

WHAT DO POTENTIAL PARTICIPANTS WANT TO KNOW
ABOUT LOW RISK INTERVENTIONAL RESEARCH? A
FEASIBILITY STUDY OF ELECTRONIC INFORMATION
PROVISION AND A RANDOMISED CONTROLLED TRIAL OF
AN INTERACTIVE INFORMATION SHEET (IIS)

by

HELEN MICHELLE KIRKBY

A thesis submitted to the
University of Birmingham
For the degree of
DOCTOR OF PHILOSOPHY

MRC Midland Hub for Trials Methodology Research
School of Health and Population Sciences
College of Medicine and Dentistry
The University of Birmingham
August 2012

UNIVERSITY OF
BIRMINGHAM

University of Birmingham Research Archive

e-theses repository

This unpublished thesis/dissertation is copyright of the author and/or third parties. The intellectual property rights of the author or third parties in respect of this work are as defined by The Copyright Designs and Patents Act 1988 or as modified by any successor legislation.

Any use made of information contained in this thesis/dissertation must be in accordance with that legislation and must be properly acknowledged. Further distribution or reproduction in any format is prohibited without the permission of the copyright holder.

ABSTRACT

This PhD considered provision of information to potential research participants. It gathered data on the types and detail of information potential participants accessed, and determined the feasibility of electronic information provision.

A systematic review found limited empirical evidence to suggest what information potential participants want when making a participation decision.

An Information Provision study was designed and embedded in an existing piece of low risk interventional research. This had three components; a feasibility study of electronic communication; a RCT of an Interactive Information Sheet (IIS); an observational study that recorded information accessed by potential participants.

Results suggest electronic communication did not affect consent rate (although study was not powered to detect this) and understanding and satisfaction were unaffected by level or mode of information provision. Traditional participation information sheets (PIS) may only satisfy 11.4% participants, undersupply 9.1% and oversupply 79.5%. Participants were often unable to accurately recall what information they had accessed.

In conclusion, the majority of potential participants to this study would have been satisfied with a streamlined PIS. An IIS could provide additional tailored information to those who require it, with standardised verbal information provision at consent interviews ensuring consent is given in accordance with GCP guidelines.

DEDICATION

To my mother who is always proud of me and my father who always was.

ACKNOWLEDGEMENTS

This PhD studentship was funded by the Medical Research Council Midland Hub for Trials Methodology Research (MRC MHTMR) (Medical Research Council Grant ID G0800808).

To my supervisors, Dr Melanie Calvert and Professor Heather Draper for the continual help and support they have provided over the past 3 years. My thanks also go to Professor Sue Wilson who provided supervisory support during the first year.

To members of the Educational Technology Team, Dr John Couperthwaite and Chris Withers.

To all of those working on the Bp-Eth study for allowing the IIS RCT to be embedded into the study and for accommodating data collection. With special thanks to Professor Richard McManus, Ramandeep Kaur and Dr Paramjit Gill.

To the Midlands Hub for Trials Methodology Research Hub for the on-going support provided during my PhD studentship. In particular, Professor Cindy Billingham for her encouragement of both me and the research, Karen Biddle for the fantastic administration support and Thomas Keeley for helping with the systematic review validation.

To Teresa Hawkins, Thomas Keeley and Jeremy Fallowfield for helping to proof read the thesis.

CONTRIBUTORSHIP

The PhD was based on work by Antoniou Et al¹ and developed from a research proposal submitted to the MRC Midland Hub for Trials Methodology Research by Professor Heather Draper, Dr Melanie Calvert and Professor Sue Wilson.

To date, two papers have been published from this PhD: 1) 'Using e-mail recruitment and an online questionnaire to establish effect size: A worked example.' This paper was co-authored by Helen Kirkby, Sue Wilson, Melanie Calvert and Heather Draper, and published in *BMC Medical Research Methodology*; 2) 'What potential research participants want to know about research: a systematic review.' This paper was co-authored by Helen M Kirkby, Melanie Calvert, Heather Draper, Thomas Keeley and Sue Wilson, and published in *BMJ Open*.

An information specialist from the University of Birmingham library helped to design the search strategy used in the systematic review. Thomas Keeley undertook the validation of the systematic review reference database.

The information to be included in the unfolding interactive information sheet (IIS) was drafted by Helen Kirkby, discussed with Dr Melanie Calvert and Professor Heather Draper, and then revised by Helen Kirkby to take into account comments made.

¹ Antoniou E, Draper H, Reed K, Burls A, Southwood T, Zeegers M. An empirical study on the preferred size of the participant information sheet in research. *Journal of Medical Ethics* 2011; 37:559-562

Chris Withers undertook the programming of the IIS website to allow data to be captured from the website into a database.

The meeting held with NRES to discuss the work of this PhD and proposals for future work was attended by Helen Kirkby, Dr Melanie Calvert and Professor Heather Draper. Helen Kirkby gave a presentation of the results of the PhD and streamlined participant information sheet. Professor Heather Draper led the discussion on proposals for future work.

Helen Kirkby was the sole author of the thesis. Dr Melanie Calvert and Professor Heather Draper provided comments on the thesis, which was revised to take their feedback into account.

TABLE OF CONTENTS

1	Introduction	1
2	Background	7
2.1	Consent criteria	9
2.2	The information that should be provided to potential research participants	18
2.3	Problems with reading and understanding participant information sheets ..	28
2.4	Previous efforts to improve PIS's	33
2.5	The role of the Internet in research	39
2.6	Using the Internet to provide study information to participants – A study by Antoniou et al.....	47
2.7	Aims and objectives of the PhD	51
3	Systematic review of the literature	54
3.1	Aims	56
3.2	Methods	57
3.2.1	Inclusion Criteria	57
3.2.2	Outcome measures.....	57
3.2.3	Search Methods	58
3.2.4	Study identification	65
3.2.5	Validation of Screening	67
3.2.6	Data Extraction.....	68
3.2.7	Study selection.....	69
3.2.8	Study Characteristics.....	75
3.2.9	Analysis	75
3.3	Results	81
3.3.1	Categories with no studies reporting relevant results.....	88
3.3.2	Categories with studies reporting general results	89
3.4	Discussion.....	92

3.5	CONCLUSIONS.....	98
4	Information Provision study protocol.....	101
4.1	Study Design.....	103
4.2	Aims.....	104
4.3	Parent study (in which the information provision study was embedded) ...	106
4.3.1	Identification of a suitable parent study.....	106
4.3.2	Outline of the parent study.....	108
4.3.3	How the Information Provision study was embedded.....	109
4.4	Participants.....	111
4.5	Sample Size Calculations.....	115
4.5.1	Estimating an effect size.....	115
4.5.2	Sample size calculations for the IIS RCT.....	118
4.6	Randomisation.....	121
4.7	Interventions.....	123
4.8	Outcomes.....	129
4.9	Statistical analysis.....	131
4.10	Ethical approvals and considerations.....	133
4.11	Changes made to the protocol after commencement of the study.....	136
5	Development of the Interactive Information Sheet (IIS).....	141
5.1	Contributorship of chapter 5.....	142
5.2	Design and implementation.....	142
5.3	Development of content.....	151
6	Results.....	167
6.1	Participant recruitment.....	169
6.2	Key results.....	175
6.3	Demographics.....	177

6.4	Information accessed by participants	182
6.5	Time spent reading information	187
6.6	Adjusted analysis for information accessed	191
6.7	Predictors of information accessed	194
6.8	Effect of IIS on consent rate	200
6.9	Understanding and satisfaction	203
6.10	Estimation of costs.....	220
6.11 Error! Bookmark not defined.	
6.12	Limitations of the Information Provision study.....	224
6.13	A streamlined PIS	226
6.14	Future of the streamlined PIS	234
7	Discussion – The Future of Information Provision in Research	240
7.1	The feasibility of electronic information provision	242
7.2	Influences on the participation decision	260
7.3	Consent when participants choose to read little information	272
7.4	Autonomy, paternalism and consent	278
7.5	Mandatory information	285
7.6	Providing verbal information.....	292
7.7	Is an IIS a solution to informing the minority?.....	295
7.8	Future of information provision in research	298
8	Conclusion.....	304
8.1	Considerations for future research	311
9	Appendices.....	314

9.1	- Kirkby HM, Calvert M, Draper H, Keeley T, Wilson S. What potential research participants want to know about research: a systematic review. BMJ Open 2012.....	315
9.2	Kirkby HM, Wilson S, Calvert M, Draper H. Using e-mail recruitment and an online questionnaire to establish effect size: A worked example. BMC Research Methodology 2011, 11:89.	329
	331
	332
	333
9.3	Information included in the IIS.....	334
9.4	Pre defined data extraction sheet for the SR	352
9.5	Blood Pressure Monitoring in Different Ethnic Groups study protocol.....	353
9.6	Electronic invitation letter	371
9.7	PIS for Interviews with parent study pilot participants and research nurses	
	372	
9.8	Proportions of participants accessing each level of information for each FAQ by age, gender and ethnicity.....	373
9.9	Information included in the streamlined PIS.....	378
9.10	Appendix 7 – Minutes from meeting with NRES Expert Panel.....	379
10	Reference List.....	384

LIST OF ILLUSTRATIONS

Figure 1 - NRES suggested PIS headings ²²	26
Figure 2 – Internet use by age group ¹⁰¹	40
Figure 3 - Search strategy: MEDLINE (OVID).....	61
Figure 4 – Agreement rate between reviewer one and two for phase one reference screening.....	68
Figure 5 – Number of citations identified at each round of screening.....	74
Figure 6 - Forest plot of the proportion of participants that wanted to know about investigator COI (random effects)	90
Figure 7 – Recruitment flow chart	114
Figure 8 - Questionnaire to determine understanding	125
Figure 9 - Questionnaire to determine satisfaction for those randomised to IIS	127
Figure 10 - Questionnaire to determine satisfaction for those randomised to PDF-PIS or paper PIS	128
Figure 11 – Outline of the IIS website	144
Figure 12 – Unfolding content of the IIS website	147
Figure 13 – Images of the unfolding content of the IIS website.....	148
Figure 14 - Distribution of participants through the Information Provision study.....	172
Figure 15 – Proportion of participants that opened the email.	173
Figure 16 – Number of participants that took part in the IIS RCT	174
Figure 17 - Number of satisfaction and understanding questionnaires returned	205
Figure 18 – Household Internet access with linear future predictions, adapted from ONS data ¹⁰²	245

LIST OF TABLES

Table 1 - Key Journals identified	63
Table 2 - References identified from each electronic database.....	70
Table 3 – Reasons for full paper exclusion	73
Table 4 - Summary of studies included in the systematic review	76
Table 5 - NRES recommended headings against papers that report evidence	82
Table 6 - Number of studies providing evidence for each category of information with pooled results.....	93
Table 7 - Results from the effect size questionnaire	117
Table 8 - Estimate sample sizes for the range of baseline consent rates.....	119
Table 9 - Sample sizes for a consent rate of 70%.....	120
Table 10 - The minimal information participants thought should be included in a PIS	156
Table 11 - Extended information participants thought should be included in the PIS	159
Table 12 – Participants included at each stage of recruitment	171
Table 13 – Baseline data for study population	178
Table 14 – Proportion with an email address broken down into demographic groups (age, gender, ethnicity).....	181
Table 15 – Proportion of participants accessing each level of information for each FAQ.....	183
Table 16 – Average stay time measured in seconds for each level and expected time (in seconds) it would take the average adult to read each level of each question (based on average adult reading 200 words per minute)	189

Table 17 - Adjusted proportion of participants accessing and time spent on each level of information (with all those who accessed no information taken out)	193
Table 18 – Proportions of participants accessing each level of information for each FAQ by participation (did consent or did not consent).....	195
Table 19 – Demographics that predict the total number of levels accessed and total time spent.....	199
Table 20 – Consent rate by study group	201
Table 21 – Comparison of consent rate between groups	202
Table 22 – Participant score on the understanding questionnaire split by study group	208
Table 23 – The average score on the understanding questionnaire, split by method of information provision and demographics	211
Table 24 – Participants’ satisfaction with the method of information provision, split by method of information provision	217
Table 25 – Estimate of cost for electronic and postal invitations	221
Table 26 – Estimate of cost to develop the content for the IIS	222

LIST OF ABBREVIATIONS

RCT.....	Randomised Controlled Trial
PIS	Participant Information Sheet
IIS.....	Interactive Information Sheet
ICH	International Conference on Harmonisation
GCP	Good Clinical Practice
NRES	National Research Ethics Service
GMC.....	General Medical Council
REC.....	Research Ethics Committee

1 INTRODUCTION

Medical research is required for medicine to advance and effective care to be provided^{1:2} but raises ethical concerns when participants are involved³. It is widely accepted that research participants must give their consent before any intervention is made (or proxy consent for vulnerable persons, i.e. children and incapacitated adults^{4:5}). This thesis reports studies of one aspect of consent - the provision of information. The studies reported in this thesis are a systematic review of the literature to determine the evidence base for what potential participants want to know when they are considering participating in research, a feasibility study of providing electronic information, a randomised controlled trial (RCT) that explored an alternative to the traditional paper based participant information sheet (PIS) and an observational study that recorded what information potential participants actually accessed when deciding whether to participate in a low risk interventional study.

The overall aim of the thesis was to gather evidence on the topics and level detail of study information potential research participants accessed when deciding whether to participate in a piece of low risk interventional research, and to determine the feasibility of electronic information provision. This aim was met by answering four research questions –

1. What does the current evidence suggest potential participants want to know when they are deciding whether to participate in research?
2. Is electronic information provision in research feasible?
3. What information did potential participants access when they made a decision about whether to participate in a piece of low risk interventional research?
4. What are the implications for the future of information provision given answers to research questions 2 and 3?

The thesis comprises seven chapters; background information, methods and results of a systematic review of the literature, the Information Provision study protocol, development of an Interactive Information Sheet (IIS), results, a discussion of the future for information provision in research in light of the results, and conclusion to the thesis.

The background chapter puts the thesis aims into context over three areas. The first outlines the ethical principles driving the process of consent to research participation before focusing on what information should be provided to potential participants to obtain valid consent. The second section describes common problems encountered when providing study information and reviews research on interventions that have been introduced to improve the information provision process. The final section explores the role of the Internet in research and how it could be used to provide electronic information to participants. The chapter finishes with an outline of the objectives used to answer the four research questions of the PhD.

The first study conducted for this PhD was a systematic review to answer research question 1 and establish the evidence base for what information potential participants wanted to know when considering participating in research. Chapter 3 describes the methods and results of this systematic review. The resulting evidence base is then compared to the NRES guidance of what to include in a participation information sheet (PIS). This systematic review has been published in *BMJ Open* and is included as Appendix 9.1.

Chapter 4 describes the methods for the design and implementation of the Information Provision study, the second study of this PhD, which aimed to answer research questions 2 and 3. The chapter begins by describing the process that identified a suitable parent study in which to embed the Information Provision study. The Information Provision study had three components; a feasibility study of electronic information provision in research, a randomised controlled trial (RCT) of an IIS compared to a PDF copy of a standard PIS, and an observational study that recorded the information accessed when potential participants were considering participating in a piece of low risk interventional research.

No established effect size was available on which to calculate a sample size for the RCT, so part of Chapter 4 (Section 4.5) outlines how a small study was conducted to determine an effect size on which to calculate a sample size. The novel method developed for this study has been published in *BMC Research Methodology* and is included as Appendix 0.

The Information Provision study included an alternative way to provide information to potential study participants by using an Interactive Information Sheet. The IIS allowed potential participants to choose the amount and types of information they accessed when considering participation in a piece of low risk interventional research. The IIS was based on work by Antoniou et al⁶ and Chapter 5 outlines the development of the IIS for use in the Information Provision study. The first section of Chapter 5 presents the development of the website that hosted the IIS and enabled the IIS to unfold and record information accessed into a database. The second

section of Chapter 5 outlines the development of the content included in the IIS. The information in the IIS is included as Appendix 9.2

Chapter 6 provides the results of the Information Provision study. It reports participant numbers and presents demographic data followed by the information accessed by participants, the effect of the interventions on recruitment rates, the feasibility of using electronic recruitment and electronic information and participant understanding of and satisfaction with the information provided.

