treating it, so I had already heard that it was a good method to get in to." (ID: 5)	'Reasons for choosing this form of treatment'	'Participants who had previous experience of treatment (mainly counselling) felt that it had not worked as they had expected and wanted to try a different approach. Some health-related students had heard positive things about CBT. Most of the participants who had not received previous treatment were attracted to the availability, flexibility and privacy of iCBT. Some participants thought that their ED was not severe enough to justify seeking

			medical help and they thought that iCBT would be more appropriate for them'.
11	"You know that a computer isn't gonna judge you and a computer isn't gonna go and talk about your problems with somebody else." (ID: 4)	'Experiences of treatment' 'Confidentiality/privacy'	'The importance of confidentiality was acknowledged by all participants. Some participants thought that receiving treatment through a computer was secure in terms of privacy, confidentiality and anonymity'.
11	"I felt a bit self conscious because I had to use it in the library computer room so sometimes the big headings of Bulimia! And Fighting Bulimia! […] I kind of not necessarily want everyone else to know what I'm doing." (ID: 5)	'Experiences of treatment' 'Confidentiality/privacy'	'Most participants expressed concern regarding accessing iCBT in a public place for fear of others finding out about their ED. These concerns were often related to the heading 'Overcoming Bulimia' situated on the screen of the programme. As a result some participants had to be extremely careful when they accessed iCBT using a public computer. Others said that if they had not had a computer at home they would have not used iCBT at all'.
11	"You can do it whenever, any day. Like you can just to do it anywhere in time and that was good." (ID: 6)	'Experiences of treatment' 'Flexibility'	'Many interviewees had busy schedules associated with their university courses. The flexibility that iCBT offered in terms of time, place of access and having both the computer programme and the workbooks covering the main parts of the sessions was seen as an advantage for all participants'.

11	"…especially to do it at home, you come back, it's tiring, then 'you'll do it tomorrow' and then tomorrow comes and then 'I'll do it this weekend because I will understand better' and then during the weekend 'I'll go to the park' […] it's very easy if you don't have someone that says 'you have to do it right now'." (ID: 9)	'Experiences of treatment' 'Flexibility'	'Nevertheless, some interviewees noticed that the flexibility meant that self-discipline and motivation were required to complete regular sessions. A sense that the programme was "lower in the priority list" (ID: 9) resulted in postponing the sessions in some participants'.
11	"It's very easy to use so that was good, the whole programme itself." (ID: 1)	'Experiences of treatment' 'Ease of use'	'All participants said they found iCBT easy to use and to understand'
11	"I don't think I have the self motivation to do it whereas […] it's just a computer but you know that at the end of the line there is people who were watching your responses and your progress and that's encouraging." (ID: 4) "Without the email support maybe it would have been dry, the email support makes it more real." (ID: 9)	'Experiences of treatment' 'Feeling supported - including help with motivation'	'Interviewees expressed the importance of feeling supported by email during the treatment. Being aware that there was someone they could contact if they needed help played a crucial role, even for people that preferred not to use the support. Some participants found that their motivation for doing the sessions was related to the sense of having someone giving them support. One participant found the whole experience of using iCBT, including the email support, impersonal'.
11	"Parts of it are relevant and parts of it are not but I mean […] that was fine, I think if you got in your head that this is a computer programme for everyone, you just get on with it." (ID: 5	'Experiences of treatment' 'Content of programme'	'For most participants the content of the programme felt appropriate. Some said that certain aspects were irrelevant to them, but there was a general understanding that the programme had to be suitable for a broad spectrum of people'
11	"Part of me felt like some of it was quite repetitive […] seems quite mechanically generated and it was just like a little bit tedious." (ID: 3)	'Experiences of treatment' 'Content of programme'	'Two participants said they found the programme repetitive at certain points'.
11		'Impact of treatment'	Overall, participants had a positive impression regarding the impact iCBT had on them. They had a sense that it contributed to giving them strategies to overcome their ED. The topic of impact of treatment fell into four categories'

11	"…I hoped I would completely resolve all my issues and that I would never make myself sick again but it is quite obvious that there is a lot more than that; definitely it was a step and I am getting there." (ID: 1)	'Impact of treatment' 'Expectations about outcome'	'Interviewees talked about their expectations of treatment outcome prior to starting iCBT. Some identified that their expectations were high and difficult to fulfill. Nonetheless, they had a sense that iCBT had placed them on the right track for getting better'.
11	"Even though I would say on the whole, the package didn't really shift me from anywhere, I have learned little sort of tools that would help me." (ID: 3)	'Impact of treatment' 'Tools for coping in the future'	'Two people did not feel that iCBT helped them much. However, they thought that parts of it provided them with useful tools'
11		'Comparison between iCBT and other forms of treatment'	'Interviewees discussed their previous experiences of treatment and many of them compared these with using iCBT. A few participants with no previous treatment experience talked about how they thought other treatments differed from iCBT. This theme was divided into three categories'
11	"I think that I can deal with it myself with such a thing like this programme […] Also I don't like to go to doctors. I feel like very hypochondriac […] I always think 'lets wait, lets wait'. […] I fear that the doctor can judge or say…'why you are coming here?" (ID: 8)	'Comparison between iCBT and other forms of treatment' 'General Practitioner (GP)'	'Some participants talked about how they felt about approaching their GP for help with their ED. Two participants said that they had seen their GP and had subsequently been referred to a specialist service. Several participants said they felt uncomfortable with seeing their GP and expressed concern at being labelled or not being taken seriously. Others did not feel that their problem was serious enough to discuss with their GP'

11	"…it took you through step by step… the computer can do much more than a book because a book […] can say take a pen and do this, and you go 'yeah, I'll do it later', and you just skip through whereas if it's on the computer you have to go step by step and then you can't move on until you've thought about it and done it so that, I think, was a lot more effective." (ID: 5)	'Comparison between iCBT and other forms of treatment' 'Other Forms of Self-help'	'Some interviewees discussed how iCBT comparedwith using a self-help book. The main highlighted difference was the structure of the sessions. For instance, in iCBT the patient has to complete the therapeutic exercises in order to continue with a session whereas in a book it is easy to postpone exercises and lose continuity. One participant mentioned the support associated with iCBT "which you don't get in a book." (ID: 9)
11		'Feedback'	'Interviewees gave suggestions for how the treatment package could be improved. Some focused on technical aspects of the programme such as the timeout function and others suggested having a broader range of examples so that more people could identify with them. Participants were asked if they would suggest using this form of treatment to others suffering with similar difficulties and all answered in the affirmative. Some participants considered iCBT particularly appropriate for people with privacy and confidentiality concerns. Two categories related to how treatment could be improved:
11	"I think it's probably better to talk rather than to email […] to organize like every Wednesday evening you get a 5, 10 minutes support call […] it would make you feel…'By that day I need to do this work and think about it'" (ID: 9)	'Feedback' 'Other methods of support'	'Some participants suggested that other methods of support should be added to the programme such as face-to-face contact or telephone calls to improve motivation and to make the experience more personal'.
11		Feedback' 'Other methods of support'	'Another common suggestion was to have email or telephone contact with a therapist after the end of treatment'.