In order to answer the final research question, the results of the Information Provision study were used to develop a streamlined PIS for the parent study. The streamlined PIS incorporated the information that participants accessed when they were deciding whether to take part in the low risk interventional study and the information that is required by the International Conference on Harmonisation⁷ (ICH) and the four statutory instruments for Good Clinical Practice (GCP) required by UK law. The results of the Information Provision study and the streamlined PIS were then presented to the National Research Ethics Service (NRES) expert panel. They provided feedback on these results, their opinions on the streamlined PIS for interventional research and how the research could be taken further. The final section of Chapter 6 reports the feedback received at this meeting.

Chapter 7 discusses the results of the thesis. It considers firstly whether using electronic PIS would be feasible in research and looks at the practicalities of providing information and recruiting electronically. The chapter then considers the

ethical concerns of information provision regarding consent in light of the results of the Information Provision study and offers potential solutions for future research.

In the concluding chapter the key points of the work undertaken for the thesis are brought together and it is argued that improvements in information provision for low risk interventional research are required.

2 BACKGROUND

Three areas of background information are needed to put the thesis aims into context. First, the ethical principles involved in consent (Section 2.1) and the information that should be provided to potential research participants (Section 2.2). Second, the common problems with providing information to potential participants (Section 2.3) and the previously reported interventions in information provision (Section 2.4). The Internet was used in the main project of this PhD as the platform to provide study information to potential research participants, so the third area of background information explores the role of the Internet in research (Section 2.5) and how it can be used to provide study information to potential participants (Section 2.6). The chapter concludes with the detailed aims and objectives of this PhD (Section 2.7).

2.1 CONSENT CRITERIA

Consent is a pre-requisite for participation in research and researchers should normally obtain the 'free and informed consent' of potential participants before they enrol⁸⁻¹¹. Gaining participant consent is not merely a legal requirement or formality but a moral obligation to ensure that potential research participants fully understand and voluntarily make decisions regarding participation.

The requirement for consent prior to research participation comes from a respect for autonomy. Although respect for autonomy is a complicated philosophical concept that will not be debated in this PhD, when the research community use 'respect for autonomy' in terms of consent it is generally understood to mean that potential participants make a choice about participation based on their own values, for their own reasons and should have that choice respected¹²⁻¹⁴. In order to respect a potential research participant's autonomy and for their consent to participate in research to be considered valid, it has to fulfil three criteria: 1) The participant is given specific detailed information about the study. 2) The participant is capable of understanding the information provided and using it to make a decision regarding participation. 3) The decision is made voluntarily^{2;3;15;16}. In addition, potential participants should be given sufficient time to make their participation decision. Although not compulsory, it is considered good practice to allow participants at least 24 hours to make a participation decision where appropriate¹⁷⁻¹⁹. Participants should be given as much time as they personally require to make a decision - for some participants and/or studies this may require much more time and for others much less.

The consent process should also be on-going and reviewed throughout a research study. Researchers should ensure that even after participants have given their initial consent they remain willing to participate, and their consent should be updated if changes are made to the study²⁰.

The participant is given specific detailed information about the study

For the first consent criterion to be fulfilled the participant must be given specific, adequate information about the study. In order to determine what information potential research participants need to know to provide their consent we need to understand why they should be informed.

The nature of clinical trials often means that the absolute benefit to potential participants is unknown, the potential for harm has not been established and there may be known and unknown (serious) adverse events or reactions. In some research studies there may also be no expected direct potential benefit to participants, for example, an early phase clinical trial where only the safety and efficacy of a new drug is tested for the benefit of future patients³. The uncertain nature of research means that potential participants put themselves at risk of harm (and/or a chance of benefit) in order for medical knowledge to be gathered. There is a greater expectation of unknown toxicity and/or side effects in research than for standard treatments, and so the risk is considered greater. Providing autonomous individuals with study information allows them to decide if participating in the research is consistent with their values, interests and preferences^{2;3;14;21-23}.

It has been argued that 'fully informed' consent can never be achieved because only those with expert knowledge can understand all aspects of a research study²⁴.

Although consent may rarely be *fully* informed, it does not mean it cannot be *adequately* informed. The question to address here is a subjective one of how much information needs to be imparted to a potential research participant for it to be considered adequate for them to make a participation decision. To help explain the term 'adequately informed' the example given by Hewlett³ of a potential customer considering a car purchase is useful. The customer might choose to buy a car based on information about its history and performance rather than full information about the workings of its engine. The customer would not be fully informed of the purchase if they chose not to understand precisely how the engine works, but they consider themselves to be adequately informed because they have the information they wanted to know about the car's history and performance. Similarly, whilst one potential research participant may consider himself adequately informed solely by information relating to the potential risks and benefits of participating, the values and beliefs of another mean that sources of funding are a significant factor, for example. The topics of information important to decision-making are, therefore, likely to differ between potential research participants.

Returning to the car sale analogy, the level of detail of information about the car considered adequate to make the purchase decision is also likely to differ between customers. A racing driver is likely to be more interested in knowing the specifics of a car's predicted performance than someone buying a car to get to local shops once a week. In this situation, one may accept that the latter does not want or need to know information about the car's performance. If so, imparting information about the car's performance would not affect the purchase decision, and the customer may not understand the information or not be interested in it. Although the latter buyer is not

fully informed about the car, they are adequately informed because the information they have is sufficient to meet their personal requirements. Similarly, whilst one potential participant may neither understand nor be interested in the pharmacological actions of a research drug, another may require this level of detailed information before they consider themselves adequately informed.

A further point to consider is the level of understanding that is considered adequate for a potential participant to be able to make a participation decision. For anyone to have complete understanding of a research study they would need to have the same depth and level of understanding as a physician and scientist, since fully understanding how a drug works would need in depth knowledge of both anatomy and the pharmacological actions of the drug. To require understanding in the same way and to the same extent that a physician and/or scientist understands is an unreasonable and impractical expectation to have of potential lay participants^{14;25}

Consent criteria require potential participants to be given 'adequate' study information on which to make their participation decision. The amount of information considered adequate, however, is likely to differ between research participants. This makes it difficult for researchers to decide exactly what types and how much information to include in a PIS. The IIS used in this PhD aimed to adequately inform all potential participants. Instead of providing a fixed amount of information, it allowed potential participants to tailor study information to their individual requirements.

Other reasons why potential participants should be provided with study information relate to protecting the integrity of the research rather than protecting participant autonomy. For example in a clinical trial where a treatment for a chronic disease may initially make the participant feel worse before they feel better, giving potential participants information about what to expect may improve the chances of their continued co-operation with the study and reduce the dropout rate²⁶. Reducing the dropout rate of a study improves the integrity of the collected data and validity of results²⁷. Since researchers have a responsibility to conduct research in such a way that can meet its aims, there may also be ethical connotations if the dropout rate biases results to such an extent that results are no longer deemed to be useful²⁸.

The participant is capable of understanding the information provided and using it to make a decision regarding participation

For the second criterion for consent to be fulfilled the potential research participant must be capable of understanding the information provided and using it to make a decision regarding participation: to have the capacity to make a decision to take part^{29;30}. The Mental Capacity Act (2005)⁵ states that in order to have capacity the person must be able to understand the information provided, retain the information, use the information as part of the decision making process and be able to communicate their decision.

In order to understand information, a potential participant has to understand the consequence of that information. To have an adequate understanding of the consequences of consenting to research does not mean that a potential participant needs a deep understanding of, for example, how a study drug works and how it has its effects on the body. Instead, they require an understanding of the types and

severity of potential side effects that drug may have and how they can report any they experience. The manner in which information is provided will influence adequacy of understanding (Sections 2.3 and 2.4), and since not understanding the information is part of the test for incapacity, study information needs to be communicated in a way that does not render a potentially competent participant incapacitated.

Usually in research, potential participants are provided with information in a paper PIS that is verbally reinforced during the consent interview. Participants' inability to recall information from the PIS at the time of the consent interview does not mean they lack capacity to consent. The Mental Capacity Act⁵ states that a person is unable to make a decision only if they cannot "retain that information, to use or weigh that information as part of the process of making the decision" (Section 3, 1b and 1c). This means that providing potential participants are able to retain and recall the verbal information given at the time they are asked to make a participation decision, they are considered to have capacity to consent since they are able to retain the information long enough to use it to make a participation decision⁵.

Finally, after making a decision, the potential research participant needs to be able to communicate that decision to researchers. Their decision may be communicated in any way appropriate to their circumstances, for example, using sign language or visual aids. Anyone not able to communicate their decision is rendered incapacitated by the Act because they cannot engage in decision-making, even though they do not actually lack inherent capacity³⁰⁻³². In order to protect, for example, those who speak a different language, from being rendered incapacitated, the Act guidance notes³³

require considerable effort to be made to enable potential participants to communicate their decision regarding participation. Language is a particularly challenging area for communication in research since it is often difficult to ensure that translations are appropriate. The Act guidance notes³³ stress that there are very few participants unable to make a participation decision because they cannot communicate it in any way, and the example provided is that of 'locked in syndrome' where participants can only communicate through blinking. These participants can still communicate and, therefore, should not be rendered incapacitated to consent³⁰.

The decision is made voluntarily

The final criterion for valid consent is that it is given voluntarily. This criterion requires that potential participants are not coerced into participating, i.e. they are not subject to the undue influence of a third party. For example, if a GP offered a patient a particular treatment in return for participating in one of their studies, it would be considered coercive and their consent not voluntary^{14;15;34}.

Potential participants may be concerned that they will receive a reduced standard of care if they do not 'comply' by participating in research they are invited to take part in. Participants that agree to take part only because of these concerns for future care would not be giving their consent voluntarily as a coercive influence is the overriding factor for their decision. In order for their consent to be given voluntarily, potential participants should be assured that they do not have to take part in the research and their healthcare would not be affected if they refused to participate.

Another aspect related to voluntariness is the right to withdraw, which ensures participants continue to take part in the research voluntarily after they have given

their initial consent to participate. International and UK guidelines state that ‘the subject should be informed of the right to withdraw consent to participate at any time without reprisal’^{22;35}. This right to withdraw is meant to reassure potential participants that their consent now does not mean that they cannot reduce or withdraw their commitment at a later date³⁶. Participants may wish to withdraw from the study for many reasons, for example, they could experience life changes that mean they have difficulties meeting the study demands and wish to withdraw completely from the study. Or they could struggle to cope with side effects of a trial drug and no longer wish to continue taking it, but agree to be followed up and for their data to be used in the study. There are, however, logistical problems in allowing participants to withdraw from the study “at any time”, for example, participants could not withdraw their consent for individual results to be used in analyses once study results had been published. The process of and problems with withdrawing consent are outside the scope of the thesis and will not be discussed further.

This section has explored what consent is and has shown that it is far more than a potential research participant simply agreeing to take part in a study. In order for consent to be valid, a potential research participant has to have sufficient information about the study, be able to understand that information and use it to make a voluntary decision about whether to take part. When thinking about consent to research it is important to have an understanding of all criteria needed for valid consent, but the rest of this PhD concerns only one aspect of consent: the provision of information.

Key points

Consent is normally a pre-requisite for participation in health research.

The requirement for consent is based on respect for autonomy that focuses on the potential participant making a choice based on their own values, for their own reasons.

In order for consent to participate in research to be valid, it has to fulfil three criteria –

- 1) The participant is given specific detailed information about the study.
- 2) The participant is capable of understanding the information provided and using it to make and communicate a decision regarding participation.
- 3) The decision is made voluntarily.

2.2 THE INFORMATION THAT SHOULD BE PROVIDED TO POTENTIAL RESEARCH PARTICIPANTS

This section explores why information provision differs between clinical treatment and medical research and then outlines current UK and international guidance and guidelines.

Differences between treatment and research

Guidelines for information provision in clinical care are provided by the General Medical Council (GMC) and state that physicians have a duty to engage participants in decisions as much as possible, share information and maximise patients' ability to make autonomous decisions for themselves². The GMC also acknowledges that no single approach to discussions about treatment or care will suit all patients or apply in all circumstances, and their guidelines allow the doctor to use specialist knowledge, experience and clinical judgement to tailor the amount of information provided (with guidance from the GMC² and Department of Health³⁷).

The conduct of research is controlled by regulatory codes and overseen by ethics committees and institutional review boards²⁶ and there are specific guidelines that recommend what information should be provided to potential research participants that do not exist for clinical care^{22;35}. Whilst the physician may recommend a particular option they believe to be best for the patient, when this is done in research there is a question of whether the doctor's advice constitutes coercion to participate and, therefore, undermines autonomy and invalidates consent³⁸. The other side to this argument is that if the researching doctor does not offer advice that would be pertinent to the potential participant's decision-making, even if it is likely to be

coercive, they have not met their clinical obligation of providing the information they think is required for their patient to make a decision³⁸. There are currently no clear guidelines as to where the balance between these two points lies.

In research, study information is traditionally conveyed to potential participants by a written participant information sheet (PIS) with sufficient time to consider the information, before it is reinforced by a verbal consent interview and participants are asked to make a consent decision^{3;22}. The consent process may differ from this traditional model - for example, in clinical trials initial information is often provided verbally to the patient during a consultation with their doctor, and the patient is then provided with a paper PIS to take away³⁹⁻⁴¹.

There are many differences between clinical care and research settings, with the biggest difference being in what they aim to do. Whilst the focus of clinical care is solely the well-being of the patient, the goal of research is primarily the acquisition of knowledge to benefit future patients²⁶. Standard therapies are usually well understood, are thought to be the best treatment for a particular clinical problem and associated risks and potential side effects can often be quantifiable²⁶. Clinical research, by virtue of it being research, may put the participant at risk of unknown side effects and risks, since the intervention has not been evaluated. There may, however, also be an anticipated or unknown benefit with trial therapies that do not exist with the standard therapy.

Researchers are legally required⁴²⁻⁴⁵ to disclose more information than physicians and some experts argue that this should remain the case⁴⁶. A greater level of disclosure may be required in research than for clinical care, both because of the

greater risk of unknown side effects and toxicities in research, and because the aim of research is to benefit future patients rather than being in the best interests of the potential participant (even though results may show that participating is beneficial for the participant). For some, a decision to participate may be affected by simply knowing how information is being collected and used for research, so a greater level of disclosure allows potential participants to access additional information regarding research processes that may be decisive to them⁴⁷.

Physicians are able to make a choice between two treatments where there is clinical equipoise⁴⁸ without telling the patient the risks and benefits of each treatment. If, however, these same two treatments were used in a research study to determine if one was superior, the doctor-researcher must inform the potential participant of all the potential risks and benefits of both treatments. Some experts argue that the discretion to provide tailored information for clinical care should extend to research and the amount of information to be provided to potential participants should remain the decision of the doctor-researcher^{47;49}, especially when the drugs being evaluated are already available for use in other situations.

Disclosure of information in both the clinical and research setting is supposed to facilitate an autonomous decision to be made. Some experts argue that the amount of information to be disclosed in both treatment and research should be based on the level of risk likely to occur⁴⁹, so the amount of information a person considers adequate to make a research or treatment decision may be similar. Research and treatments considered low risk arguably require less information to be provided than those considered high risk⁴⁹. Alternatively it may be that respect for autonomy and

protection from harm are paramount in both clinical care and research settings alike and guidelines for information provision should be similarly strict in both settings.

There are differences of opinion on whether information provision should differ between clinical and research situations. In order to determine how much information should be provided to potential research participants, we need to firstly determine what information potential participants actually use to make a participation decision.

Key points

Information provision in research is tightly controlled by regulatory codes and is overseen by ethics committees and institutional review boards. In clinical care the decision of how much information to provide is left with the treating physician.

Health research requires information to be shared with potential participants to make a decision, whereas in clinical care it is controlled by physicians.

Information provision differs between research and clinical care due to their-

- Respective aims.
 - Clinical care focuses on the well-being of the patients.
 - The focus of research is primarily the acquisition of knowledge to benefit future patients.
- Relative risks.
 - A trial therapy may put the participant at risk of potential unknown side effects and toxicities since the intervention has not been evaluated.
 - Not all research is considered high risk – for example, questionnaire based studies.

Current guidelines for informing research participants

The first published guidelines for informing potential research participants were the Nuremberg Code (1949) that occurred as a result of human rights abuses in Germany during the Second World War. The Nuremberg code provides 10 points that should be observed for all trials, the first of which concerns voluntary consent of participantsⁱⁱ. Following this, an important international statement, the Declaration of Helsinki³⁵, was produced by the World Medical Association in 1964 (with subsequent amendments). This provided further guidelines on what information should be provided to potential research participantsⁱⁱⁱ. In terms of information provision, both The Nuremberg Code and Declaration of Helsinki state that potential participants should be adequately informed about research but do not provide guidance on the detail that should be provided.