12	“To gain a bit more knowledge on my body and how I can better manage my health” “Guidance to make sure that I was doing the right thing as far as exercising a bit more and eating properly” “To record what I was doing and then talk to your consultant and actually see ways of improving either fitness or health” “A solution to weight loss” “Documenting what I was doing/motivation to continue”	‘Users’ Desired Outcomes’	‘Overall, the outcomes people anticipated from engaging in the program largely reflected their motives for participating. Most were expecting to receive guidance and counseling from the project team to help them enhance their diet and participation in physical activity. For some, this guidance and advice were expected to be specific, such as a prescriptive diet plan to follow or support for their particular sport and activities. For others, the type of advice and support expected were described more generally, such as “tips and suggestions” to live a healthier life. Strategies to help participants stay disciplined and to take action were also expected, such as the provision of materials to record diet and physical activity behaviors. A few participants also expressed that they expected to improve their lifestyle behaviors and/or weight status as a result of participating in the study’.
12	“The program made me focus more on my physical activity and diet after actually seeing the data” “Overall I think it’s great” “I got a little bit out of it. It actually encouraged me to start walking a lot more. In my particular job I'm out of town a lot so there are not a lot of regular exercise programs I can actually sign up for. Whereas, I ended up buying myself a pedometer and I have been walking” “It was easy to read” “I really liked seeing the visual record of my progress” “I like the idea of being able to use the calendar to record progress” “I’m not high tech minded but I could still use it”	‘Users’ Positive Emotions’	‘Participants from both intervention groups liked that the information they were provided with was easy to read, use, and had an appropriate tone (ie, not derogatory). Participants from both groups liked that the materials could be used as a benchmark and reference tool when thinking about their own health. Participants who received the IT-based intervention liked the ability to record and view a visual summary of their progress’

12	"I wanted to be told what the outcome would be if I did specific amounts of activity" "I wanted to count cross training exercise but didn't think that it was really designed for this "It wasn't prescriptive enough" "It didn't give me the outcome I was looking for" "I think I may have let the system down by not following through as much as I should. Initially I was recording my activity weekly but it was a routine that didn't change much so I sort of fell off on the updating sort of sense" "I think I would have done better with the Web-based stuff, more motivation that way" [Print]	'Users' Negative Emotions'	'Some participants who received the printed information found that the booklet was too long and that some of the text was long-winded. Furthermore, there were a few participants who expressed disappointment with the level of interaction and feedback provided and felt they would have done better with the "Web-based stuff." Among those who received the IT-based intervention, some participants expressed that they would have liked functional aspects of the website to be improved, such as the ability to enter and keep track of different types of activities, the ability to enlarge text, and the progress calendar. Furthermore, a few participants raised sustaining self-monitoring as an issue, especially when personal physical activity routines did not change (ie, self-monitoring via the website was considered less useful) or when in out-of-service areas (ie, when self-monitoring could not be done immediately and conveniently due to a lack of Internet connection). A few participants also expressed disappointment with the intervention content, with some participants reporting that the physical activity and nutrition content was not prescriptive enough, and others reporting that they would have liked to have received more personalized information and feedback about how their changes in health behavior were likely to impact on their health'.
12	"I would have liked reminder emails with link to direct entry without log-in" "Capacity to enter data when no reception is available and then sync when phone has reception" "Post challenge-report that detailed progress over time period of the entire challenge" "I would have liked to have been able to measure total physical activity across different types of activity I'd have liked a calorie conversion option on my progress chart" "I would have liked to have been able to set my own challenge metrics and timeframes" "I'd like to be able to pause my challenge or reset for when I am sick or away" "I think one method to address some of my habitual failings, is if it was on either a mobile phone app or an Internet version. Cause I'm more of a technology orientated person than I am paper orientated. I probably would have addressed and achieved more of the challenges purely because, you know, if it's on the phone or on my computer it's more ah, it's more interesting and more accessible for me" [Print]	'Attributes Desired by Users'	'Suggestions on how to improve the print-based intervention included providing more tips and helpful hints that are based on the experiences of their peers, and transferring the intervention onto a Web or mobile phone platform to make it more interesting and accessible. Suggestions on how to improve the IT-based intervention were more varied and included both suggestions on how to improve the website usability and for improving intervention content. Specific functional components requested by participants included a facility to report IT-based issues, reminder emails offering direct links to participant profiles (without logging in), the capacity to use the mobile app when there is no Internet connection, and to sync the data with the website at a later date. Suggestions on how to improve intervention content included providing links to nutrition and physical activity information on a separate page of the website, allowing participants to set their own challenge metrics, providing more detailed and iterative feedback, and providing access to other useful tools, such as a calorie conversion calculator. Some of these suggestions, namely

			a facility to report IT-based issues and links providing further lifestyle information, were actually included on the website'.
13		'Themes'	'The themes which emerged were mixed between themes related to research (altruism), the intervention itself (using the tool as a substitute for online help, continuing benefit from the intervention) and both (trust in brand, salience, language of the tool)'.
13	"It was password protected and I trusted the fact it was by the NHS and it was part of a study so those were the kind of things that made it, I felt secure in that sense. I just felt because of the source of it. If I had found it in a different way, I probably wouldn't have felt the same about it. Because it had come through the NHS and I knew it was part of the study and everything seemed very well run I didn't worry about that at all ". [interviewee 14, a 35– 49 year old woman]	'Trust in the brand'	'The most prominent theme that emerged from the interviews was the importance of a trusted (offline) brand to participants during enrolment. The branding took the form of the logos of the NHS (UK National Health Service) and the lead University conducting the research. The value of this branding was in providing legitimacy to an online site and giving participants both trust in the content and that any information they provided would be used securely'. 'This worth of the branding translated both to participants choosing to take part in the trial, enrol and also following enrolment, during the trial, participants were asked to upload details of their emotional states. When asked about the reasons they felt secure in providing this information, the most common response (8 interviewees) related to the branding of the tool and trial by the NHS or the academic institution undertaking the research.
13	"I mean obviously with it being from a University, that's always useful, rather than, shall I call it a private organisation, you know, it didn't feel as if anybody was trying to make any money out of it".[interviewee 18, a 55–59 year old woman]		'Three interviewees provided reasons why this made them feel secure'

13	"I suppose because the NHS has you know, my medical records and they assure me that they are confidential because I felt comfortable with that. Also I knew it was the University and they were doing some research, so I knew that they would use possibly use my information but it would be used in the right way" [Interviewee 11, a 55– 59 year old woman]		'The trust that was engendered by the brand had a dual role in ensuring participants both that there were no alternate motives by the researchers (particularly financial), but also that the organisations would have the facilities and ability to store their data confidentially'.
13	" in participating in research which might help others in the future" (interviewee 4, a 40– 45 year old woman)	'Motivations to enrol' 'Altruism'	'Participant altruism was a frequently cited motivator to enrol in the trial. 10 interviewees discussed altruistic reasons and were interested when asked about their feelings about participating in the trial'
13	"because it was Internet-based it is easier to put down and think about it and stuff that I may not wanted to have talk about, I am not a person who would go for counselling or anything, I'm just not that kind of person but I'm quite happy to put some stuff into the internet and let it tell me what I'm thinking if that makes sense, so it deals with me personally". (interviewee 14, a 35– 39 year old woman).	'Motivations to enrol' 'Using the online tool as a substitution for offline help'	The second motivation across the interviews was related to the way an automated internet intervention provided the opportunity to access some level of help, without interacting with a health professional. 10 participants, although acknowledging that they needed some help to improve their sense of wellbeing, described not wanting to attend a medical appointment, either feeling that their problems did not warrant professional attention, or that they wanted a less intrusive method of seeking help'
13	"the right place at the right time really" (interviewee 10, a 40– 44 year old woman).	'Motivations to enrol' 'Salience to current health condition'	Despite the trial being advertised a s being concerned with the improvement of mental wellbeing, and not with treating mental health problems, a major motivator was participants' current low mood. The promotion of mental wellbeing had more salience for those whose wellbeing was not good. Most participants who had entered the PsyWell study were experiencing or had experienced – recently or in the past - periods of low mood or difficulty coping, and were looking to either help themselves through this period (n = 14), or understand the periods of low mood in the past (n = 2). These periods of low mood had a wide range of aetiology, including bereavement, physical illness, mental illness such as anxiety or depression, stressful periods at work or unemployment.