Following the Nuremberg Code and Declaration of Helsinki, the International Conference on Harmonisation^{7:50} (ICH) aimed to harmonise clinical research processes, in order ensure that research is conducted safely, effectively and in the

ⁱⁱ Relating to the voluntary consent of participants, the Nuremberg Code states the potential participant:

"should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonable to be expected; and the effects upon his health or person which may possible come from his participation in the experiment."

ⁱⁱⁱ In terms of information provision in research the current version of the Declaration of Helsinki states that:

'In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal.'

most efficient and cost-effective manner⁵¹. The ICH gave rise to the first set of Good Clinical Practice (GCP) guidance to become mandatory for all commercial clinical research. One aspect of GCP concerns the protection of participants and in part covers the information that should be provided to potential participants before consenting to a study. Following ICH guidance, the European (EU) Directive on GCP in Clinical Trials (2001/20/EC) aimed to harmonise research processes within the EU and covered both commercial and non-commercial research. The EU Directive first became UK law on 1st May 2004 by use of statutory instrument 'The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 1031)⁴²'. There are currently four statutory instruments that regulate clinical trials in the UK – 1. Medicines for Human use (Clinical Trials) Regulations 2004 (SI 1031)⁴². 2. Medicines for Human use (Clinical Trials) Amendment Regulations 2006 (SI 1928)⁴³. 3. Medicines for Human use (Clinical Trials) Amendment No. 2 regulations 2006 (SI 2984)⁴⁴ 4. Medicines for Human use (Clinical Trials) and Blood Safety and Quality (Amendment) Regulations 2008 (SI 941)⁴⁵.

One part of GCP concerns information provision to research participants and the ICH GCP provides a list of information that potential participants must be provided with before they consent to research. The National Research Ethics Service (NRES) provide guidance²² to help researchers write PIS's that meet the requirements of the ICH GCP. NRES guidance suggests headings (Figure 1) of information that should be provided in a PIS (where relevant). The guidance suggests that one size of PIS will not fit all and the length should be matched to the complexity and risk of the individual study. It also notes the concern that PIS are becoming increasingly long and complex.

Even with the extensive NRES guidance, researchers often find it difficult to decide how much detail to include in a PIS^{52;53} since each potential participant is likely to find different types of information important and require different levels of detail before they are able to make a participation decision. It is often particularly difficult to know how much information to include in PIS for low risk studies, in particular questionnaire-based studies where less information is likely to be provided in a PIS since reading the questionnaire itself provides information on the types of questions being asked.

Figure 1 - NRES suggested PIS headings²²

What is the purpose of the study?

Why have I been invited to participate?

Do I have to take part / What will happen if I do not want to carry on with the study?

What will happen if I take part / What will I have to do?

Will I be paid expenses or payments for participating?

What are the alternatives for diagnosis and/or treatment?

What are the disadvantages and risks of taking part / Side effects of any treatment received?

Information relating to the radiation and Ionizing Radiation Regulations.

Could participating could cause harm to an unborn child?

What are the benefits of taking part?

What will happen when the research study stops?

What will happen if there is a problem?

Will participation be kept confidential?

What will happen if relevant new information becomes available?

Will by GP/family doctor be involved?

What will happen to any samples I give?

Will any genetic tests be done?

What will happen to the results?

Who is organising and funding the research?

Who has reviewed the study?

Key points

Research in the UK must adhere to four statutory instruments.

One aspect of GCP is the provision of information to potential participants.

The National Research Ethics Service (NRES) provides extensive guidance on how to write PIS that adhere to statutory instruments.

Even with the extensive guidance provided by NRES, researchers often find it difficult to decide on the level of detail to provide in a PIS, especially in low risk interventional research and questionnaire based studies.

2.3 PROBLEMS WITH READING AND UNDERSTANDING PARTICIPANT INFORMATION SHEETS

This section outlines the problems associated with writing and communicating study information and the following section describes the reported interventions that have aimed to improve these processes.

It is essential that a PIS is readable and understandable to research participants (or their representative) if it is to be used to aid decision making. The average reading age of the UK population is estimated to be around that of an educated 9 year old and the need to write PIS's at a suitable level has been noted for decades⁵⁴. Despite this, PIS often contain complex language that is above the recommended reading age^{55;56}. Potential participants often struggle with the language and content of a PIS with even a low level of readability⁵⁷ and the general population finds medical and scientific language particularly difficult to read⁵⁷, so the task of writing a readable PIS can be difficult. The readability of a PIS is directly linked to a potential research participant's understanding of the study⁵⁸. A PIS that requires a high reading level or contains excessive clinical jargon is more difficult to understand than a simple disclosure and participants particularly struggle to grasp scientific concepts such as 'randomisation', 'equipoise', 'risk' and 'probability'^{57;59;60}. Participant demographics can also have an effect on understanding with lower educational levels and reading ability linked to poor levels of understanding⁶¹⁻⁶³. There are many other aspects of a PIS that can influence participant understanding, for example the layout, presentation and length⁶⁴⁻⁶⁶. Investigators have long been required to disclose relevant information to participants, but ethical guidelines make little explicit reference to the need to test understanding.

There are problems with ensuring and demonstrating that potential participants understand the study they are asked to participate in. Firstly, research questions and study details vary between studies and study specific methods limit the ability to generalise or compare consent processes¹. As such, most studies of participant understanding have used measurement strategies tailored toward the individual study and no standardised measure to demonstrate understanding exists¹. Secondly, determining the distinction between recall and understanding of study information is a difficult task. Understanding information suggests an ability to apply the information, whereas recall is the ability to reproduce specific pieces of information⁵⁸. Most methods to assess understanding test the short-term recall of technical information, which cannot be equated with understanding since the ability to repeat information is not the same as being able to apply the information to appreciate the consequences of the decision, i.e. understanding the information²³. Differentiating between recall and understanding is a significant problem and this, together with the lack of a standardised tool, means that most assessments of understanding of study information actually measure recall. As we have already seen, the reason potential participants are provided with study information is so they can use it to make a participation decision.

Another method of assessing understanding is to ask participants if they believe they have a good understanding of the information. Studies reporting this as an outcome often found the majority of participants were satisfied with the consent process and considered themselves well informed. Further examination, however, showed that many were unaware of particular features of research (including the unproven nature of the treatment and uncertainty of benefits to themselves) and were considered to

have low levels of understanding^{60;67-69}. If participants often believe they understand the information when, in reality, they have not fully grasped the ideas, this poses a further problem for determining potential participant understanding. The reason for this difference could be explained by potential participants not actually wanting to know all of the information provided in a PIS and so consider themselves to be well informed because they understand the aspects of the study they wish to know. It may be that the information researchers think participants need to make an informed decision differs from the information that participants think they need to make a decision⁷⁰.

A potential participant's level of understanding requires a compromise between knowing basic study elements and having sufficient knowledge to understand the finer methodological points that are required for someone to fully understand what taking part means²⁵. Potential participants should understand the information sufficiently well enough to be able to make a choice that makes sense for them, in the manner in which they would normally make similar choices²⁵. Allowing potential research participants the chance to ask questions and gather further information to use in the formulation of their decision has been shown as one way to improve their understanding⁶⁷.

There are clear limits to what written information alone can do to overcome the complex barriers to understanding and the quality of communication between the person obtaining consent and the potential participant is fundamental to the consent process⁷¹. Methodologies that assess the consent procedure require greater attention. Without a standardised method to assess understanding, interventions that aim to improve potential participant understanding cannot be meaningfully

compared. Despite this, the next section shows that there have been many attempts to improve participant understanding.

Key points

Potential participants have to be able to understand the information in the PIS in order to make a consent decision.

Potential participants are more likely to understand information in a PIS when its readability level is lower.

It is difficult to determine whether participants have understood the study:

- There are no standardised methods to measure understanding.
- Recall, rather than understanding, is often measured by researchers.

Participants think themselves to be well informed but when tested are often considered by researchers to have low levels of understanding.

The information researchers think participants need may differ from what participants think they need.

Different potential participants are likely to want different types and amounts of information in order to consider themselves adequately informed.

2.4 PREVIOUS EFFORTS TO IMPROVE PIS'S

There have been many attempts to design interventions that improve the readability and understanding of PIS. Two systematic reviews; by Flory and Emanuel (2004)⁶⁴ and Cohn and Larson(2007)⁶⁵; have been published that aimed to evaluate these interventions. In this section, the methods for each of the two systematic reviews are compared and then the results from both reviews are combined and reported together.

Flory and Emanuel (2004)⁶⁴ aimed to determine what interventions actually work to improve potential participant understanding and how well they work. They included all trials published between 1966 and March 2004 that quantitatively compared the understanding of research participants who had undergone a standard consent process (as defined by the individual study; most commonly a PIS followed by a verbal consent interview) with the understanding of participants who had received an intervention. Thirty publications reporting 42 trials were identified and included in the review. Each study reported four quality criteria; if it was randomised, included a real or simulated consent process, number of participants and whether it was published in a peer-reviewed journal. Peer-reviewed randomised trials in a real setting with relatively large enrolment (size not defined) were given the greatest validity. The primary outcome was the significance of differences ($p < 0.05$ = statistically significant) between understanding scores for control and intervention groups.

Cohn and Larson (2007)⁶⁵ aimed to critically analyse studies published between 1996-2007 about potential participants' understanding of study information in research and to identify promising intervention strategies. Each study was given a

quality score based on its performance on six quality indicators; sampling method, use of controls/comparison group, response rate, outcome measurement, clear description of the intervention/comparison and method and using a statistical method appropriate to the study. Ten interventional studies were identified, although eight of these were included in the review by Flory and Emanuel.

Interventions from the two reviews were categorised into five groups; multimedia, enhanced PIS, extended discussion, test/feedback and other approaches. The intervention could be in place of or in addition to the standard PIS. All studies aimed to improve the level of understanding of participants. As discussed previously (Section 2.3), it is likely that these studies do not report the level of understanding of participants since current tools to measure 'understanding' actually measure recall. The term 'understanding' (rather than 'recall') will remain the term used to report results in this PhD, however, since studies report what is currently understood (with the current tools available) by most researchers to be the measure of understanding.

Multimedia interventions

Multimedia interventions used any form of computer or video technology to present information to potential participants. Twelve multimedia interventions were compared to standard PIS/consent processes to determine if the intervention increased the potential participants' understanding of the study. Seven interventions were supplementary videos⁷²⁻⁷⁶, three were computerised presentations^{72;76;77}, one a supplementary touch screen computer presentation⁷² and one an interactive computer program⁷⁸. Studies of these twelve interventions provided little evidence to suggest that a multimedia presentation of study information improved potential

participant understanding since only one study found a statistically significant improvement ($p=0.01$)⁷⁷.

Enhanced PIS interventions

Interventions were classed as 'enhanced PIS' interventions if the study PIS was thought to be improved in some way. Sixteen enhanced consent form interventions were compared to standard PIS/consent processes to determine if participant understanding of the study was improved. Five PIS were enhanced by re-arranging the information in the PIS but not removing any information^{72;76;79;80}, three by improving readability alone⁸¹⁻⁸³, three by improving readability, providing less detailed information and re-formatting information^{63;84;85}, two by reformatting and providing less detailed information (but not improving readability)^{86;87}, two by providing less detailed information^{88;89}; and one by allowing a consumer group to revise the study PIS⁹⁰.

Understanding was thought to be improved by reformatting the PIS and/or improving readability to be more accessible^{79;81;86;87}, by providing less detailed information^{88;89} and allowing patient input to the design of the PIS⁹⁰. Interestingly, none of the interventions that combined improving readability, providing less detailed information and re-formatting the information in the PIS improved understanding^{63;79;84}. Of the seven interventions that showed a statistically significant improvement in understanding ($p<0.001$ ⁸⁶⁻⁸, $p<0.005$ ⁸¹, $p<0.02$ ⁸⁹, $p=0.03$ ⁹⁰, $p<0.05$ ⁷⁹), five evaluated hypothetical consent processes where the PIS was the only means to convey study information to participants. In most real situations potential participants also receive verbal information about the study, which may dilute the effect of the PIS on

understanding. Any effect of improvement to understanding in the hypothetical studies, then, is more likely to be indicative of the effects of the PIS on level of understanding.

Extended discussion interventions

Extended discussion interventions evaluated the use of a meeting with a researcher or neutral educator to discuss the information in the PIS. Six^{62;73;91-94} extended discussion interventions were tested that aimed to improve study understanding. Interventions tested were a 30 minute semi-structured telephone conversation with a research nurse⁹¹, detailed repetition of clinical trial information⁹², three 40 minute meetings with a counsellor⁹³, a meeting with an independent educator⁷³, a meeting to discuss the trial with the enrolling physician⁹⁴ and a video followed by discussion with a consent educator⁶². Three interventions showed a statistically significant improvement in understanding ($p < 0.001$ ⁹¹⁻⁹³) and two showed a trend towards improved understanding ($p = 0.054$ ⁷³; $p = 0.08$ ⁹⁴). It is likely that encouraging potential participants to have an extended discussion about the information included in a PIS improves their understanding of that information.

Test and feedback interventions

Five interventions^{80;95-97} tested participants' understanding of study information, provided feedback for incorrect answers and then repeated the understanding questionnaire. Understanding was shown to be improved in all five studies^{80;95-98}.

Any other approaches

A series of five other interventions^{72;80;98-100} not classifiable into any other category were identified, two of which were combinations of other approaches (extended discussion, computerised presentation and other simple teaching aids¹⁰⁰, and extended discussion, additional pamphlet and other teaching aids⁹⁸). These both showed a statistically significant improvement in understanding ($p < 0.05$ ⁹⁸, $p = 0.001$ ¹⁰⁰). The other three interventions included allowing potential participants to experience the tests (multi-frequency bioelectrical impedance analysis and questionnaires) used in the study before deciding whether to participate⁹⁹, to have a neutral facilitator present at the potential participant's meeting with investigator⁸⁰ and educational vignettes included with the PIS⁷², all of which did not show a statistically significant improvement in understanding.

Of all the tested interventions in the two reviews, re-arranging the information in a PIS, providing less detailed information and allowing potential participants to have extended discussions with researchers showed an improvement in understanding that was both clinically relevant and statistically significant. Part of this PhD tested a developing intervention - an interactive participant information sheet (IIS) - that allowed participants to choose the level of detail of study information they wanted. Since results from these reviews showed that reformatting and providing less detailed information improves a potential participant's understanding of study information, it was hypothesised that this intervention would also improve participant understanding.

The IIS intervention utilised the Internet to recruit and provide information to potential participants, so the next section of this chapter outlines current use of the Internet in research.

Key points

Two published systematic reviews^{64;65} evaluated interventions that aimed to improve the readability and understanding of PIS.

Understanding was found to be improved by –

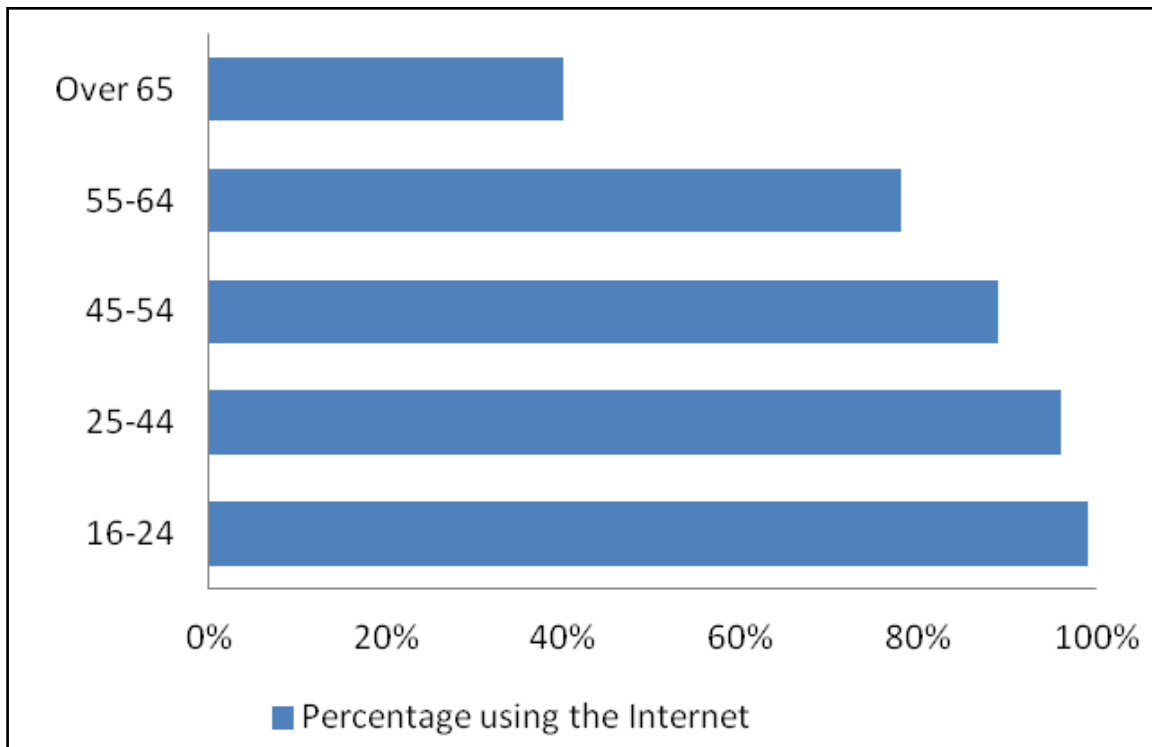
- Re-arranging the information in a PIS.
- Providing less detailed information.
- Allowing potential participants to have extended discussions with researchers.

2.5 THE ROLE OF THE INTERNET IN RESEARCH

This section of this chapter explores the use of the Internet in medical research and outlines the advantages and disadvantages of conducting research online when compared with traditional non-Internet based methods. The interactive nature of the Internet makes it an attractive method for conducting research and there are many advantages, as well as some disadvantages, of using the Internet to facilitate research.

The last 15 years have seen a substantial increase in the proportion of the population using the Internet. According to data collected between 2000 and 2012 by the Office for National statistics (ONS)¹⁰¹⁻¹⁰³ 99.3% of 16-24 year olds now use the Internet (up from 69% in 2000) and 80% of households in the UK have an Internet connection (up from 25% in 2000). Internet use declines with increasing age (Figure 2) and use is affected by location (85.9% London and the South East vs. 72.7% Northern Ireland), marital status (92% single vs. 81% married), occupation (91% managerial/professional occupations vs. 67% semi-routine/routine occupations), health (86% healthy vs. 61% disabled), education (97% >degree level vs. 45% with no formal qualifications) and income (98% >£41,000 vs. 69% income <£10,399).

Figure 2 – Internet use by age group¹⁰¹



As the proportion of the population using the Internet has increased so have its uses and many day to day tasks such as banking are now carried out online^{101;104}. A growing number of people search the Internet for health related information and often use this to self-diagnose and self-medicate ailments^{105;106}. The Internet is also used regularly in medical research with tasks from writing a protocol to data entry utilising the Internet¹⁰⁷⁻¹¹⁹. Since one of the earliest pieces of online research, a web-based survey on the effects of ulcerative colitis on quality of life by Soetikno et al in 1996¹²⁰, Internet research methodology has advanced substantially. Clinical drug trials have been conducted electronically where participants were recruited, completed study questionnaires, had study medication automatically dispensed to them (via mail) and logged adverse events online^{118;121-123}.

Designing research and writing a study protocol often uses information sourced from the Internet. Online medical literature databases are routinely used to review current literature¹⁰⁷⁻¹¹⁰, requirements for ethical approval can be located¹¹¹ and experts in the field can be contacted for advice on specialised matters¹¹². The Internet can be used to recruit potential participants, for example, via websites that list clinical trials by disease type¹¹³⁻¹¹⁶, by putting links to a research websites on social network sites^{112;117}, or by using email mailing lists to send study information to large numbers of addresses¹¹².

There is also scope for using the Internet to provide study information to potential participants. Once potential participants are directed to a study website it can be used to provide them with study information and screen them for eligibility¹¹². A PIS presented online may have many advantages over a paper one. It could, for example, be made to be interactive so those who want lots of background information could easily access it, or potential participants with sight problems could increase the size or change the colour of the text to allow them to see it more easily¹¹⁷.

Once the potential participant has read the information and decided they would like to take part, an online eligibility-screening questionnaire^{112;118} may be used to automatically determine if they are eligible, which could reduce trial personnel involvement and related costs¹¹². Traditionally, study participants have signed consent documents by hand, but, new technologies mean digital signatures¹²⁴⁻¹²⁶ could be used for Internet based studies. This would make all aspects of participant recruitment achievable online.

Many aspects of study administration are already conducted using the Internet, for example, randomisation, communication and data collection. In randomised controlled trials where it is common to use a central co-ordination centre for randomisation, the Internet often replaces expensive 24-hour phone services with an online service where participants have a study group randomly allocated to them by a computer¹¹². Study websites may be used by potential participants and study personnel to access study information, contact details and download required paperwork and a section is often made secure (by password protection) to allow trial personnel/participants to communicate^{112;118;119}. Data can be remotely entered into a central database using Internet technology and advantages of this include the data being immediately accessible for analysis, time savings due to fewer steps in the data collection process and reduce handling and storage costs due to the near elimination of paper source documents^{112;127}.

There are functionality benefits to conducting research online. For example, web-based forms used to collect participant responses to online questionnaires have advantages over their paper-based alternative, such as automatic collating of information^{112;128;129}. The ability of web-based forms to be interactive allows questionnaires to be actively tailored towards population subgroups; for example, text can be translated at the click of a button. Missing data can be minimised by configuring web-based forms to automatically reject incomplete questionnaires^{130;131} and scripting language can build dynamic questionnaires that randomise certain items to minimise the risk of systematic influences of the order of items upon responses¹³².

Online research can be conducted confidentially and anonymously, providing the correct electronic safeguards are in place. Web-based forms can allow questionnaires to be completed anonymously as technological identifiers (such as IP addresses) can remain uncollected, or they can be placed in a password protected area of the Internet to protect personal information. Previous research has shown that Internet completers skipped fewer sensitive questions and were less likely to conform to social desirability when compared with those completing a mailed questionnaire^{128;133;134}. Participants may feel more comfortable completing personal questions online than for a postal survey because of the “increased perception of anonymity”¹³³.

Online questionnaires can also speed up the research process; for example, study information and questionnaires can be distributed to large numbers of potential participants very quickly and at a lower cost than traditional paper ones^{112;118;128;129;135;136}, and they allow rapid prototyping and pilot testing of instruments (for example an automatic time stamp can be used to calculate the time needed to complete the questionnaire)¹³¹.

Response rates and participation rates can be calculated by assigning a unique ID to every questionnaire viewer (a cookie) and multiple responses from the same user can be filtered out by removing questionnaires completed at the same computer¹³¹. Calculating response rates to online questionnaires can be tricky, however, and there are many concerns over who has received, opened and completed the questionnaire¹³⁷.

With potentially reduced costs, global access and real time data collection, the potential size of research studies that can be practically implemented is increased by using the Internet and global studies could be run in shorter time frames. There are, however, disadvantages to conducting research online. The most significant disadvantage is the potential for selection bias due to the non-representative nature of the Internet population^{101;138;139}. Considering whether the topic chosen for study is suitable for the Internet population should be the first consideration when deciding whether to conduct online research. An online questionnaire would be unsuitable if the target population were elderly with major morbidities, for example. Several studies have tested the validity of Internet-based surveys by comparing their results to identical traditional paper-based studies and they seem to suggest that the validity and reliability of data obtained online are comparable to those collected by conventional methods^{140;141}. This may mean results can be collected online that are generalisable to the population as a whole, but this is only likely to occur when the majority of the study sub group population have Internet access. The generalisability of results collected using Internet technologies remains a limitation for research in populations where the majority do not have Internet access.

In a population where most were competent computer and Internet users, Pealer et al¹³³ found no statistically significant differences in participants' demographics or response rate between those completing a postal questionnaire and those completing an Internet survey and other studies have shown similar results^{139;142}. It can be expected that if the trend of increasing Internet access continues, it will eventually reach a point where Internet access is as common as postal access. When this point is reached, conducting research online would have no greater risk of un-generalisable results than conducting the survey by post or by telephone.

Paul et al¹¹² outline other potential disadvantages of conducting research using the Internet. Online communications may not be as secure as more traditional means (telephone, fax and mail) and some participants and study centres may decline involvement because of concerns over the security of online data. Internet studies often require experienced computer professionals to set up and maintain the online system. If the study experiences problems with the online system, potential participants may be deterred from participating if they are unable to access the website the first time they try. Studies may need to have paper-based back-ups for all aspects of research conducted online, in-case Internet connection and/or online systems fail. Finally, the expense of developing an online system may not be feasible for smaller studies.

There are many advantages to conducting research online that make it an attractive prospect. This PhD considers two aspects of Internet research; electronic communication and provision of electronic study information.

Key points

Many people use the Internet for a variety of daily tasks and use of the Internet in research is a growing area.

Whole research studies can now be conducted online; from writing a study protocol to analysing data; and tasks are often much quicker using electronic methods.

There are many advantages to using the Internet in research including flexibility of data provision, automatic collating of information, minimising missing data, and reduced costs of distribution, completion and return of research items such as questionnaires.

Disadvantages of conducting research online include the generalisability of the online population, potentially less secure communications and the need for experienced computer professionals to set up and maintain online systems.

2.6 USING THE INTERNET TO PROVIDE STUDY INFORMATION TO PARTICIPANTS – A STUDY BY ANTONIOU ET AL

A study by Antoniou et al⁶ piloted a new way to provide study information to potential participants and aimed to explore how information is used to make a decision about whether to participate in research. The study was embedded within a nation-wide population-based study investigating the development of twins during early childhood and involved the completion of an electronic questionnaire accessed via the study's website by a study participant. Participants of the 'development of twins' study were either parents or legal guardians of twins.

Before deciding whether to participate in the development of twins study, potential participants were directed to an interactive PIS that allowed them to access up to three levels of information 'unfolding' on request from each of six frequently asked questions (FAQ's). Participants clicked a (+) sign next to the FAQ in order to access the information. Level one gave them a broad understanding of the project and what would be required of them if they chose to participate. The information in level two was longer and comparable to the level of detail required in a standard REC reviewed PIS. Level three was more sophisticated and contained links to external sources of information, such as academic articles. The information that potential participants chose to access, along with how long they spent on it, was tracked. This allowed the authors to determine what information was accessed by each participant deciding whether to complete an online questionnaire and to apply average reading times to the time spent on each level. Demographics collected enabled the amounts of information accessed to be compared between sub groups of the population. Results showed that whilst the first level of information (for at least one FAQ) was

accessed by 70 to 82% of participants, only 9 to 18% accessed level two (for at least one FAQ) despite this being the level of information RECs suggest participants should be given and only 3 to 12% accessed all three levels of information in any FAQ. On average participants spent more time reading information about why the survey was being conducted. No overall statistically significant differences were seen in the pattern of accessing and the time spent reading the information between ethnic groups, the educational level of participants, age or gender, although a trend was seen for some individual FAQ's.

As well as collecting information about what information participants accessed, participants were asked questions about the information they read in the PIS and were asked to choose options that applied to them from a list provided. The results of this questionnaire often conflicted with what participants actually did. For example, 4% (20/552) said they did not click any of the (+) sign options whereas the activity monitored showed this to be 18%. Interestingly, 20% (93/552) said they wanted more information about what would be done with the results of the study, even though only 9% chose to click through to the second and 6% to the third level of information for the corresponding FAQs.

The majority of the potential participants sought very little information before making a decision about whether or not to participate in the questionnaire-based study, and a clinically significant minority (18-30%) had accessed no information at all.

This study by Antoniou et al provided useful information as to what information participants want to know when they are deciding whether to participate in questionnaire-based research where completing the questionnaire itself provides

direct information about what participating entails. As the authors acknowledge, study results are not readily generalisable to all potential participants in clinical research since the study population were all parents of young twins and were mostly white, well-educated women. The authors also acknowledge that the study also only collected the information from those who took part in the study and not those who did not choose to participate, and results may differ for these two groups⁶.

Results from this study also only concern what information participants of low risk questionnaire-based studies wanted to know and the amount of information participants of other studies - particularly those involving an intervention or greater risks - want to know may be very different. Further research needs to be conducted to determine if these results are generalisable to the whole research participant population. This PhD aims to add to this knowledge base by developing the Interactive Information Sheet (IIS) used by Antoniou et al and using it to collect the information accessed by participants deciding whether to participate in low risk interventional research.

Key points

Antoniou et al designed an 'unfolding' electronic information sheet that enabled them to observe the information accessed by potential participants before they participated in an Internet-based questionnaire study.

The participants chose to access very little information before participating.

Reported and actual patterns of information access differed, suggesting that asking participants what information they use to make a participation decision may not be an accurate way of determining what they did use.

Results of this study are not generalisable and further research is required.

2.7 AIMS AND OBJECTIVES OF THE PHD

Aims of the PhD:

To gather further evidence of the topics and level of detail of information potential participants access when deciding whether to participate in a piece of low risk interventional research, and to determine the feasibility electronic information provision.

Research questions:

1. What does the current evidence suggest potential participants want to know when they are deciding whether to participate in research?
2. Is electronic information provision in research feasible?
3. What information did potential participants access when they made a decision about whether to participate in a piece of low risk interventional research?
4. What are the implications for the future of information provision given answers to research questions 2 and 3?

Objectives:

1. Systematically review the literature on what information potential participants want to know when they are deciding whether to participate in research by:
 - i. Devising a systematic review study protocol
 - ii. Using the protocol developed in (i) to conduct a systematic review of the literature

2. Devise and conduct a study that allows a) participants to be contacted electronically b) study information to be provided electronically and c) collects data on what information potential participants accessed when making a participation decision for a piece of low risk interventional research by:
 - iii. Identifying a suitable parent study in which to embed the study
 - iv. Calculating a sample size for the information provision study
 - v. Developing a study protocol
 - vi. Designing a website to host the IIS and develop programming code required to record the information accessed
 - vii. Testing the website designed in (vi) for errors and participant usability
 - viii. Identifying the information to be included in the IIS using the results of the systematic review (1), interviews with potential participants and key research staff and discussion with experienced academics
 - ix. Designing a questionnaire to determine understanding and satisfaction of participants with the information provided
 - x. Obtaining ethical approval for conducting the study
 - xi. Collecting and analysing data on the feasibility of electronic information provision and the information accessed by potential participants

3. Consider the implications of study results from objective 2 by
 - xii. Designing a PIS using the information potential participants wanted to know from results collected from objective 2 and the information current guidance stipulates participants need to know, for the parent study identified in (iii)
 - xiii. Gathering expert opinions on how to take forward the research conducted for this PhD

3 SYSTEMATIC REVIEW OF THE LITERATURE

This chapter will answer the first research question of the thesis and meet objective one. It will establish the evidence base for the information that research participants want to be included in a PIS. As was discussed in the previous chapter, valid consent to research requires potential participants being given the information they need to make a decision. The information potential participants want to know may be different to the information experts think they want to know⁷⁰. The systematic review reported in this chapter identified all literature reporting what information research participants wanted to know before they were able to make a participation decision. It then compared this evidence base to the information that NRES²² guidance suggests should be included in a PIS.

3.1 AIMS

To assess the level of detail and the types of information potential research participants report they should be given in order to make a decision regarding participation in medical research.

To assess how this evidence compared with the kinds of information that NRES guidance suggests participants should be given.

3.2 METHODS

Methods, including inclusion criteria and analysis plan, were specified in advance and documented in a protocol as detailed below.

3.2.1 INCLUSION CRITERIA

Any primary research published between 1950 and 27th October 2010 with no limit to language, participant age, medical condition or participant group (including vulnerable participants). Literature was included if it asked potential research participants to indicate how much/which types of information they wanted to be told about a research study or to rate the importance of a specific piece of information.

Studies reported in multiple journals were included only once with the latest known reference used. Where reports noted different aspects of the research, results were included from all publications. The review was limited to studies of participant opinion, excluding studies of health care professional or other expert opinion.

3.2.2 OUTCOME MEASURES

The percentage of participants that wanted to know a specific item of information about a study (spontaneous and prompted responses) or rated a piece of information as important. Qualitative information, for example from focus groups, where participants indicated what information they wanted to know.

3.2.3 SEARCH METHODS

Electronic databases

An information specialist from the University of Birmingham library helped to design the search strategy used for this systematic review. The search of electronic databases combined Mesh terms 'Patient', 'Research Subjects', 'Consent forms', 'Informed Consent' and 'Research ethics' with terms relating to information provision (Figure 3). The search was applied to Medline (Ovid platform)¹⁴³ and adapted for Web of Science¹⁴⁴, Applied Social Sciences Index and Abstracts on the Web (ASSIA)¹⁴⁵, Sociological Abstracts¹⁴⁶, The Health Management Information Consortium (HMIC)¹⁴⁷ and the Cochrane Library¹⁴⁸. The last search ran on the 27th October 2010.