			Some participants conveyed the sense that the trial invite appeared at …'
13	"After his (husband's) death I was, well in a state of great grief, so browsing the net, I came across your site. I don 't know whether it was through looking at sites to do with bereavement or whether it was a second phase of my sort of emotional set up, and I started to look, once I had looked at everything to do with bereavement I then moved on to positive thinking, trying to access something that might actually help, and I came across your research project and I thought it was based on CBT which I knew a little about, not much but a little and I wondered ir that might help me, and that 's why I accessed it and that's why I decided to go through with it to see if it would help ". (Interviewee 4, a 60– 64 year old woman).	'Motivations to enrol' 'Salience to current health condition'	'The theme of participants having volunteered for the trial as a result of a difficult period Interviewee 4, a 60– 64 year old woman who had recently experienced a bereavement of her husband'
13	" sort of after a couple of weeks when the reminder came I thought oh no, not this again, you know, it wasn' t holding my attention and I didn't want to log on" (interviewee 11).	'Continuing: feeling benefit from the invervention'	'In looking for interviews which deviated from the above, we identified two participants who described no benefit from the intervention'
13	"thought it was patronizing … I don't appreciate somebody telling me that I have got to think differently". (Interviewee 20) "Just so that you would have somebody who completed the trial". (Interviewee 20)	'Continuing: feeling benefit from the intervention'	'One described it as repetitive and boring .. 'I continued with the trial for the purposes of the research'

13	"When it was talking about depression and how you saw things, they would ask you what you felt about something, how did you perceive this certain situation and then they'd say kind of, and then they'd talk about students at college or going out with your friends, where I'm sort of late fifties, so that to me, I couldn't quite relate to it. I understood what they were talking about and understood what they were trying to get out, how you can see different situations in a different light depending on your mood, but the situations they were putting me in were for a younger person ". (interviewee 13 (age group 55– 59) "Some of the questions were over long and they were definitely geared to American college students which I found very irritating". (Interviewee 9, a 50 –59 year old woman)	'Negative experience: language of the tool'	'The only consistent negative theme arising from participants' experience was that the language of the internet tool was not tailored towards them as individuals. Interviewees described a negative perception that the tool was designed for a group other than themselves. Seven interviewees described the language as aimed at a younger age group, and five interviewees felt the language was aimed at an American audience'
14	"simple, concise and clear" (P2)	'Website Format Is Acceptable'	'All participants reported that the website was well designed, easy to understand, and written in simple, non-specialist language'
14	"I found it time consuming, you know, to log in, and I'm not one of those on the computer all day. I found it a bit time consuming and sometimes I must admit I thought I can't be bothered to do this today and I didn't but as I said, things had started to improve quite early on with the early part of the sessions". [P13]	'Website Format Is Acceptable'	'However, all participants reported that the website took time to complete, and several mentioned that a user had to be self-motivated to work through the material'
14		'Engagement With the Regul8 Website' 'Overview'	'Analysis revealed three types of engagement with the Regul8 website that emerged from participants' discussions: (1) limited or no engagement, (2) engagement with content on how practical lifestyle changes may affect IBS, and (3) engagement with content on how emotions and thoughts may affect IBS (as well as practical lifestyle changes)'

		'Engagement With the Regul8 Website' 'Limited or No Engagement With the Regul8 Website'	'Ten participants reported either that they did not use the website at all or that they did not find it relevant and did not see it as a way to help them manage their IBS. Despite this, most participants in this group were recorded as completing 4 or more website sessions and therefore being compliant. As participants were able to click through website pages and select different sessions easily, it is possible that these participants browsed the majority of
14	"I don't think I have much time, I think if I had time and I did some of the sort of more relaxation techniques at the time that the website was talking about them, then that would help, but to do some of these techniques I feel I need that, you know, almost one-on-one, you know, I think things like yoga could almost help it but I couldn't just pick up a book and learn yoga, you know, it's that kind of training I would love to do but um, time unfortunately doesn't permit it and so I sort of put up with the symptoms, which is why I hoped it would be a wonder drug". [P5]	'Engagement With the Regul8 Website' 'Limited or no engagement with the Regul8 Website'	'We identified three common obstacles that appeared to deter participants from engaging with the website. The first was an ongoing search for a Participants who were searching for a "magic pill" to "cure" their IBS resisted the idea that they might be able to (or would even want to) manage their illness through changing their thoughts and/or behaviors. They were hoping for a treatment that would enable them to "by and large lead a normal life" (P25) without disrupting their daily lives or taking time away from preferred or prioritized activities such as work and leisure'.
14		'Engagement With the Regul8 Website' 'Limited or no engagement with the Regul8 Website'	'Consequences of prioritizing a medical solution to IBS included seeing the website as unimportant within the trial and not seeing the website as a form of management in its own right. Indeed, 2 participants reported having made a conscious choice to abandon the website because they had stopped taking the trial medications'

14	“it wasn’t extensive information, it was quite limited, I think I expected more” (P1).	‘Engagement With the Regul8 Website’ ‘Limited or no engagement with Regul8 Website’	‘Participants’ preconceptions about the impersonal nature of websites constituted a second obstacle to engagement. Some participants saw websites as a means to provide factual information and were expecting the website to provide extensive, authoritative, and new facts about IBS and its management. They were disappointed that the website did not meet their expectations’
14	“I just found the whole sort of process a little bit, um as I say a little bit sort of condescending, you know, to how a website, on an impersonal device like a computer, trying to give me a sort of counseling approach to managing the symptoms. [Interviewer: yes, yeah] so you know it was sort of, it was very impersonal [Interviewer: mm hmm] didn’t, didn’t gel with me at all.” [P5]	‘Engagement With the Regul8 Website’ ‘Limited or no engagement with the Regul8 Website’	‘the website was interactive and did not merely provide information but required participants to self-assess, write down their own goals, or keep a written record of any unhelpful thoughts. This was difficult for some participants who believed that websites are unsuitable for interventions that require exploration of one’s personal thoughts and feelings about IBS. Regardless of their views on the legitimacy of a psychological approach to IBS in general, these participants did not feel that a website was the appropriate means of delivering such an intervention’ ‘Interestingly the majority of the participants who felt this way were in the group who did not receive the nurse telephone session to support their progress with the website’
14	“Well the trial wasn’t too bad, the website was ok, I think I would have put more effort into it if, like I say, I was having the issues with serious symptoms at the time but like I said I wasn’t really, so [there is] less motivation to work your way through the pages of the website.” [P4]	‘Engagement With the Regul8 Website’ ‘Limited or no engagement with the Regul8 Website’ “the website is not right for me’	‘The third obstacle to engagement related to poor perceived fit between the website and the individual and can be summarized by the phrase, “the website is not right for me”. Sometimes this centered on the psychological elements of the website..’‘Poor perceived fit was also related to perceived symptom severity and existing levels of knowledge. When they felt the website was not right for them, participants politely suggested other groups for whom it might be more suitable, including patients with more or less severe symptoms (with participants usually recommending the website for people who had different symptoms from themselves) or newly diagnosed patients who were assumed not to have an understanding of IBS and self-management techniques’

14	"I thought [the website] might have some suggestions as to things you could do to help relieve it. Which was sort of implicit there somewhere, so that was quite good. I think it was probably reassuring in a way…that obviously the symptoms I'd had were very common and were similar to other people...'cause I hadn't really talked to anyone else about it". [P9]	'Engagement With the Regul8 Website' 'Limited or no engagement with Regul8 Website'	'Despite not engaging with the interactive parts of the website, some participants nevertheless found it reassuring to have their existing beliefs about IBS confirmed and took comfort from feeling that they were not alone in their experiences of IBS. The latter might be a particularly valuable feature of websites for conditions such as IBS that patients often find difficult to discuss in everyday life'
14	"[The nurse] made me feel perhaps better and realize that things perhaps had helped at the time that I hadn't realized if you get what I mean? But that was not to do with the drugs, it was more with the [website] advice that was given, I found that more helpful". [P12]	'Engagement With the Regul8 Website' 'Engagement With Content on Practical Lifestyle Changes'	'As well as engaging with the content of the website, participants also commented on how they favored the interactive format of the Web-based program, which encouraged them to keep records of their thoughts and behaviors, and the nurse telephone support session, when available, and how these helped them to engage with the information'
14		'Engagement With the Regul8 Website' 'Engagement With Content on Psychological Aspects'	'Several of the participants who had engaged with the psychological aspects mentioned how they had joined the trial because they were very eager to find something to help their IBS. Participants mentioned joining "out of desperation" because they had previously been "through hell" as a result of their IBS and because they felt they were "living on medication". One participant specifically stated that she had joined the trial because of the "cognitive therapy" that was offered as part of the website'.
14	"I think I got more out of it by having even the interim call with [nurse], during it, because um, the website can't cater for everything without it being over-complex and pages and pages of options". [P2]	'Engagement With Regul8 Website' 'Engagement With Content Psychological Aspects'	'As for group 2, this group also liked the nurse telephone support when it was available to them'
14	"[The website] explained [IBS] and it forced you to be quite open and honest probably more so than you would be in face to face conversation um, especially, um…you know it's not the most pleasant of topics to discuss". [P2]	'Engagement With Regul8 Website' 'Engagement With Content Psychological Aspects'	'Interestingly some felt that the website was a particularly good format for discussing a sensitive subject that some people may not want to talk about face-to-face'