The types of literature included in each electronic database were:

- 1) Medline (Ovid)¹⁴³: A database of life sciences and biomedical literature that includes medical journals and literature from academic journals within the subjects of medicine, nursing, pharmacy, dentistry and health care. It includes literature from 1950 to the present day.
- 2) Web of Science (WoS)¹⁴⁴: A platform providing access to seven databases covering journals, book-based and journal conference proceedings within the subjects of science, technology, social sciences, arts and humanities. It includes non-medical journals not indexed by Medline. It includes literature from 1900 to the present day.

- 3) ASSIA¹⁴⁵: Includes topics of literature such as social services, psychology, sociology, economics, politics, race relations and education not indexed by Medline or WoS. It includes literature from 1987 to the present day.
- 4) Sociological abstracts¹⁴⁶: A database of literature from disciplines within social and behavioural sciences not indexed by other databases. It covers literature from 1952 to the present day.
- 5) HMIC¹⁴⁷: A platform that provides access to the Department of Health's Library and Information Services, and the King's Fund information and Library Service. It includes literature relating to health and social care management information, health service policy that is not included in other databases searched. The majority of the literature included in this database ranges from 1983 to the present day.
- 6) The Cochrane Library¹⁴⁸: The Cochrane Library is a collection of six databases that contain evidence to inform healthcare decision-making (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Cochrane Methodology Register, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database and the NHS Economic Evaluation Database). It covers literature from 1988 to the present day.
- 7) Index to Theses¹⁴⁹: A comprehensive listing of around 500,000 thesis titles and abstracts that have been accepted for higher degrees by universities in Great Britain and Ireland, since 1716.
- 8) Grey literature includes papers, reports, technical notes or other documents produced and published by governmental agencies, academic institutions and other groups that are not distributed or indexed by commercial publishers but

nevertheless may include information relevant to this review. The following sources of grey literature were accessed:

- a) System for Information on Grey Literature in Europe (SIGLE)¹⁵⁰: An open access database of bibliographical references of reports and other grey literature produced in Europe. Examples of grey Literature included in this database are technical or research reports, doctoral dissertations, conference papers and official publications. It covers topics of pure and applied science and technology, economics, other sciences and humanities.
- b) GreyNet International; The Grey Literature Network Service¹⁵¹: Provides listings of potential places to search for grey literature.
- c) Health Information Resources (formerly National Library for Health)¹⁵²: Provides access to medical documents, including evidence based reviews, guidance documents and reports, specialist collections for specific areas of medical practice, health care databases (for example HMIC and Medline), collections of medical images, and up-to-date drug libraries (for example the British National Formulary (BNF)).
- d) UBIRA¹⁵³: The ePapers repository contains research material produced by members of the University of Birmingham. It includes working papers, images and contains material that has not been through a formal peer-review process.

Figure 3 - Search strategy: MEDLINE (OVID)

```
"research patient*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
exp Patients/
"participant*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
exp Research Subjects/
1 or 2 or 3 or 4 or 5 or 6
exp Consent Forms/
"information leaflet*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
"information sheet*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
(consent adj4 form*).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
8 or 9 or 10 or 11
exp Informed Consent/
exp Ethics, Research/
"medico legal".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
"medicolegal".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
exp Disclosure/
(informed adj4 consent*).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
(research adj4 ethic*).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
"disclos*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
"want to know".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
"want*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
"information*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
"require*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
"desire*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
"need*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
"choice*".mp. [mp=title, original title, abstract, name of substance word, subject heading word]
23 or 24 or 25 or 26 or 27 or 28
7 and 21 and 29
12 or 22 or 30
31 and "Humans" [Subjects]
```

References and cited article lists

Secondary citations were identified from reference lists of included papers. Medline (Ovid Platform) was also used to search for any literature citing articles identified for inclusion in the review, and all returned references were included as secondary citations.

Expert authors

Expert authors were identified as authors of papers included in the review. A list of expert authors was compiled (from authors of identified included papers) and contacted by email. They were asked to identify articles relevant to this systematic review and identify further expert authors to contact. A reminder email was sent after one month if they did not respond.

Key Journals

Some ethics and law journals may not be indexed on the electronic databases searched because they are not classed as medical journals. Given the nature of the review topic, these types of journals had the potential to include relevant articles and, therefore, needed to be searched. Relevant journals were identified through Internet search engines 'www.google.com' and 'www.google.com/scholar', with searches using the key words 'consent' and 'research'. Any journal that published papers within the subject of research ethics was classified as a relevant journal for this review. Of the 33 relevant journals identified (Table 1) thirteen were not indexed on electronic databases, although tables of contents were available electronically and were reviewed (from the first issue available or from 1950, whichever was earlier) to identify papers for inclusion.

Table 1 - Key Journals identified

Journal Title	Indexed in an electronic database?	Database
Acta Bioethica	Yes	Web of Science
American Journal of Bioethics	Yes	Medline
Bioethics	Yes	Medline
Bioethics Bulletin	No	-
BMC Medical Ethics	Yes	Medline
Cambridge Quarterly of Healthcare Ethics	Yes	Medline
Community Ethics	No	-
Eubios journal of Asian and International Bioethics (EJAIB)	No	-
Ethics and Behaviour	No	-
Ethics and Medicine	No	-
Hastings Centre Report	Yes	Medline
Health Ethics Today	No	-
Health Expectations	Yes	Medline
JONA's Healthcare Law, Ethics and Regulation	Yes	Medline
Journal of Clinical Ethics	Yes	Medline
Journal of Law and Medicine	Yes	Medline
Journal of Law, Medicine and Ethics	Yes	Medline
Journal of Medical Humanities	Yes	Medline
Journal of Medicine and Philosophy	Yes	Medline
Journal of Medical Ethics	Yes	Medline
Kennedy Institute of Ethics Journal	Yes	Medline
Medical Law Review	Yes	Medline
Medicine, Health Care, and Philosophy	Yes	Medline
New Zealand Bioethics Journal	No	-

NTM: International Journal of History and Ethics of Natural Sciences, Technology and Medicine	Yes	Medline
Nursing Ethics: An International Journal for Health Care Professionals	Yes	Medline
Online Journal of Health Ethics	No	-
Penn Bioethics Journal	No	-
Philosophy, Ethics and Humanities in Medicine	Yes	Medline
Princeton Journal of Bioethics	No	-
Theoretical Medicine and Bioethics	Yes	Medline
American Medical Association Journal of Ethics	No	-

Internet search engines

Other relevant articles were identified by searching two Internet search engines (Google and Google Scholar) using the key words 'Patients', 'Informed consent' and 'Research'. Only the first 30 results (3 pages) of each search were reviewed because article relevance diminishes substantially with each page of results¹⁵⁴.

3.2.4 *STUDY IDENTIFICATION*

Given the unspecific nature of search terms in the research questions, a broad searching strategy was implemented to maximise the possibility of identifying all relevant literature. For example, editorials and letters were not eligible for inclusion in the review but were included in the search to identify expert researchers in the field.

MeSH terms were used in conjunction with key words and wildcards. The first 500 references retrieved from Medline were reviewed to identify any key words that commonly appeared in relevant papers and the search strategy was refined. There were no key words found consistently across irrelevant papers that could be incorporated to narrow the searching strategy. Figure 3 shows the search strategy that was used to conduct the Medline search and adapted for other electronic databases.

Due to the broad search strategy implemented there was a large number (n=11,943) of unique references retrieved. Decisions for inclusion, therefore, utilised three phases of screening with irrelevant references being excluded at each phase. Phase one involved reviewing reference titles alone, phase two involved reviewing abstracts and phase three involved reading full papers to determine if they met study inclusion criteria.

Phase one – Title reading

Titles were scanned for an indication the paper met the inclusion criteria. References were included in phase two if they appeared to refer to any of the following topics:

1. Information research participants wanted to know.
2. Information patients wanted to know about treatment.
3. Ways to alter or improve informed consent procedures.
4. Addition of information to consent forms/patient information sheets (e.g. adding a rare complication to an information sheet).
5. Ways to improve recruitment.
6. Participants/patients asked to help with the design of a participant/patient information sheet.

Phase two – Reviewing Abstracts

Phase two involved reading the abstracts of references that had not been excluded in phase one. References were marked for inclusion in the next phase of screening if they appeared to meet the inclusion criteria for the full review (where inclusion could only be confirmed once the full paper had been read), if no abstract was available, or it was not clear from the abstract whether it met inclusion criteria.

Phase three – Reading full papers

Full papers of the references identified from phase two for inclusion in phase three were accessed and reviewed and those meeting the inclusion criteria were marked for data extraction.

3.2.5 VALIDATION OF SCREENING

Validation was independently conducted on approximately 10% of the references identified from electronic databases. Reference Manager was used to store citations, and give each reference a unique ID. Figure 4 shows the agreement rate between the two reviewers. The two reviewers agreed that 91 references should be included (thereby excluding 870 papers) in the next phase of screening. A kappa calculation determined an inter-rater agreement of 80.0%¹⁵⁵. Using figures from Table 1, the equation used to calculate kappa was:

$$K = [\text{Pr}(a) - \text{Pr}(e)] / [1 - \text{Pr}(e)] = [0.96 - 0.8] / [1 - 0.8] = 0.16 / 0.2 = 0.80 = 80.0\%$$

$$\text{Pr}(a) = [91 + 870] / 997 = 0.96$$

$$\text{Pr}(e) = p(++) + p(--) = 0.01 + 0.79 = 0.8$$

$$p(++) = ([91 + 16] / 997) \times ([91 + 20] / 997) = [107 / 997] \times [111 / 997] = 0.01$$

$$p(--) = ([20 + 870] / 997) \times ([16 + 870] / 997) = [890 / 997] \times [886 / 997] = 0.79$$

There were 36 references where the reviewers disagreed about inclusion.

- 16 references were marked for inclusion in the next phase of screening by reviewer one but excluded by reviewer two. Since reviewer one (the author of this thesis) completed the full screening process on all references, if this reviewer included more papers in each round of screening, it would not have meant relevant papers were missed. These papers, therefore, needed no further consideration.
- 20 references were excluded by reviewer one but included by reviewer two. This initially suggested a potential 2% error rate (20/997) but when the abstracts were reviewed, none of the papers were relevant.

Figure 4 – Agreement rate between reviewer one and two for phase one reference screening

		Reviewer 1 (HK)	
		+	-
Reviewer 2 (TK)	+	91/997	20/997
	-	16/997	870/997

Key:

+ indicates the reviewer thought the paper should have been included

- Indicates the reviewer thought the paper should have been included

3.2.6 DATA EXTRACTION

Data were extracted from papers using a pre-defined data extraction sheet, designed to extract quality indicators from papers (Appendix 9.3). Items extracted were year of publication, country of study, study design, study setting, sampling strategy, participant group, analysis procedure, number of participants, response rate and results relevant to this systematic review. The data was extracted (by the author of the thesis) and 10% were checked for accuracy by a colleague (Thomas Keeley). Disagreements were resolved by discussion.

Themes used to categorise the data were based on NRES recommended headings²² with similar headings combined to make one variable.

3.2.7 *STUDY SELECTION*

Figure 5 provides an overview of how many references were identified from each source.

Electronic Databases

The breakdown of the references identified by each electronic database is presented in Table 2 and shows that each of the electronic databases identified unique references. Once the latest update was conducted (on 27th October 2010), a total of 10838 unique references were identified from searching electronic databases. Fourteen of these references were identified for inclusion in the review.

Table 2 - References identified from each electronic database

Database Name	No. references identified	No. after duplicates deleted	% Unique references	No. papers included in review
Medline	6322	6322	Reference source	13
ASSIA	953	833	87.4%	1
Sociological abstracts	1181	957	81%	0
HMIC	695	550	79%	0
Web of Science	2884	1380	47.9%	0
Grey Literature	204	204	100%	0
Thesis	592	592	100%	0
Total	12831	10838		14

References and cited article lists

Searching reference lists of relevant articles provided 404 references and an additional 69 were identified by reviewing the cited article lists of relevant articles. All 473 reference titles were examined for relevance and 42 met phase two inclusion criteria. Twenty-two were duplicates of references identified by the electronic database search and a further twenty were excluded after reviewing the abstract. No unique references meeting inclusion criteria were identified by this method.

Expert authors

Fourteen expert authors were identified (corresponding authors from included papers) and written to. Twelve responded to an email request with relevant papers and three identified three further expert authors who all responded to our correspondence. Thirty-seven references were identified; 13 were duplicates from the electronic database searches and 24 did not meet inclusion criteria. No unique references meeting inclusion criteria were identified by this method.

Key Journals

Eight potentially relevant articles were identified from hand searching journal content pages of the 13 key journals not indexed on electronic databases (Table 1); none met inclusion criteria once full papers were read.

Internet search engines

The search engines Google Scholar (returned 896,000 results) and Google (returned 11 million results) returned 11,896,000 results. The first 30 results from each search engine were reviewed for relevance; however, none of the articles or websites retrieved identified any papers relevant to the review that had not been identified from other sources.

Total number of references identified from all sources

A total of 13379 citations were identified. Once duplicates had been deleted there were 11943 unique references to be screened (Figure 5). Of these, 11291 were discarded on the basis of the title alone (phase one screening), for example, 'Should non-invasive ventilation be used with the do-not-intubate patient?'¹⁵⁶ and 'Sex

offender re-entry courts: a cost effective proposal for managing sex offender risk in the community¹⁵⁷.

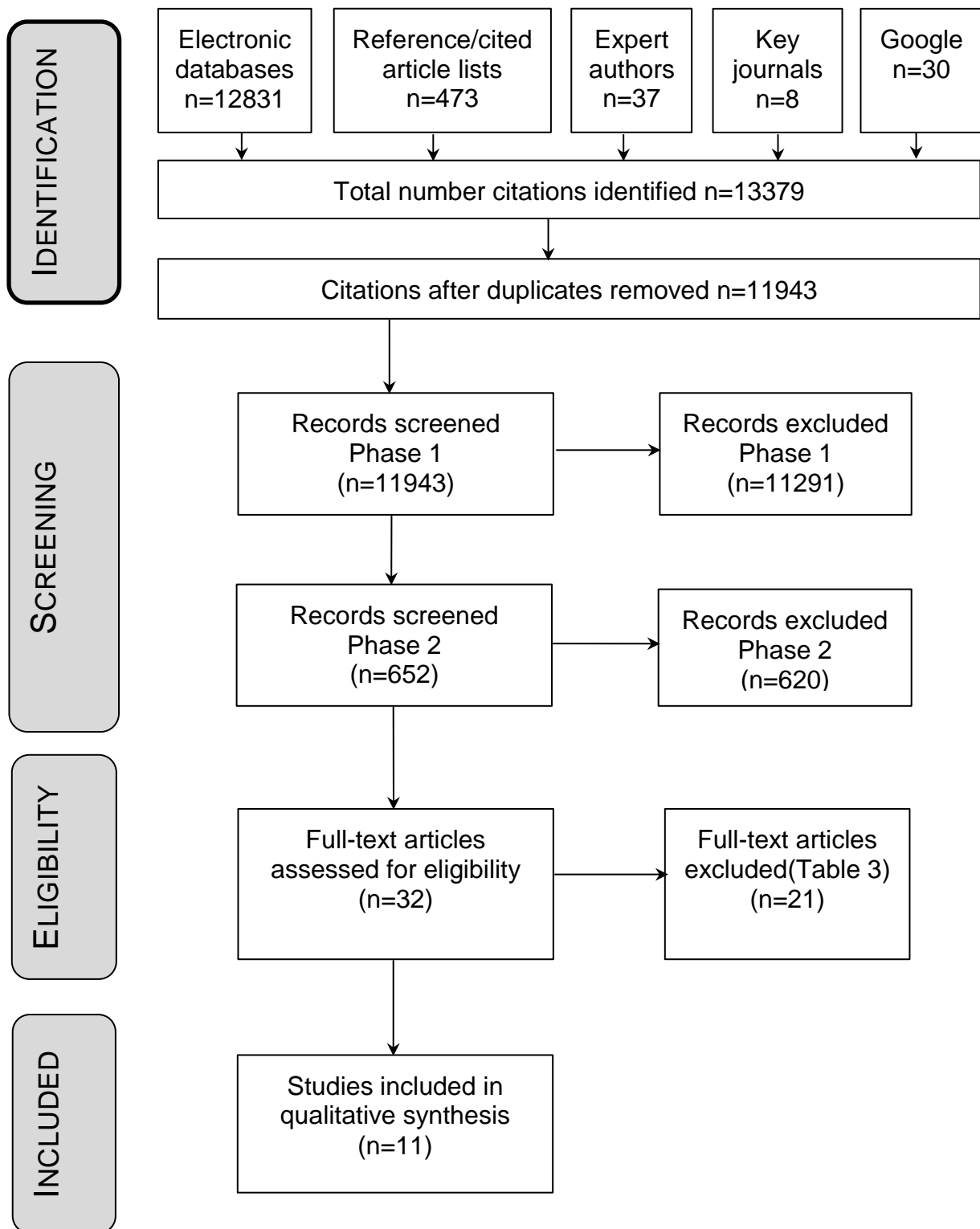
There were 652 references included in phase two, of which 620 (95.1%) were discarded because the abstracts confirmed that they did not meet the inclusion criteria. Types of studies discarded at this phase included those asking patients to comment on what information they wanted to know about their treatment in routine clinical care, studies asking health professionals what information they thought participants should be told and studies that determined readability of participant information sheets and participant understanding of them.

There were 32 papers that proceeded to phase three, of which 11 papers met the inclusion criteria (and 21 were excluded). An example of a paper excluded at this phase was entitled 'Consent of use of personal information for health research: do people with potentially stigmatizing health conditions and the general public differ in their opinions?'¹⁵⁸. On reading the abstract it seemed the paper may meet inclusion criteria, but when the full paper was read the study aim was to determine whether patients thought they should have to give their consent for their details to be used in various different types of research; it did not ask them what they wanted to know about the research in order for them to give that consent. Exclusion reasons for the 21 papers are included in Table 3.

Table 3 – Reasons for full paper exclusion

Reason	Number of studies excluded
Determine participant understanding of the study or satisfaction with the information provided. These studies did not ask participants if they wanted to know the information or rate how important the information was to know, and so did not meet inclusion criteria for the systematic review	5
Reasons why participants may refuse/consent to participate in research	4
Concerned only whether research participants would want results of the study to be returned to them following completion of the study	3
Expert opinions of what should be included in a PIS	3
Asked participants if they would be happy for their details to be given out for other research studies without their consent	2
What patients wanted to know about treatment	1
Who should convey study information to participants	1
Asked participants to talk about ethically important processes in research, but did not if they would want to know them when deciding whether to participate in research	1
Asked participants if they wanted a long or short PIS but not what information they wanted included in it	1

Figure 5 – Number of citations identified at each round of screening



3.2.8 *STUDY CHARACTERISTICS*

Table 4 shows the study characteristics and results for each of the eleven studies included in the review. No papers were published before 1994 and most (n=8) were published after 2005. Most (n=7) were conducted in the USA with only one study conducted in the UK¹⁵⁹. Five studies used questionnaires to produce quantitative results, four used qualitative semi-structure interview and two used focus groups.

3.2.9 *ANALYSIS*

A meta-data analysis used basic thematic analysis to split results from identified papers into themes (topics of information). Where more than one quantitative study reported the proportion of participants wanting to know a topic of information, results were pooled with random effects.

Table 4 - Summary of studies included in the systematic review

Lead author / Country / Year	Inclusion / exclusion criteria	Participant illness	Participant demographics	Total number of participants (response rate)	Study design	Sampling strategy	Analysis	Key Themes explored	Study strengths	Study limitations
Walkup ¹⁶⁰ USA 2009	None provided	None	<u>Gender</u> : Not reported <u>Age</u> : Not reported <u>Education / deprivation</u> : Not reported <u>Ethnicity</u> : Not reported	57 (not provided)	Exploration of conversation and questionnaire	Convenience	Descriptive summary statistics	Study purpose, voluntariness, study method, risks, benefits, confidentiality, review board approval	Participants approached in a public setting and invited to complete a questionnaire and researcher recorded study information spontaneously requested Did not specify a disease group	No inclusion/exclusion criteria Participant demographics not reported Participants questions may have been answered by looking at the questionnaire
Bento ¹⁶¹ Brazil 2008	Female participants aged 18-49 who had taken part in a clinical trial of women's health in the previous 12 months and lived in Metropolitan area of Campinas, Sao Paulo, Brazil	Women's health	<u>Gender</u> : Only women <u>Age</u> : 18-49 <u>Education / deprivation</u> : 4 focus groups 8 th grade or less, 4 focus groups above 8 th grade education <u>Ethnicity</u> : Not reported	51 participants 8 focus groups (not provided)	Focus groups	Convenience	Framework analysis	Study methods, risks and benefits	Participants of different ages and educational level likely to have different needs and opinions regarding topic Focus groups homogenous for age and educational level; suitable to ensure they were comfortable expressing opinions Recruitment continued until data saturation point	Demographics not representative of the general population as the study only included women and was limited to participants from a trial of a contraceptive intervention

Casarett ¹⁶ 2 USA 2001	Participants with a current telephone number, enrolled at a pain clinic, who had chronic non-malignant pain, were taking scheduled opioids and had experienced the pain for at least 6 months	Chronic pain	<u>Gender:</u> 40% male <u>Age:</u> Mean age 47 [range 30-86] <u>Education / deprivation:</u> Range of backgrounds <u>Ethnicity:</u> 85% White	40/86 (46.5%)	Semi structured telephone interviews	Convenience	Descriptive summary statistics and Bivariate analysis with non-parametric tests	Voluntariness, study methods, expenses, risks and the drug/device/procedure being tested	Validated interview topic guide Questions spontaneously asked by participants were recorded	Demographics not representative of general population as participants were more often male and limited to chronic pain patients
Maslin ¹⁵⁹ UK 1994	Attending a breast unit and were patients with a breast cancer diagnosis or asymptomatic women with a family history of breast cancer	Cancer	<u>Gender:</u> Only women <u>Age:</u> Median 47 [range 24-81] <u>Education / deprivation:</u> Not reported <u>Ethnicity:</u> Not reported	213/300 (71%)	Postal questionnaire	Random	Simple descriptive statistics	Study purpose, voluntariness, study methods, risks, benefits and confidentiality	Participants chosen at random but from a subset of those attending a breast unit	Demographics not representative of general population as the study only included females and was limited those with breast cancer

Sand ¹⁶³ Norway 2008	Participants eligible for the parent study (all lung cancer patients)	Cancer	<u>Gender</u> : 57% male <u>Age</u> : Median age 69 [range 44-84] <u>Education / deprivation</u> : Range of backgrounds <u>Ethnicity</u> : Not reported	21/33 (64%)	Semi structured interviews	Convenience	Identification and categorisation of themes and analysis based on deductive and inductive categories	Voluntariness, study methods and treatment alternatives		No inclusion/exclusion criteria stated but 11 potential participants were not invited Technical problems with 3 recordings Demographics not representative of the general population as participants were more often male, had a median age of 69 years and were limited to lung cancer patients
Hutchinson ¹⁶⁴ Australia 2008	Participants of clinical trials of COPD, asthma, diabetes, osteoporosis, rheumatoid arthritis and the influenza vaccine. Excluded if clinical trial for acute, life threatening or debilitating conditions with inadequate therapy	Chronic illness	<u>Gender</u> : 52% male <u>Age</u> : Median age 70 [range not reported] <u>Education / deprivation</u> : Range of backgrounds <u>Ethnicity</u> : Not reported	259/324 (80%)	Questionnaire	Convenience	Descriptive summary statistics and multivariate logistic regression	Conflicts of Interest (CoI)/organisation and funding of the research		Demographics not representative of the general population as median age of 70
Gray ¹⁶⁵ USA 2007	Participants enrolled onto a phase I research trial, spoke English, and were medically and mentally capable of participating	Phase I research trial	<u>Gender</u> : 52% male <u>Age</u> : Median age 61 [range 26-82] <u>Education / deprivation</u> : Range of backgrounds <u>Ethnicity</u> : 81% White	102/119 (86%)	Semi-structured interviews	Consecutive participants enrolling onto parent trial	Descriptive summary statistics, Chi squared tests and Multivariate logistic regression	Conflicts of Interest (CoI)/organisation and funding of the research	Same interviewer conducted all interviews	Demographics not representative of the general population as the median age was 61 and was limited to cancer patients participating in an early phase clinical trial

Grady ¹⁶⁶ USA 2006	Participants of HIV, Hepatitis, Arthritis and Surgical Oncology Trials who were >18 years and English speaking	Various	<u>Gender:</u> 61% male <u>Age:</u> Not reported <u>Education / deprivation:</u> Range of backgrounds <u>Ethnicity:</u> 70% White	33 (not provided)	Face to face semi structured interviews	Convenience	Transcripts coded and themes and major concepts identified	Conflicts of Interest (CoI)/organisation and funding of the research	Open questions used during interviews Data collection continued to saturation point Two authors independently conducted analysis	Used hypothetical scenario Demographics not representative of general population as participants were more often male and limited to adults participating in HIV, hepatitis, arthritis or surgical oncology trials
Hampson ¹⁶⁷ USA 2006	Participants with cancer and enrolled in a clinical trial who were English speaking and >18 years	Cancer	<u>Gender:</u> 56% male <u>Age:</u> 24% < 50, 32% 50-59, 26% 60-69, 16% >70 <u>Education / deprivation:</u> Well educated and financially secure <u>Ethnicity:</u> 92% White	252/272 (93%)	Structured face to face interviews	Not provided	Descriptive summary statistics and Fishers exact test / Kruskal-Wallis test	Conflicts of Interest (CoI)/organisation and funding of the research	Validated interview questions	Demographics not representative of general population as the study population were well educated, financially secure and limited to adult participants of a clinical trial
Weinfurt ¹⁶⁸ USA 2006	Healthy adults or those with a mild chronic illness. Excluded if they had participated in another focus group within the previous 6 months or were working or had worked for an organisation involved in the conduct of clinical trials	Healthy	<u>Gender:</u> 42% male <u>Age:</u> 12% 18-29, 51% 30-49, 37% >50 <u>Education / deprivation:</u> Well educated and financially secure <u>Ethnicity:</u> 56% White	16 focus groups (not provided)	Focus groups	Convenience	Initial content codes based on transcripts developed that were summarised and reviewed to identify main themes	Conflicts of Interest (COI)/organisation and funding of the research	Participants not limited to disease group	Only one moderator conducted focus groups Non-verbal communication not recorded Demographics not representative of general population as the study population were well educated, financially secure and the majority had previously shown interest in research

Kim ¹⁶⁹ USA 2004	Potential research participants >18 years, diagnosed with heart disease, breast cancer or depression, and listed on the Harris Interactive Chronic Illness Database	Various	<u>Gender</u> : 50% male <u>Age</u> : 4% 18-29, 16% 30-44, 61% 45-64, 19% 65+ <u>Education / deprivation</u> : Range of backgrounds <u>Ethnicity</u> : 92% White	5478/20205 (27%)	Internet-based questionnaire	Random	2-way ANOVA modified for ordinal data and multinomial logistic regression	Conflicts of Interest (CoI)/organisation and funding of the research	Validated questionnaire Participants chosen at random but from the subset of those registered on the Harris Interactive Chronic Illness Database	Demographics not representative of general population as it was limited to Internet users
-----------------------------------	---	---------	---	------------------	------------------------------	--------	---	--	---	---

3.3 RESULTS

A meta-data analysis used basic thematic analysis to split results from the 11 papers into themes based on the FAQ titles provided in NRES guidance. Individual results were coded based on their relevance to each theme and then collated and used to report results (Table 5).

Table 5 - NRES recommended headings against papers that report evidence

NRES Heading*	Evidence from literature
What is the purpose of the study?	<p>2 studies provided relevant data^{159;160}</p> <p>Between 51% (29/57; 95% CI 38%;63.9%)¹⁶⁰ and 94%(200/213; 95% CI 90.7%;97%)¹⁵⁹ wanted to know about the scientific purpose of the study.</p> <p>Pooled results (with random effects) showed that 80.0% (229/27; 95% CI 83%; 91%) of participants wanted to know about the scientific purpose of the study.</p>
Why have I been invited?	No studies reported this
Do I have to take part? / What will happen if I don't want to carry on with the study?*	<p>4 studies provided relevant data^{159;160;162;163}</p> <p>Between 0% (0/57)¹⁶⁰ and 95% (202/213; 95% CI 91.9%;97.8%) wanted to know¹⁵⁹ about this. One study reported that participants thought it was the most important piece of information to be included in a participant information sheet¹⁶³</p> <p>Pooled results (with random effects) from the 3 quantitative studies^{159;160;162} showed that 38.8% (215/310; 95% CI 2.5%;99.5%) participants wanted to know this.</p>

What will happen to me if I take part? / What will I have to do?*

3 studies provided relevant data^{159;160;162}

Two studies showed that around 40% of participants wanted to know the time needed to complete the study (42% [17/40; 95% CI 27.2%;58.8%]¹⁶²; 37% [21/57; 95% CI 24.3%;49.4%]¹⁶⁰), whilst the third study had conflicting results and showed that 96% (204/213; 95% CI 93.1%;98.5%) wanted an indication of the nature and extent of the time commitment¹⁵⁹

Pooled results (with random effects) showed that 61.4% (242/310; 95% CI 15.7%; 96.9%) participants wanted to know this.

1 study provided relevant data¹⁶²

68% (27/40; 95% CI 53%;82%) wanted to know the frequency of additional study visits¹⁶²

Only one study provided results, so no pooled results could be calculated

No studies reported this

Two studies reported relevant data^{162;163}

The proportion of people wanting to know what would happen to them ranged from 9.5% (2/21; 95% CI 0%;22.1%)¹⁶³ to 20% (8/40; 95%CI 7.6%;32.4%)¹⁶² depending on what the specific information was. For example, 20% (8/40; 95% CI 7.6%;32.4%) wanted to know about burdens to friends or family caused by study participation¹⁶², 12% (5/40; 95% CI 2.3%;22.8%) wanted to know how much work they would miss because of study participation¹⁶², 10% (4/40; 95% CI 0.7%;19.3%) wanted to know how much time would be spent waiting in clinic during study visits¹⁶², and 9.5% (2/21; 95% CI -3%;22.1%) wanted to know practical information about trial procedures¹⁶³

Specific information types varied considerably between studies, so no meaningful pooled results could be calculated

Expenses and payments

1 study provided relevant data¹⁶²

25% (10/40; 95% CI 11.6%;38.4%) wanted to know if free medication would be available during or after trial¹⁶²

<p>What is the drug, device or procedure that is being tested?</p>	<p>Two studies provided relevant data¹⁰⁶</p> <p>One qualitative study showed that participants wanted to know how to use the intervention¹⁰⁶</p> <p>One study¹¹⁵ showed that specific questions about the medication regime ranged from 25% (10/40; 95% CI 11.5%;38.4%) that wanted to know what control they had over medication dose during the study to 70% (28/40; 95% CI 55.8%;84.2%) that wanted to know the frequency with which study medication must be taken¹¹⁵</p> <p>The same study showed that 62% (25/40; 95% CI 47.5%;77.5%) wanted results of previous studies of safety and 45% (18/40; 95% CI 29.5%;60.4%) of efficacy, and 15% (6/40; 95% CI 3.9%;26.1%) wanted to know if study medication had been approved for clinical use¹¹⁵</p>
<p>What are the alternatives for diagnosis or treatment?</p>	<p>1 study provided relevant data¹¹⁶</p> <p>5% (1/21; 95% CI 0%;13.9%) wanted as much information about treatment alternatives as they received about the study medication¹¹⁶</p>
<p>What are the possible disadvantages and risks of taking part? / What are the side effects of any treatment received when taking part?*</p>	<p>4 studies provided relevant data^{104;10516106}</p> <p>Results ranged from no participants that asked about study risks (0/57)¹⁰⁵, to 97% (207/213; 95% CI 95%;99.4%) who wanted to be informed about any possible emotional or physical discomforts and side effects¹⁰⁴</p> <p>Specific information types varied considerably between studies, so no meaningful pooled results could be calculated</p>
<p>Radiation and the Ionizing Radiation Regulations</p>	<p>No studies reported this</p>
<p>Harm to the unborn child: therapeutic studies</p>	<p>No studies reported this</p>

What are the possible benefits of taking part?	<p>Three studies provided relevant data¹⁰⁴⁻¹⁰⁶</p> <p>Results ranged from 0% (0/57)¹⁰⁵, to 98% (209/213; 95% CI 96.3%;99.9%) that wanted to know about study benefits¹⁰⁴.</p> <p>Pooled results (with random effects) of the two quantitative studies^{104;105} suggest that 57.2% (209/270; 95% CI 7.2%; 98.4%) wanted to know about study benefits</p> <p>Two studies provided relevant data relating to specific benefits^{115;116}</p> <p>Specific requests ranged from 14% (3/21; 95% CI -0.7%;29.3%) that wanted to know about hopes for better treatment¹¹⁶ to 55% (22/40; 95% CI 39.5%;70.4%) that wanted an opportunity to learn about condition or medication under study¹¹⁵</p> <p>Specific information types varied considerably between studies, so no meaningful pooled results could be calculated</p>
What happens when the research study stops?	<p>1 study provided relevant data¹¹⁵</p> <p>55% (22/40; 95% CI 39.6%;70.4%) wanted to know about the availability of medication after the study is over¹¹⁵</p>
What if there is a problem?	<p>No studies reported this</p>
Will my taking part in the study be kept confidential?	<p>2 studies provided conflicting data^{104;105}</p> <p>2% (1/57; 95% CI 0%;5.2%) asked about data privacy¹⁰⁵ and no participants asked about data maintenance (0/57) in one study¹⁰⁵, whereas the other study showed that 75% (160/213; 95% CI 69.3%;80.9%) wanted to be assured that all information concerning them would be kept confidential¹⁰⁴, and 66% (141/213; 95% CI 59.9%;72.6%) wanted to be given information on the protection of their privacy¹⁰⁴</p> <p>Pooled results (with random effects) showed that 43.7% (302/483; 95% CI 9.8%; 8.2%) participants wanted to be given information about confidentiality and the protection of their privacy</p>

Involvement of the GP/family doctor	No studies reported this
-------------------------------------	--------------------------

What will happen to any samples I give?	No studies reported this
---	--------------------------

Will any genetic tests be done?	No studies reported this
---------------------------------	--------------------------

What will happen to the results of the research study?	No studies reported this
--	--------------------------

Who is organising and funding the research?