14		'Engagement With the Regul8 Website' 'Engagement With Content Psychological Aspects'	'We explored differences between participants who had engaged with the content on the psychological aspects of IBS and those who had not engaged with it. The majority of participants who did not engage with the psychological components of the website had only limited engagement with the website overall and seemed to miss out on the information on the influence of thoughts and emotions on IBS symptoms because of their lack of interaction with the website'
15	A1: "how would you do a blood sample at home? I wouldn't trust myself to do it, I'd rather go somewhere and see healthcare professional to have it done. [prompt: swab?] A swab would be OK". (Male, 20-29, tabloid.)	'Willingness to consent to the online study'	'The majority of respondents (32/42, 76%) said they would be willing to give their consent to participate in the online genetics study. Although based on a small sample, younger respondents appeared less likely to participate (9/14) than older respondents (13/14). Reluctance from younger respondents was more likely to be related to the logistics of taking blood samples at home (they had mistakenly thought it required home based venipuncture), the time commitment of participation, and suspicions over the origins and credibility of the website'
15	B14: "My only concern would be the safety of information and what happens to the information when its finished with. If there's a change in organisation or someone [leading the study] in the future, will the information be secure? How safe is the DNA in the future? Is this government funded? Who owns the information?" (Female, 40-49, tabloid.) B1: "What will they do with it? Is it possible to test a sample 5 years from now? What kind of research are they going to use this for, any examples? I wouldn't want my DNA to help someone develop a 'keep you young' cream". (Female, 40-49, broadsheet.)	'Willingness to consent to the online study'	'The middle age group seemed more aware of the potential risks involved in participation, more concerned about DNA testing, security of the DNA samples, and sharing medical records. The middle age group were also more sceptical of the purpose to which their personal data and DNA would be put'
15	C8: "I'm interested in these diseases - my father had cancer, mother dementia, different diseases; now more young people are obese and dying eating the wrong foods". (Female, 60-69, tabloid.)	'Willingness to consent to the online study'	'Older respondents were generally more enthusiastic about participating than the other age groups and were willing to overcome obstacles to do so. Thirteen of the 14 respondents in this age group were willing to participate in the genetics study. Older respondents voiced fewer concerns, appeared more trusting of the content of the website and more comfortable with the process of reaching consent through the website than those from other age groups. Part of their motivation to participate stemmed from their own experience of ageing and health problems and witnessing family members live with illnesses'

15	A7: “I don’t know. I mean how is the DNA going to be stored?” (Female, 20-26, broadsheet.)	‘Willingness to consent to the online study’	‘We found little overall difference between the broadsheet and tabloid readers’ willingness to take part in the study. However, this overall result masked several distinct differences between the two groups. Broadsheet readers were more demanding of both the quality and quantity of information given on the website than their tabloid counterparts. They were more likely to say that they had not been given enough information to make an informed decision and more likely to voice concerns about genetic research. They were more sceptical of the uses their DNA might be put to and less likely to agree to provide a DNA sample or access to their medical records’
15	B8: “DNA sample – yes - the police already have one”. (Male, 40-49, tabloid.) C13: “It’s bound to be helpful. Helpful to me. Find out more about health”. (Female, 60-69, tabloid.)	‘Willingness to consent to the online study’	‘Tabloid readers were more relaxed about these concerns, readily linking DNA samples to the police database. In contrast to broadsheet readers who were able to suggest specific benefits for health and the treatment of disease from understanding the links between genes and our environment, the tabloid readers were less able to see clear benefits from the study. They offered generalised benefits’
15	B7: “I’m very suspicious and worry as I know things can be duplicated - I would need evidence that it really is Cardiff University”. (Male, 40-49, tabloid.) A4: “If I know it’s authentic, then OK”. (Female, 20-29, tabloid.)	‘Trust’	‘A number of themes emerged from the interviews. The most common theme was related to trust. Respondents frequently referred to trust in the organization - Cardiff University – as a reason for feeling comfortable and agreeing to take part in the study. Respondents used a variety of references to trust (eg, reassurance, authenticity, reputation, credibility). Respondents appeared to be making a quick intuitive decision about whether they could trust that the website was a product of Cardiff University or whether it could be attributed to an impostor posing as Cardiff University. In doing so, they looked for evidence to satisfy their scepticism’
15	B14: “This separation [of names and data] is meaningless. Someone can put it back together”. (Female, 40-49, broadsheet.)	‘Trust’	‘Some respondents were deeply sceptical about the site and had difficulty trusting the content, and its promises of safety, security and privacy’

15	C3: “Abuse of information: can anybody else access this information? You can’t keep tabs on everything. What will happen to this information? Phone calls? Spamming?” (Female, 60-69, broadsheet.) B13: “Police - would they have access? It’s Big Brother like in 1984 - there’s so much data already out there it could be used to control people. I’m thinking of eugenics, use of my DNA in a negative way. Biowarfare even”. (Female, 40-49, tabloid)	‘Security’	‘Security of personal data was a major preoccupation of many respondents. It was feared their personal information may be misused, which might range from unwanted communication through to the use of their DNA for development of biologicalwarfare or eugenics’.
15	C12: “Only if the security is in place – ir encryption is in place. It’s a matter of time before they can overcome any obstacles in place. I’m not keen on government centralized information - as long as this information isn’t part of that it would be OK.” (Male, 60-69, tabloid.)	‘Security’	‘There was a well articulated concern that all personal data given for the purposes of this study should be ring fenced and protected from any other database or government use. A few made references to the police database but more common references were made to how the ‘government’ might use the data’.
15	B2: “Yes, would be OK to provide a DNA sample. No crime”. (Male, 40-49, broadsheet.)	‘Security’	‘Respondents who said they had ‘nothing to hide’ were also making subtle references to potential exposure of personal information to government or police databases. Having nothing to hide was mentioned frequently as a reason to participate, although interestingly respondents appeared to relate to this in terms of information from their personal history (address, previous convictions, etc) rather than their health history’
15	A3: Risks? Just personal information being mislaid. (Female, 20-29, broadsheet.)	‘Security’	‘Security concerns extended beyond the security of the website itself - there were concerns about how data would be handled and how any potential for it to be lost would be mitigated. Some respondents mentioned worries over laptops or removable storage with personal data on being mislaid’
15	A3: “Because my DNA has never been analysed, it’s fascinating”. (Female, 20-29, broadsheet.) B3: “If there’s something on my side of the family I would like to know”. (Male, 40-49, tabloid.) C7: “For my own sakedto see that I’m OK. My daughter is bipolar”. (Female, 60-69, tabloid.)	‘Curiosity’	‘Surprisingly, the request for a DNA sample did not provoke heated debate or discussion among most respondents. The majority said that they would be happy to provide a DNA sample, given provisos that their personal information would be safe, the site was secure, and the DNA would only be used for medical research purposes and not commercial research. Respondents were often enthusiastic and interested in the study because they thought they were going to learn something about their own genes. They were intrigued about their own genetic