4 studies provided relevant data^{107;109-111}

There was general disagreement over whether patients wanted to be told about financial COI. Pooled results showed that 65% (95% CI 64%;66%) wanted to know about any type of COI.

3 studies provided relevant data relating to what participants wanted to know about specific aspects of COI^{110;113;117}

When financial COI were broken down into subcategories, 82.5% (4519/5478; 95% CI 81.48%;83.5%) wanted to be told about commercial funding¹¹³, 69% (3779/5478; 95% CI 67.8%;70.2%) about personal income¹¹³, between 41% (105/259; 95% CI 34.6%;46.5%) and 82% (4492/5478; 95% CI 81%;83%) about patents and stocks and shares^{113;117}, and 40% (101/253; 95% CI 34%;46%) thought researchers should have told participants only about the oversight system¹¹⁰

One study reported that participants wanted to know specifically how money was spent, with proportions ranging from 25% (65/259; 95% CI 19.8%;30.4%) that wanted to know how much of the funding was spent on administration¹¹⁷, to 38% (98/259; 95% CI 31.9%;43.8%) that wanted to know how spare accrued funds were used at study completion¹¹⁷

One qualitative study reported that participants wanted to know the name of the sponsor¹¹¹, and one quantitative study reported that 57% (148/259; 95% CI 51.1%;63.2%)¹¹⁷ wanted to know the name of the funder.

Some participants wanted help understanding the potential consequences of COI, some did not¹¹¹

Specific information types varied considerably between studies, so no meaningful pooled results could be calculated

Who has reviewed the study?

1 study provided results¹⁰⁵

No participants asked about institutional review board approval (0/57)¹⁰⁵

*Similar headings have been merged

3.3.1 CATEGORIES WITH NO STUDIES REPORTING RELEVANT RESULTS

Of the twenty NRES suggested headings for inclusion of information in a PIS, there were seven categories where no research evidence was identified to suggest what information potential research participants wanted to know. These were:

- Why have I been invited?
- Radiation and the Ionizing Radiation Regulations
- Harm to the unborn child: therapeutic studies
- What if there is a problem?
- Involvement of the GP/Family doctor
- What will happen to any samples I give?
- Will any genetic tests be done?

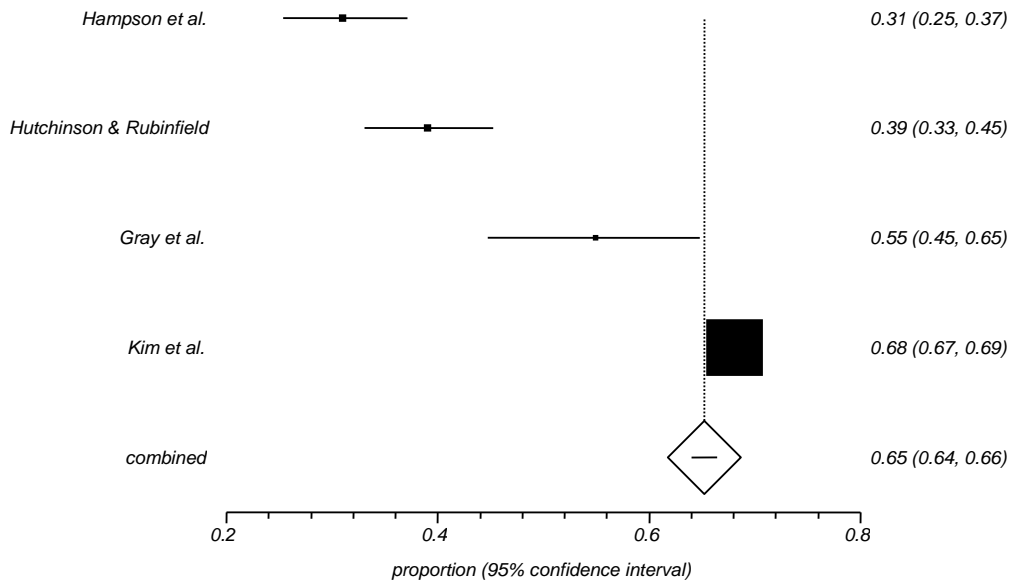
Four of these categories ('Radiation and the Ionising Radiation Regulations', 'harm to the unborn child: therapeutic studies', 'will any genetic tests be done?' and 'what will happen to any samples I give?') are very specific and NRES suggests their inclusion only for relevant studies. There were four other categories where no studies reported relevant results ('why have I been invited?', 'what if there is a problem?', 'involvement of the GP/family doctor' and 'what will happen to the results of the research study?') and these categories of information are likely to be relevant for the majority of research studies.

3.3.2 CATEGORIES WITH STUDIES REPORTING GENERAL RESULTS

Six studies considered what potential participants wanted to know about investigator conflicts of interest (COI). Six studies reported research participants' preference for information about investigator COI in a research study. When the results of the four qualitative studies were pooled (with random effects) (Figure 6), 65.2% (95% CI 64.0%; 66.4%) wanted to know about any type of COI. The forest plot (Figure 6) showed that individual study results varied widely with one large study providing the majority of the weight. The two studies that produced substantially different results to the pooled percentages^{164;167} had problems with generalisability to the wider research population and the use of defined sub populations may account for the differences seen. Given that the one study providing the majority of the weight in the calculation¹⁶⁹ agreed with results of the two qualitative studies (most participants wanted to be informed of any COI^{166;168}), this is likely to be the best evidence of where the true value lies, given the limited data available.

All six studies collected only hypothetical opinions of what participants wanted to know. It is generally held that hypothetical opinions may not reflect real opinions¹⁷⁰⁻¹⁷² and participants may think differently when they are considering what information they require to decide to participate in an actual study.

Figure 6 - Forest plot of the proportion of participants that wanted to know about investigator COI (random effects)



Of the remaining eleven categories, pooled results were calculated for four categories. Results showed that participants wanted to know about the purpose of the study (84.8%; 229/270), voluntariness (69.4%; 215/310), what they would have to do (78.1%; 242/310), and confidentiality (62.5%; 302/483). There were seven categories where pooled results could not be calculated because they included qualitative results, only one study provided results or studies reported specific information types that varied considerably between studies.

Only five studies looked generally at what potential research participants wanted to know when deciding whether to participate in research (the remaining six studies looked at what potential participants wanted to know about conflicts of interest). The proportion of participants that wanted to know study information varied according to

the topic. Results ranged from 5% (1/21) that wanted to know about alternative treatments¹⁶³ to 98% (209/213)¹⁵⁹ that wanted to know about potential benefits. Different study methodologies may account for this variability. For example, studies that asked participants if they wanted to know specific information often reported high proportions (i.e. 75% [160/213] wanted to be assured that all information concerning them would be kept confidential¹⁵⁹), whereas studies that reported spontaneous information requests generally reported low proportions (i.e. only 2% [1/57] wanted to know about data privacy¹⁶⁰). One study was a qualitative focus group study and did not report proportions¹⁶¹. There were also limitations to generalisability of findings in all studies.

3.4 DISCUSSION

Of the eleven papers identified; six only provided information on what participants wanted to know about COI in research^{165;164;166-169}. Only five looked more broadly at what research participants want to know¹⁵⁹⁻¹⁶³. All eleven studies were shown to have limitations when applying their findings to the wider research population (Table 4). This systematic review, therefore, found no good quality evidence to suggest what information the general research population wants to know before they decide whether to participate in research. Table 6 shows a summary of the number of studies providing evidence for each category of information with pooled results where they could be calculated.

Table 6 - Number of studies providing evidence for each category of information with pooled results

NRES suggested title	Number quantitative (/ total number) studies	Pooled results (%)
Study purpose	2/2	Yes (84.5)
Why they have been invited	0/0	No
Voluntariness	3/4	Yes (69.4)
What will happen to them	3/3	No
Expenses and payments	0/0	No
What is being tested	0/1	No
Alternatives	1/1	No
Disadvantages, risks and side effects	0/0	No
Radiation and the Ionizing Radiation Regulations	0/0	No
Harm to the unborn child: therapeutic studies	0/0	No
Benefits	2/3	Yes (77.4)
When the research study stops	0/0	No
If there is a problem	0/0	No
Confidentiality	2/2	Yes (62.5)
Involvement of the GP/family doctor	0/0	No
Samples	0/0	No
Genetic tests	0/0	No
Results	0/0	No
Organising and funding of the research	2/4	Yes (65)
Ethical review	1/1	No

Incomparable study methodologies

Of the five studies that looked more broadly at what research participants wanted to know¹⁵⁹⁻¹⁶³, differences in research methodology and design meant that that application of pooled results was also limited. An example of this is the category 'What is the purpose of the study?' where two studies provided relevant results. The study by Walkup and Bock¹⁶⁰ was an observational study and reported what information participants spontaneously requested about a questionnaire survey, whilst the study by Maslin¹⁵⁹ asked participants to indicate if they wanted to know each of a series of prompted pieces of information. Walkup and Bock reported a much lower proportion of participants that wanted to know the study purpose (51%¹⁶⁰ vs. 94%¹⁵⁹). When asked directly if they wanted to know this information, as in the Maslin study, participants said they did want to know the information because they found it interesting. In the study by Walkup and Bock, however, they did not ask for that information spontaneously. The differences in results caused problems when trying to determine if participants wanted to know this information, as the studies were not comparable. Ideally, a separate meta-analysis would have been conducted for each type of methodology, but the limited literature meant this could not be done.

A second potential cause of the variability in study results could be attributed to differences between hypothetical studies and collecting actual opinions. Walkup and Bock¹⁶⁰ reported what participants wanted to know about a real study, whereas Maslin¹⁵⁹ reported what participants said they wanted to know about a hypothetical study. It is generally held that what people say they want to know in a hypothetical

situation differs to what they would actually do when presented with a real scenario¹⁷⁰⁻¹⁷².

The final difference between these two papers lies in the level of risk in the studies participants were asked about. Walkup and Bock¹⁶⁰ conducted a low risk questionnaire study, compared with Maslin's¹⁵⁹ high-risk breast cancer trial. It would be reasonable to expect that participants wanted to know more information when being asked to participate in a higher risk study. This again makes comparisons between the two study results difficult.

These differences in the design of the studies papers may account for the different proportions of participants that wanted to know about the purpose of the study. Given these differences in the study designs, data could not be pooled to determine an overall proportion of how many people wanted to know each piece of information about a study.

Similar problems were seen with other NRES categories, for example 'Do I have to take part? / What will happen if I don't want to carry on with the study?' Two papers reported the questions that participants asked about a study when they were being invited to take part^{105;115} and both reported that few participants wanted to know information about whether they had to take part in the study (0% [0/57] and 32% [13/40; 95% CI 18%;47%] respectively). In comparison, the two studies that asked participants if they wanted to know specific pieces of information^{159;163} both reported a very high proportion of participants that wanted to know this information (95%

[202/213; 95% CI 91.9%;97.8%]¹⁵⁹ and “it being the most important piece of information to be included in a PIS”¹⁶³).

Level of detail

There were also problems with the level of detail provided by the five studies that reported generally what participants wanted to know. Most papers asked participants if they wanted to know pieces of information or recorded what information they requested, but the methodologies used did not allow information to be collected on the level of detail potential participants want. Real time observational studies need to be conducted that track the level of detail of information accessed by potential participants when they are given a choice.

Generalisability

A further problem with the studies identified for inclusion in this review was the selected populations used in the studies. Many studies used specific subsets of the population, such as cancer patients, and did not look broadly at what all research participants might want to know about research. Given that NRES guidance provides general guidance to writing a PIS (i.e. not guidance specific to subgroups), the views of the overall research population need to be taken into account when writing guidance on how much information to include in a PIS. This would suggest that work needs to be conducted with a range of key stakeholders to address differing needs, i.e. to ensure that future PIS are written in such a way as to provide the information that potential participants want, meet regulatory requirements and also provide information to legally protect researchers. Given that this systematic review provided little evidence to suggest exactly what information research participants wanted to

know, PIS may not currently include the information they want to make a participation decision.

Limitations

The unspecific nature of the topic and the broad search strategy used in this systematic review led to the identification of a large number of citations (n=11943) and it was not feasible to review all abstracts. The sifting process included scanning titles for relevance in the first instance, so there is a possibility that relevant papers were excluded where a title was not sufficiently informative. Whilst this is a limitation to the review, the lack of overall evidence means it is unlikely that many (if any) relevant papers were missed.

3.5 CONCLUSIONS

This systematic review has demonstrated differences between what participants wanted to know before they decide to take part in research, depending on the methodologies, context and population used in the studies.

The studies showed that participants spontaneously requested less information than they said they wanted to know when they were prompted. It is difficult to conduct future research to determine what information potential participants want, since asking potential participants what information they want to know may not accurately reflect what information they will use when faced with a participation decision¹⁷⁰⁻¹⁷². Future research should focus on real time observational studies that collect the information accessed by participants when making a participation decision.

A paper by Dixon-Woods et al (2007)¹⁷³ is worth discussing in relation to the results of this systematic review. Embedded within the genetic GRAPHIC trial, interviews were undertaken with 29 healthy participants to explore their views and experiences of research. They found that participants often decided to participate without a great deal of thought and the decision was not based on the information included in the PIS, but rather based on four other main factors: a positive attitude towards medical research; a desire to do good; a possibility of some personal gain in the form of a health check; and confidence in the research process and its governance and a perception of low risk. Participants suggested that the precise nature of the study was unimportant so long as the research appeared to be worthwhile and well run; something they attributed to recognising funders and organisers of the research i.e.

an issue of trust. This research sheds a new light on the meaning participants may give to information included in a PIS, and whilst they may not need to know all of the information included in a PIS, they may use it to form an overall opinion of whether the study is worthwhile participating in.

For firm conclusions to be drawn from the speculations made in this systematic review, further research is needed. There is real need for a large, good quality study to determine what information research participants actually want to know about a research study, so that information provided in the PIS can be tailored towards what participants feel they need to know in order to arrive at an informed decision.

This systematic review has been published in the BMJ Open¹⁷⁴ and is included as Appendix 9.1.

Key points

There is limited evidence about what information potential participants want to know at the time they are deciding whether or not to participate in research.

Asking potential participants what information they want to know may not accurately reflect what information they will use when faced with a participation decision.

Real-time observational studies need to be conducted to explore what information potential participants access when given a choice. This will enable us to determine exactly what information research participants want to know and could, in addition to other sources such as expert opinion, help tailor PIS towards specific population subgroups and enable appropriate high-quality information to be provided to meet individual needs.