			inheritance, how their genes influence their health, and were both curious and concerned about learning something detrimentaltabout their future health. When the interviewer reiteratedtthe absence of direct clinical feedback in this study, respondents were disappointed and although thistdid not deter anyone from participating, it definitely reduced enthusiasm for engagement with the research'
15	C1: "If by any chance they do discover something wrong with you will they tell you? Yes I think they should". (Female, 60-69, tabloid.)	'Curiosity'	'Some respondents questioned the ethics of the absence of clinical feedback and considered whether or not participants in the study should be told if a genetic marker was found in their DNA'.
15	A8: "I'm not happy taking a sample, it's about the practicalities of it rather than the privacy of data or information". (Male, 20-29, broadsheet.)	'Operational concerns'	'Concerns about operational issues relate to time commitment, providing a DNA sample and the need for more information Some respondents expressed concerns that they might be signing up to something with an unspecified time commitment. Questions related to: how often would I be contacted? How long would it take to complete the questionnaires? How long would the study go on for? A number of people were reluctant to provide a DNA sample because mistakenly they thought that it would require home based venipuncture. Some respondents were needle phobic and others thought they would not be able to operate the apparatus at home. The website states that participants will be sent the necessary equipment to take a small sample of spit or a drop of blood, and should post the sample back to the researchers. The information about how the sample should be taken and how much blood/saliva would be required had clearly not been effectively communicated by the research team'
15	B7: [Were you given enough information?] "No, I need to know what I'm contributing to, the goals of the study". (Male, 40e49, tabloid.)	'A desire for more information'	'More information was also required by some participants regarding who was conducting the study, what the purpose of the study was, and what the expected outcomes of the study were. Overall, respondents gave the impression that this aspect of the content of the web pages was insufficient and that clarification of the benefits of the study - and introducing them earlier - would aid recruitment'

CHAPTER 6 APPENDIX

APPENDIX 6A - TOPIC GUIDES

What are the views and experiences of researchers, participants, and the public concerning participation in internet-based randomised controlled trials (RCTs)

1. Researcher interview topic guide

1. Introductory question to find out about the general background and context of your research, and your specialty or interest area.
2. Tell me about whether you have used the internet, or internet-enabled devices in your research, to either conduct or deliver an online RCT?
    - used the internet to conduct an ibRCT
    - used the internet to manage an ibRCT
    - used the internet to deliver an intervention within an ibRCT
3. Was this trial part of a wider programme of research?
If so, what was the context?
Where is the programme based?
How many researchers are actively engaged in your group on iRCTs?

[is there anything else you would like to add about the background/context of your trial or research programme that relates to the use of the internet?]
4. Thinking back to when you first started using the internet, what do you think were the main factors led you to use the internet?
    - What did you think the benefits would be?
    - What did you think the problems or issues would be?
5. I'm interested in hearing what you think about the main impacts of the use of the internet for your trial on your participants, can you summarise:
    - what you think from their perspective worked well for them – positive or beneficial factors
    - what didn't work well for them – negative factors
6. How did running the trial using internet technologies impact on the way that you communicated with participants?
    - How do you think this was perceived by participants?
    - What were their main concerns?
7. Were any patients or members of the public involved in the planning and design of the trial?

If yes, who were they and how were they recruited?

- At what stage of the trial were they involved?
- How successful was this?
    - What went well?
    - What didn't go so well?

8. Did you ask participants about their views or experiences within the trial, or how they felt about taking part?

If so, did this include questions about the use of the internet specifically?

What conclusions did you draw from this?

7. How would you summarise the main benefits and problems you experienced as a researcher using these technologies?

- Benefits
- Problems

8. Would you use the internet again in the future trial?
9. Closing questions and summary of next steps

Thank you for taking the time to participate in this study

2. Public interview topic guide

Opening - When I think of 'health research' I think of……

What do you think is involved in a 'clinical trial' ?

1. Have you ever taken part in a research study about your health?

    If yes, what did it involve?

2. Did you need to use the internet or a web site, computer or phone during the study, and if so, what did you have to do?

3. Were you asked what you felt about taking part at any time?

    If so, when were you asked, and in what way?

    What did you say?

4. Would you be likely to agree to take part in a clinical trial, and if so why?

If not, why not?

Clinical trials

5. Some research involves the use of the internet or mobile phone, for instance to collect data, or communicate with participants -

Do you think this would make people more likely (or less likely) to take part?

What kind of issues do you think might influence a decision to take part?

    What did you think the benefits, the good things might be?

    What did you think the problems would be?

    What worries do you think people might have about taking part?

6. What information should we give people might help you understand more about the study?

What would you want to know if you were deciding whether to take part?

How would you like this information to be given to you?

Researchers

7. I'm interested in hearing what you think about why trial researchers might want to use the internet in research studies:

Why do you think you think it might help them?

What might not work so well for them?

8. People taking part in health research often have more contact with a health professional or visit a clinic or hospital more often. In an internet-based study, this might not be the same, people might not see a health professional at all:

- How do you think people would feel about this?

- How would you feel about it?

    - Would it stop you wanting to take part?

9. How would you feel about taking say, your own measurements or activities, and entering the results yourself, say through a web site or through your phone?
Why/Issues
Involvement
10. Some researchers are hoping to get members of the public more involved in the planning and design of research studies
What ways do you think patients or the public could help or get involved?
How might this help researchers?
Closing
11. Finally, if I asked you to take part in a study today that was going to use the internet or phone to collect data and for communication, that was investigating looking a topic or health issue that you were really interested in, would you consider taking part?
If not, what would stop you?
If yes, what would the reasons be, and what information would you want to have?
Any problems you could foresee?

Thank you for taking the time to participate in this study

3. Public focus group topic guide

Opening - welcome the group, introduce myself, and the purpose and context of the focus group, explain what a focus group is and how it will work, and make the introductions.

Going to start with a general question for everyone to complete in a couple of words.

"When I think of 'health research' I think ……"

"What do you think is involved in a 'clinical trial' ?"

Taking part

1. Being asked to take part in a clinical trial

"What do you think people feel about being asked to join a clinical trial"

"What sort of things do you think would make them want to join?"

"What sort of things would make them less likely to agree to take part?"

2. Being asked to take part in an internet-based clinical trial

We are now going to consider how people feel about being asked to join a clinical trial that used the internet in some way. (Clarify what we mean by 'internet" i.e. some research involves the use of the internet or mobile phone, for instance to collect data, or communicate with participants)

"Do you think this would make people more likely (or less likely) to take part?"

"What kind of things do you think might influence their decision to take part?"

"What would make it different from a more traditional research trial"

Communication and contact

3. People taking part in health research often have more contact with a health professional or visit a clinic or hospital more often. In an internet-based study, this might not be the same, people might not see a health professional at all:

"How do you think people would feel about this?"

"How would you feel about it?"

"Would it stop you wanting to take part?"

4. What information should people be given to help them make a decision to take part in a clinical trial?

"What would you want to know if you were deciding whether to take part?"

"How would people feel about their data being used for other research"

Involvement

5. Some researchers are hoping to get members of the public more involved in the planning and design of research studies

"What ways do you think people could help or get involved?

“How might this help researchers?”

Closing

6. Finally, if I asked you to take part in a study today that was going to use the internet or phone to collect data and for communication, that was investigating looking a topic or health issue that you were really interested in, would you consider taking part?

“If not, what would stop you?”

“If yes, what would the reasons be, and what information would you want to have?”

“Any questions, or thoughts that people have had that they want to add?”

Closing section:

Thank the participants

Explain again how the data will be used and when the wider research will be finished. Say that they will receive an e-mail thanking them for their time, and giving them an opportunity to find out what the results of the study were, and how they are being used. Incentives will be given out, and a receipt completed.

APPENDIX 6B - PRIMARY STUDY INFORMATION SHEETS

What are the views and experiences of researchers, participants, and the public concerning participation in internet-based randomised controlled trials (RCTs)

Participant Information Sheet

I would like to invite you to participate in my research project on the use of the Internet in randomized controlled trials. The following will give you a short overview of what this means for you and the information you decide to give me. 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.

What is the purpose of this study?

The purpose of the study is to explore the experiences and attitudes that researchers, patients, and the public have towards the use of the Internet in clinical trials. The study aims to find out what will help researchers who use the internet in their research understand more about the attitudes and experiences of participants, improve their ability to recruit and retain participants, and find ways to involve patients and the public all stages of their research.

This study is not about research into any specific type of health issue or condition, but about the impact more generally of technology on people who have taken part, or may be asked to take part, in this type of research. We want researchers to understand more about how people feel about this, and what impact it might have on whether people choose to take part in research of this kind. Participants for the researcher interviews will be sought from the international community of researchers who have developed or conducted internet-based controlled clinical trials.

What does taking part involve?

Potential participants will be contacted in person, via e-mail, and via social media and networks, and asked to take part in an interview. The interview will be held using Skype, Loop up, or similar web-enabled telecommunications software, and will last for about 45 minutes. As participants are sought from a wide range of countries, all efforts will be made to fit in with preferred times and technologies.

If you agree to take part, you will be asked to sign a consent form. You will be free to withdraw at any time, without giving a reason.

Who can join in this research?

Anyone who has either used, or would like to consider using Internet technologies in the conduct of randomised controlled trials in health and wellbeing research. We want to get as broad a view as possible from a wide range of the international research community.

What are the views and experiences of the public about taking part in internet-based health research.

Participant Information Sheet

I would like to invite you to participate in my research project on the use of the Internet in health research. The following will give you a short overview of what this means for you and the information you decide to give me. 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.

What is the purpose of this study?

Doctors, other healthcare professionals, and patients need evidence from clinical trials to know which treatments work best. Clinical trials are research studies involving people. They test whether particular treatments are safe and how well they work. Without well-conducted trials, there is a risk that people will be given treatments that do not work and which may even be harmful. Small studies produce less reliable results than large ones, so studies have to be carried out with a large number of people before the results are considered sufficiently reliable. Recently, researchers have started using the Internet in the way they carry out studies, both as a way of delivering a particular treatment or service, and as a way of getting more people to take part in the research.

This study aims to explore the experiences and attitudes that people have towards the use of the Internet in health clinical trials. The study aims to help researchers who use the Internet in clinical trials find out more about what people think about taking part in this type of research, and to find ways to involve patients and the public in all stages of the research process.

This study is not about research into any one type of health issue or condition, but about the impact more generally on people who have taken part, or may be asked to take part, in any clinical trials that use the Internet. We want researchers to understand more about how people feel about this, and what impact it might have on whether people choose to take part in research of this kind.

What does taking part involve?

Taking part in this study will involve joining a focus group. The focus group should take about an hour. You will be asked about your experiences or views about health research, and what you think about the use of the Internet in carrying out these types of studies. There are no right or wrong answers to the questions – the aim of the group discussion is to find out your real thoughts and opinions. The focus groups will be recorded and then typed up so that I have a record of what is said. No individuals will be named or identified in the record.

The groups will be held in a local community centre or meeting room in London or Newcastle upon Tyne, depending on your location. If it is not convenient for you to

APPENDIX 6C - PRIMARY STUDY CONSENT FORMS

Public and researcher perspectives on participation in internet-based randomised controlled trials

INFORMED CONSENT FORM

I have read the participant information sheet and I understand:

That this project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee.

The Department of Research and Development at ThinkWell and Public led online trials (PLOT) supports the practice of protection of human participants in research. The following will provide you with information about the research that will help you in deciding whether or not you wish to participate. If you agree to participate, please be aware that you are free to withdraw at any point throughout the duration of the experiment without any penalty. The maintenance of confidentiality of information is subject to normal legal requirements.

This study will explore the experiences, perceptions and attitudes of researchers, trial participants and the public towards the use of the Internet in clinical trials. The study aims to help researchers who use the internet in clinical trials find out more about what people think about taking part in this type of research, to improve the way they recruit and retain participants, and to find ways to involve patients and the public all stages of the research process.

This study is not about research into any specific type of health issue or condition, but about the impact more generally on people who have taken part, or may be asked to take part, in any clinical trials that use the Internet. We want researchers to understand more about how people feel about this, and what impact it might have on whether people choose to take part in research of this kind.

All information you provide will remain confidential and will not be associated with your name. If for any reason during this study you do not feel comfortable, you may withdraw. Your participation in this study will require approximately 60 minutes. When this study is complete you can be provided with the results of the study, and you will be free to ask any questions.

Please fill in the check boxes below:

- I have read the information above and the Participant Information Sheet, and I agree to participate in this study. ☐
- I am aged over 18 and live in the UK. ☐
- I am aged over 18 and I live in another country. ☐ Please indicate your country of residence using the dropdown box
- I have read the list of exclusions in the Participant Information Sheet, which would exclude me from this study, and I confirm that none of them apply to me. ☐

Consent Form
Version 1 (Researcher)
22.01.15
MS-IDREC-C1-2013-174

Public perspectives on taking part in internet-based health research.

INFORMED CONSENT FORM

I have read the participant information sheet and I understand:

That this project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee.

The Department of Research and Development at ThinkWell and Public led online trials (PLOT) supports the practice of protection of human participants in research. The following will provide you with information about the research that will help you in deciding whether or not you wish to participate. If you agree to participate, please be aware that you are free to withdraw at any point throughout the duration of the experiment without any penalty. The maintenance of confidentiality of information is subject to normal legal requirements.

The purpose of the study is to explore the experiences and attitudes that people have towards the use of the Internet in health research. The study aims to help researchers who use the Internet in clinical trials find out more about what people think about taking part in this type of research, and to find ways to involve patients and the public in all stages of the research process.

This study is not about research into any specific type of health issue or condition, but about the impact more generally on people who have taken part, or may be asked to take part, in any clinical trials that use the internet. We want researchers to understand more about how people feel about this, and what impact it might have on whether people choose to take part in research of this kind.

All information you provide will remain confidential and will not be associated with your name. If for any reason during this study you do not feel comfortable, you may withdraw. Your participation in this study will require approximately 60 minutes. When this study is complete you can be provided with the results of the study, and you will be free to ask any questions.

Please fill in the check boxes below:

- I have read the information above and the Participant Information Sheet, and I agree to participate in this study. ☐
- I am aged over 18 and live in the UK. ☐
- I have read the list of exclusions in the Participant Information Sheet, which would exclude me from this study, and I confirm that none of them apply to me. ☐
- I have had the opportunity to ask questions about the study and I have received satisfactory answers to my questions, and any additional details I requested. ☐

Consent Form
Version 2 (Public)
22.01.15
MS-IDREC-C1-2013-174

APPENDIX 6D - SAMPLE OSOP MAP

CHAPTER 7 APPENDIX

APPENDIX 7A - DEVELOPMENT OF THEMES

Database	Descriptive map	Synthesis	Qualitative study
Terminology Location/geography Location of expertise Conditions and interventions Stage of trial Rapid growth/pace Reporting	Trial planning and design Trial management and co-ordination Recruitment and enrolment - Diversity and representativeness - incentives Screening and randomisation Data - Data capture design and collection - Data management - Self-report - Statistical analysis Acceptability and feasibility Engagement and fidelity Adherence, retention and attrition Ethical issues Perspectives and experiences - Researcher perspectives - Participant perspectives Setting or participant characteristics	Choice, consumers and expectations Autonomy and self-efficacy Perceptions of roles and relationships Information as an intervention Making it personal Obligation or burden Feeling safe and secure Being supported Technology, time and place Ethics and informed consent	Understanding of research Ethical issues: - ethical approval - informed consent - reporting research - equity - representativeness, sustainability and waste Trail design and appropriateness: - characteristics - convenience and cost - rise of technology - reach and hard-to-reach - engagement and adherence Roles, relationships and rapport: - researchers and health professionals - social support - personalised and tailored Feeling safe and secure: - trusted brand - secondary use of data - data and validity Technology and control: - convenience vs intrusion Sharing, learning and skills Patient and public involvement Making sense of the digital world
Conclusion summary themes: • Roles and relationships • Being personal • The digital world • sharing and learning • Citizens and research			

APPENDIX 7B - FINDINGS BY STAGE OF TRIAL

Trial stage	Findings
Planning and design	
Design: Appropriateness	• Views on how decisions were made about the appropriateness of an online design were varied, and sometimes contradictory, with most researchers not thinking outside their specific trial. • Internet-based technologies were usually used for the intervention delivery, and pre-dominantly in studies involving psychological therapies, behaviour change, or life-style interventions. • Online trials were viewed as offering potential solutions to some of the challenges experienced in traditional trials, in the potential for larger sample sizes, increasing reach and representativeness. • Most researchers view the ubiquitous adoption of technology in research as inevitable, but can also question its value and appropriateness, reflecting on the overall utility, and suggesting that the methods could make a trial more complicated than necessary. • Researchers were unsure of the evidence base for what works in online trials and some assumptions were influenced by findings from traditional trials and/or from other types of technology use. • Public participants saw the potential for online trials to address non-drug trials. • Researchers felt a sense of excitement by internet-based methods, and the sense of being at the forefront of technological change and development.
Design: Technology	• There is a potential lag between the rapid development and updating of technologies and their use in research, and potential adoption in practice. • Applications may be out-of-date before the trial finishes. • Researchers using internet-technologies face issues relating to their reliance on commercial developers which can prove problematic in terms of reliability, understanding of methods, and feelings of not being in control. • The interface of the trial is a vital element and requires careful design. • Some researchers distinguish between different types of online technologies, viewing some as less acceptable for research, although they may be the most popular in terms of public use.
Acceptability and feasibility	• It was not clear whether feasibility or acceptability testing methods or approaches had adapted to the new delivery methods.
Cost	• The assumption that internet-based trials were cheaper to run could mask hidden costs, such as the reliance on commercial software developers.
Ethical issues and approvals	
Ethical approval	• Ethics committees lack understanding of the online environment, and it this may always lag behind as the pace of technology change is too fast for them to keep up. • Ethics committees may feel that there is a ‘duty of care’ impact on trials where therapies are offered without professional contact.

	• Delays occurred seeking ethical approval for internet-based trials could increase costs. • There was a call for increased openness and transparency from researchers and participants relevant to all types of trial. • Researchers suggested that the public were more concerned about the risks of taking part than participants expressed themselves.
Informed consent	• Researchers felt that the online medium would generate additional problems in failure to ensure participants read or understood information and consent forms provided. • Making research more transparent could lead to greater fears, particularly in an online environment if secondary use of data is a possibility. • Researchers and participants both expressed views that a face-to-face, personal approach was more effective way of making sure information was understood. • Better, clear information at recruitment stage could help and take advantage of technical capabilities for presentation. • Having a full understanding of trials is an issue, and requires mechanisms to check understanding. • Making research more transparent could lead to greater fears. • Researchers and the public think that people don't read consent and information sheets properly. • Participants don't like to admit they might not understand - attributed to 'others'.
Ethical issues: Confidentiality	• Emergent issues re security and feeling safe in an online setting relate mainly to newer types of studies, such as genetic studies, but there are also issues regarding the way websites are designed that have to be used in public for people with sensitive conditions.
Ethical issues: Equity	• Impact on equity re access to online trials in low income countries.
Trial management	
Recruitment and enrolment	• Poor experiences of contact in other health settings could influence the decision to join an online trial, as could a wish to avoid contact with a health professional. • There was a potential issue relating to self-selection in internet-based trials that could undermine the advantages of increased ease of recruitment. • The public were worried about 'fake' online personas and this could have an impact on trust if recruitment for trials was not associated with a known setting, or trusted brand. • Unintended recruitment may occur in online trials, due to fewer boundaries or inadequate screening processes. • Concerns or risks of joining a trail were attributed to 'others'. • Convenience of online recruitment shouldn't replace good practice. Online recruitment may be used in traditional trials, and may therefore face the same issues as those reported for internet-based trials. • Researchers avoid unnecessary openness in order not to compromise recruitment.

Communication	• Personal characteristics and preferences may be harder to address in an online trial, for example in autonomy vs prescription. • Increasing the relationship and rapport between researchers and participants could have a negative effect by making the results less translatable to a real-world setting, the results less reliable, and introducing additional therapeutic benefits in some types of trials. • Researchers were worried about increased scepticism about research in general, but felt that the more hidden nature of the research team in an online trial could make this more problematic. • Researchers may find themselves altering their protocols to include more personal contact, to increase the sense of rapport. • Participant preferences in terms of automated reminders and other communications is hard to gauge or generalise due to the wide range of preferences, but can be intrusive. • Social support and sharing could enhance understanding of trials. • Some participants were less engaged with trials if they had less personal support, and had an expectation of reassurance. • Personalisation of communication is important to participants, as is usability and relevance in terms of style, language, and level of information.
Engagement, adherence and retention	
Engagement and adherence	• Engagement and expectations - it is harder for researchers to pick up nuances in an online environment. • Emphasis placed on convenience of channel may hide expectations re expert support and feedback. • Variation in perception of roles and relationships - having and unknown or unseen therapist may impact on adherence. • There can be a blurring of awareness for participants about their activities when being part of a trial and the activities of daily life. Being such an integral part of daily life could have potential unintended consequences on trial engagement and adherence. • Taking part in an internet trial can increase flexibility and convenience, but can also be offset by feelings of intrusion into daily life. • The internet may be seen as a treatment in itself. • Connectivity issues, such as speed and access, and people being in different places as part of their daily life may impact on adherence and be difficult to anticipate. • Personal benefit a motivator, but it may be difficult to meet participant expectations. • Role of researcher as expert and expectations of participants re reassurance and availability is a challenge.
Retention and attrition	• The nature of participant characteristics and preferences may be more difficult for researchers to pick up if contact or support is less available or personal, i.e. picking up feelings of guilt or burden in an online environment. • Easier to join trial but easier to leave: easier to join a trial and possibly not even be conscious of being in a trial.

	• Leaving an online trial can be seen as easier to do, as there is no need to explain if all contacts are virtual. • If internet-based trials are successful in integrating into daily life they may then have to compete with other online distraction, and need new strategies to retain participants. • Difficult for researchers to anticipate all likely preferences of participants in terms of their likelihood of remaining in a trial, and there is an interdependence between characteristics and adherence that is difficult to manage. • There is a mismatch between the time frames and commitments expressed as acceptable by participants, and as useful by researchers.
Data	
Data collection and security	• The use of aliases was a potential problem for researchers. • Specific types of data collection were viewed as potentially more worrying by the public when they involved newer types of studies, such as genetics studies. • The benefits for participants with stigmatising conditions of being able to enter data online was stated as a benefit by researchers. • Problems with data and validity were expressed, new developments such as tracking were suggested as potentially improving accuracy of data collection, however these were also seen as creating new and some researchers had experienced problems with this technology. • Some participants felt that self-report would not be as accurate or reliable in an online setting. • The public were less worried if the research was being carried out by a 'trusted brand'. • Participants were confident that their data was secure and that they had rights regarding this, although it was not clear that they fully understood the potential risks. • What happens to data, the shelf life of data, and how it might be used was raised as a concern.
Patient and public involvement; reporting, and sustainability	
PPI	• PPI is not being enhanced using potential available technologies. • Flexibility of new channels of communication could lead to better PPI. • There was a concern that the public would learn less about science in an online setting and that this would make the understanding of trials harder to achieve. • Researchers recognised the value of qualitative research to better understand public and patient views and perspectives, but had not necessarily carried this out.

Ethical issues: Reporting	• Researcher responses included the view that participants would not be interested in results, as they were part of a transient, online experience. • Participants expressed a desire to have results reported back to them.
Ethical issues: sustainability	• Tools being part of a future strategy could be a benefit, but in online access/change may be an issue. • Issue of sustainability re future use and therefore lack of benefit for community.

APPENDIX 7C - FINDINGS AND RECOMMENDATIONS BY STAGE OF TRIAL

Trial stage	Findings	Recommendations
Planning	• The pace of technological development and the pace of research are seen as incompatible, and the development of online trial methods will always lag behind. • Nature of technological change and the increasing adoption into all areas of society spark fears of inappropriate use in research, the 'rush to apps'. • There are questions as to the extent that the applicability of RCT methods and principles can be adapted in this setting.	• Researchers should ensure there is a clear theoretical framework for their trial design. • Researchers should keep up-to-date with methodological research on online trial methods and practices. • Other research designs including N of 1 trials should be considered. • ORCHID should be developed as an open access resource, and kept up-to-date.
Design	• The fact that the relevance of content can be experienced as a positive motivator or a barrier in the same trial with different participants, demonstrates the complexity and challenge inherent in designing an internet-based trial that has the flexibility to appeal to a wide range of personal characteristics. • Reliance on external companies, and the lack of a shared culture and language, can lead to problems in the design of interventions, including delays in response times, increased costs. This can lead to feelings of a lack of control, and reduced trust.	• Improved ways of conducting acceptability and feasibility testing, with greater involvement of patients and the public should be developed. • Researchers should consider both the cost, and quality assurance, implications before deciding whether to develop interventions in-house or outsource them.
Understanding of research	• The presence of online trial recruitment adverts and the subsequent delivery of a trial intervention online could lead to a blurring between the trial and everyday life, and impact on what people think they are signing up for as part of a trial. • Both the patient representatives and other public respondents found it difficult to differentiate between different types of clinical trials, and researchers fear lowering of understanding of research amongst the public.	• Researchers should increase work to raise the understanding of research amongst the public.
Acceptability and feasibility	• Poor experiences were reported relating to usability in terms of language, style of materials, level of complexity or number or questions, all of which could have an impact on adherence and attrition. • Access to technology and connectivity is still an issue, for instance in rural or other communities; impact on those with disabilities; or for participants without the language or expertise to share or exploit existing skills, software or other resources.	• Researchers need to consider health and digital literacy and ensure that content is adequately tailored to their target group.

Ethical approval	• Researchers had experienced difficulties when seeking ethical approval, and felt that ethics committees lack understanding about the specific nature of online trials, causing delays and additional costs.	• Work should be undertaken to update ethics committees on internet trial methods and standards.
Equity	• There is less funding or support for conducting internet trials in low-income countries, where there may be poorer infrastructure or capacity, poor access to equipment or connectivity for participants, which exacerbates existing inequity.	• Researchers should use existing research networks and international partnerships to build capacity in online methods.
Informed consent	• Reading detailed information online was seen as difficult, and researchers fear that the medium generates additional problems in terms of how much information is understood or even read by participants. • Researchers can underestimate the need to fully explain all the mechanisms involved in trial participation, from the rationale and reasons, to the very practical matter of what people will actually have to do.	• Researchers should consider developing technical solutions to help present trial and consent information, tailoring to different needs to address accessibility and equity. • Researchers need to consider how they gain consent, and manage the tension between the need to provide re-assurance, and acknowledging uncertainty.
Recruitment and enrolment	• Making it easier to join a trial may in itself negatively impact on participant awareness and understanding. Making it too easy to join a trial may lead to participants not even being aware that they are participating in a trial.	• Researchers should consider developing technical solutions to help present trial and consent information, tailoring to different needs to address accessibility and equity.
Communication and feedback	• Participants may anticipate a mode of communication with the researcher or therapist that is unrealistic in the context of an internet-based trial, and the unforeseen or hidden nature of the communication mechanism could lead to misunderstandings or unmet expectations. • In the studies investigating psychological therapies, relationships between the researcher and therapist role were perceived in a number of ways, with varying expectations, and with some participants feeling unsatisfied with the difference between anticipated and actual therapeutic contact. • There were variations in how roles and relationships between researchers and participants were anticipated or experienced, and a sense that expectations differ, and are not well understood by each other. • Rapport is a complex theme, and a range of views were expressed by researchers and participants. For some an absence of support was reported to have a negative impact on motivation, however, for some types of intervention a lack of personal contact could be seen as a positive feature when testing an intervention where self-management or self-treatment is intended, as it could mirror a 'real-life' setting in which patients would not have immediate or personal contact with a health professional or therapist.	• Planning appropriate and relevant feedback requires consideration at the trial design stage, and participants should be appropriately informed about the amount of contact or tailored support the trial will provide. • Researchers need to consider where and how participants will be accessing interventions, and ensure that privacy and confidentiality are maintained. •

Data collection and reminders	• Reminders can have equally positive or negative consequences for participants, sometimes perceived as stressful to receive, but for others helping to maintain motivation. • The nature of the time commitment has specific features, particularly for longer terms studies, and requires fitting in with daily life to sustain the convenience factor. This requirement is at variance between researchers looking to demonstrate long-term outcomes, and participants for whom a two-week commitment can be seen as being 'too long', and for whom dropping out from an activity is very easy. • Increased flexibility and a reduced need to travel are reported as advantages by researchers and participants, but these benefits are modified by experiences of intrusiveness. Therefore, the convenience of taking part in an online trial in one sense is offset by feelings of burden, and particularly related to data collection.	• Expectations need to be made clear about data collection and burden, preferences for feedback and reminders, and time commitments.
Data security	• Question as to whether researchers can provide adequate safeguards or assurance about data security and privacy in an era where technology is advancing rapidly, and where major threats to data are experienced even in the most well controlled sectors such as finance, government and commerce. • Confidentiality and privacy common themes arise across a number of studies, related to the security of data, the nature of the condition being investigated, and also to the potential for disclosure without permission of personal data or health status.	• The changing digital environment may lead to an increased need for very specific and clear information on data storage and security for participants.
Patient and public involvement	• Public interviewees could foresee potential benefits for greater involvement, through shared ownership of the process, or as a way of helping the public understand the 'why' of research. • Focus group members felt that greater public involvement could help direct internet-based research towards the most important patient-focused questions. • Researchers were aware of the value of involving patients and the public in the way that trials are planned and designed, but did not always do it themselves, with some viewing this as an extra burden at a busy time.	• Improved patient and public involvement in the whole trial process could offset some of the challenges, and improve the relevance and acceptability of online trials. • Researchers need to ensure that a wide range of participant and public views are taken into account, and fed into trial design, planning and conduct.
Reporting	• The enthusiastic adoption of new technologies could lead to fewer negative studies being published, leading to publication bias. • Online trials are difficult to retrieve systematically, as are methodological studies concerning their conduct and quality. • One public participant had experienced a lack of reporting back on the results of the trial in previous experiences.	• Standardisation in indexing methodology could complement transparency in research and lead to more effective searching and reporting of internet-based clinical trials research.

		• Researchers should ensure that participants are offered, and receive, trial results.
Sustainability	• There may be problems relating to how interventions and their content will be kept up-to-date, and expectations that the material will always be available. This may need to be made explicitly clear to participants. • Issues were raised concerning the transfer of online research into practice, relating to sustainability and equity. Being able to re-access or go back to online materials was experienced as a positive factor. • No accountability being held for future adoption or use of the interventions being tested, contributes to waste, and a lack of community benefit from trial activities.	• Research teams should consider whether Internet-based tools or resources tools could continue to be available after the trial, but consider issues of maintenance. • Online trial could provide a more naturalistic setting for an intervention, and offer more control for participants, potentially helping researchers understand how well study findings could be translated into real-life settings.
Sharing and learning	• Researchers were keen to share learning and have better evidence about methods and trial design, but felt that this was harder in the online trial environment. They 'learn while doing', less likely in traditional clinical trial settings, and although they would try to act on this learning, and do things differently in the future, there was less of a sense of validated testing. • There was a suggestion that there should be more collaboration between research teams, and barriers between different disciplines and types of expertise should be broken down.	• Researchers should keep up-to-date with methodological research on online trial methods and practices. • Online trial teams should be multi-disciplinary and include digital and usability expertise.