4 INFORMATION PROVISION STUDY PROTOCOL

The second objective of the PhD was to devise and conduct a study (from henceforth referred to as the Information Provision study) to collect data on what potential participants want to know to be able to participate in low risk interventional research. This chapter provides the protocol for the Information Provision study.

4.1 STUDY DESIGN

The Information Provision study had three components. The first addressed the feasibility of electronic information provision, comparing electronic information provision to standard paper format. The second was an RCT (IIS RCT) that compared responses to a PDF file of a standard PIS (PDF-PIS) with an IIS. The third component was an observational study of participants randomised to the IIS arm of the IIS RCT. This recorded the study information accessed by each participant.

4.2 AIMS

Feasibility component:

Primary aim

To determine if it was feasible to provide electronic information in low risk interventional research

Secondary aims

- To determine the proportion of potential research participants that had access to the Internet and were willing to use it to access study information and whether this varied within subsets of the population
- To determine if participants were satisfied with the way in which information was provided and whether satisfaction varied within subsets of the population
- To determine what proportion of the population had a good understanding of a study after reading the PIS and whether method of information provision affected level of understanding

IIS RCT:

Primary Aim

To determine if an IIS could improve consent rates to research

Secondary aim

To allow assessment of satisfaction and understanding as a component of the observational study

Observational study:

Primary Aim

To determine what information potential participants accessed about a low risk interventional study when given the choice of the type and level of detail of information

Secondary Aims

- To determine if informational needs differed within subsets of the population
- To determine if the type and amount of information used by potential study participants differed between those who consented and refused to participate in the study and whether this differed within subsets of the population

4.3 PARENT STUDY (IN WHICH THE INFORMATION PROVISION STUDY WAS EMBEDDED)

4.3.1 IDENTIFICATION OF A SUITABLE PARENT STUDY

Antoniou et al⁶ demonstrated the feasibility of using an IIS in an Internet questionnaire-based study. When conducting research on consent procedures, there are concerns that new interventions may mean participants will enter research without being properly informed if the introduced intervention does not appropriately inform potential participants. For this reason, it was decided that the next challenge for the IIS was to use it in low risk interventional research where the risks and disadvantages of participating would be minimal. Accordingly, the information provision study needed to be embedded within a low risk intervention study (non questionnaire-based) that had a large number of participants (Section 4.5) with a range of ages and the capacity to recruit participants and distribute participant information electronically. Clinicians and academic researchers at the University of Birmingham were approached to see what planned or on-going trials were available, but finding a study that met all criteria proved difficult.

A consultant at the Queen Elizabeth Hospital, Birmingham offered three potential studies. The first two studies (a RCT of chronic colitis patients randomised to active topical treatment vs. no topical treatment, and a randomised non blinded controlled study of a new form of oral iron for anaemic inflammatory bowel disease patients) were excluded because of small sample sizes (n=50). The third study (a RCT to test a new formula of cyclosporine) was industry-based and the clinical research

organisation was unwilling to embed a methodological question into their protocol. Several potential leads with other hospital consultants were also explored but no suitable study was identified.

Principal Investigators (PIs) within the School of Health and Population Sciences and the Clinical Trials Units at the University of Birmingham were then approached via email (and sometimes in person where appropriate). A summary of the Information Provision study was included in emails and PIs were asked to identify potentially suitable studies in which it could be embedded. Professor Richard McManus, a researcher with several prevalence studies in primary care, expressed an interest. After discussion with Professor McManus, a suitable observational study, the 'Blood Pressure Monitoring in Different Ethnic Groups (Bp-Eth)' study was identified. Bp-Eth was a large study (n=800), recruiting over 24 months, it included a range of participants and was suitable for electronic recruitment. The limitation to embedding in this study was the older participant age range (40-74) but as young people were more likely to use the Internet¹⁰², if the study found that providing study information electronically was acceptable to an older cohort of participants, it was reasonable to hypothesise that it would also be acceptable to a younger cohort.

4.3.2 *OUTLINE OF THE PARENT STUDY*

Study aims

The tri-phase “Blood Pressure Monitoring in Different Ethnic Groups Study (Bp-Eth)” (Appendix 9.4) conducted at the University of Birmingham aimed to answer three research questions:

1. How often and in what ways does monitoring of blood pressure occur and how does it differ between White and minority ethnic populations?
2. Are the thresholds for diagnosis and management of hypertension comparable for White and minority ethnic populations using three different measurement modalities: office blood pressure, ambulatory blood pressure monitoring (ABPM) and self monitoring?
3. What preferences for blood pressure measurement do people from White and minority ethnic populations have?

Outline of the three research phases

Phase I was a cross-sectional survey of 8000 participants and included representative samples from four ethnic groups, (White, Irish, Asian, and African-Caribbean) with both normotensive and hypertensive blood pressure ranges.

Phase II was a validation study to compare different modes of blood pressure measurement in diagnosing hypertension and to detect thresholds for when

medication doses should be altered. Blood pressure readings (recorded by ambulatory 24 hour blood pressure monitors; self monitored blood pressure and research office measurements) were used to ascertain whether differences in readings between methods of measurement were similar between ethnic groups. Participants were eligible for phase II if they were aged between 40-74 years and belonged to one of the four ethnic groups under investigations (White, Irish, Asian, African-Caribbean). Participants were excluded if they were unable to self monitor or use an ambulatory blood pressure monitor, were pregnant, unable to consent, had a terminal disease or their GP felt they were not suitable.

Phase III was a focus group study that included participants from each ethnic group. It considered participant preferences for, and experiences of, blood pressure measurement in each of the three ways considered in phase II.

4.3.3 HOW THE INFORMATION PROVISION STUDY WAS EMBEDDED

Participants (8000 in total) were recruited into phase I of the Bp-Eth study. At the end of the phase I questionnaire participants were asked to provide contact details if they would be willing to participate in phase II. Of the participants who returned the phase I questionnaire and expressed an interest in participating, 800 (200 White, 200 Black, 200 Asian and 200 Irish) were recruited take part in phase II of the Bp-Eth study.

To embed the Information Provision study an additional email address field was added to the contact details participants were asked to provide if they were interested in Phase II of Bp-Eth. All those who provided an email address were potentially eligible to participate in the Information Provision study.

The full protocol for the Bp-Eth study is provided as Appendix 9.4.

For the remainder of the thesis, phase II of the Bp-Eth study, where the information provision study sat, will be referred to as the parent study. The questionnaire for the phase I Bp-Eth study will be referred to as the questionnaire for the parent study. This is for clarity to distinguish between the Bp-Eth and Information Provision study.

4.4 PARTICIPANTS

Feasibility of electronic information provision

All participants who wished to continue with the parent study were included. Participants were asked to provide an email address with their contact details. If they did, they were sent an electronic invitation letter (via email) (Appendix 9.5) and link to the parent study website. If no email address was provided they were sent the standard parent study information through the post.

IIS RCT

All those who provided an email address were sent the invitation to participate in the parent study in which they were asked to click on a hyperlink to the parent study website. If they did so, they were randomised either to receive a PDF copy of the paper PIS (PDF-PIS) or the IIS.

Participants were assumed to have opened the email if they returned a read receipt, replied to the email, made a consent appointment or accessed the study website. Participants who appeared not to have opened the email within 3 days were contacted by telephone to verify their email address. Up to 10 attempts were made to contact participants at different times of the day; in the morning (9-12pm), lunchtime (12-2pm), afternoon (2-6pm), evening (6-9pm) and weekends; over a seven day period. If they did not answer the telephone after ten attempts they were deemed un-contactable and sent a postal invitation and paper PIS.

If participants made an appointment with the research nurse they were perceived to have consented for the purpose of this Information Provision study. Following this perceived consent, the potential participant still may not have participated in the parent study and changed their decision either prior to the appointment (and so did not attend the appointment) or after speaking with the research nurse. In these cases, the information in the PIS/IIS was not decisive for their final decision. This study aimed to consider only the effect of the PIS/IIS on consent, and so perceived consent was used as the outcome.

The email invitation contained contact details for researchers if participants were interested in taking part. Participants were able to make an appointment without clicking on the hyperlink to access the study website. These participants were perceived to have consented to take part without accessing any PIS.

Observational study

Participants randomised to IIS were included in an observational study that captured the information accessed by each participant using a database connected to the IIS.

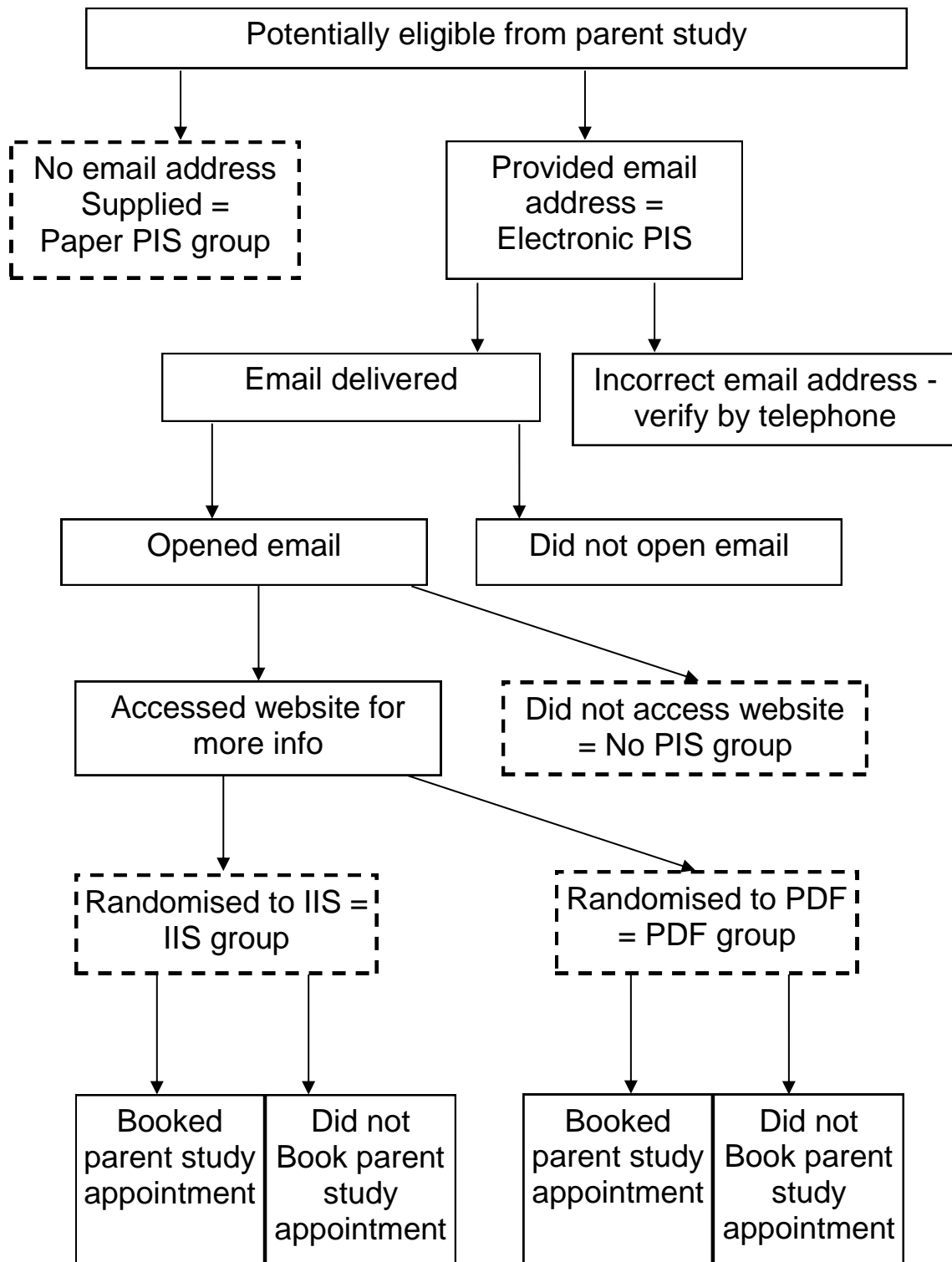
Demographic data for all participants were collected by the parent study, which was made available for use in the Information Provision study.

Figure 7 provides an overview of how participants were recruited to the Information Provision study.

Understanding and satisfaction questionnaire

All participants who agreed to participate in the parent study were asked to complete a questionnaire to determine their understanding of the study and their satisfaction with the way in which information was provided. Participants randomised to PDF-PIS or IIS were directed to complete the questionnaires after they indicated if they wished to participate in the parent study. If they did not complete the questionnaire at this time, did not take part in the IIS RCT or were sent a paper PIS, the questionnaires were sent through the post at the time they made an appointment with the research nurse for the parent study. All participants receiving a postal questionnaire were sent a reminder and duplicate questionnaire if they did not respond within two weeks.

Figure 7 – Recruitment flow chart



4.5 SAMPLE SIZE CALCULATIONS

Sample size calculations were based on the IIS RCT component of the Information Provision study.

4.5.1 ESTIMATING AN EFFECT SIZE

The primary outcome measure of the IIS RCT was consent rate to the parent study. Since the IIS had never been used as the intervention for a RCT and there was insufficient evidence to predict the likely effect size, it was not known how much of a difference its use would have on the consent rate. Without this estimate of effect size a sample size calculation could not be made¹⁷⁵⁻¹⁷⁷. Another way to estimate the effect size is to gather expert opinion and then use effect size that is required to change practise, to inform sample calculations¹⁷⁸. This method was used to establish an effect size for the IIS RCT.

Researchers were identified and invited (by email) to participate in an online questionnaire. The questionnaire described the IIS and asked how much they would need to see recruitment rates increased by, based on 90%, 70%, 50% and 30% baseline rates, before they would consider using the IIS in their research. The questionnaire was sent to 122 people; 7 responded to say they were not involved in trial design and could not complete the questionnaire, 64 attempted it and of these 26 failed to complete it. Thirty-eight completed the questionnaire and were included in the analysis (response rate 33%; 38/115). Depending upon the baseline recruitment rates presented in the questionnaire participants wanted recruitment rate to increase from 6.9% to 28.9% before they would consider using the IIS (Table 7). This study has been

reported in the BMC Medical Research Methodology Journal¹⁷⁹ and the full study is included as appendix 0.

Table 7 - Results from the effect size questionnaire

Expected consent rate without using the IIS (baseline consent rate)	90%	80%	70%	50%	30%
Mean percentage increase experts wanted	7.4	10.9	13.8	19.6	27.0
Standard deviation	3.19	5.61	24.05	8.53	18.13
Median percentage increase wanted	9	10	11	20	25
Inter quartile range	5	5	10	17.5	30
Range of responses seen	0-10	0-20	0-30	0-50	0-70

4.5.2 SAMPLE SIZE CALCULATIONS FOR THE IIS RCT

A variety of sample sizes were calculated assuming study baseline consent rates of 90%, 80%, 70%, 50% and 30%, powers (β) of 90% and 80% and effect sizes of 7.4%, 10.9%, 13.8%, 19.6% and 27% respectively (Table 7) using the calculation:

$$N = [(\alpha + \beta)^2 \times (p_1q_1 + p_2q_2)] / \text{effect size}^2 \text{ }^{176}$$

With a predicted type I error of 5% and a type II error of 10-20%, the calculated sample sizes ranged from N=122 to N=442 (Table 8).

Pilot work for the parent study (n=7) suggested that consent rate was likely to be around 70% so this was used as an estimate of the main parent study consent rate. Table 9 shows a further range of sample sizes based around a 70% consent rate for the range of effect sizes collected from the effect size questionnaire.

The sample size estimate for the IIS RCT component of the Information Provision study was 382 participants, but given the uncertainty of the effect size the study was implemented as quickly as possible to recruit the maximum number of participants from those invited to the parent study. The maximum number of participants that could have been approached was 1200 (given that 840 participants were sought for the parent study and assuming a 70% consent rate).

Table 8 - Estimate sample sizes for the range of baseline consent rates

Effect size	Consent rate	Power	N (per arm)	N (total)
7.4%	90%	90%	221	442
		80%	165	330
10.9%	80%	90%	214	428
		80%	160	320
<u>13.8%</u>	<u>70%</u>	<u>90%</u>	<u>191</u>	<u>382</u>
		<u>80%</u>	<u>143</u>	<u>286</u>
19.6%	50%	90%	126	252
		80%	94	188
27%	30%	90%	66	132
		80%	61	122

Table 9 - Sample sizes for a consent rate of 70%

Effect size	Consent rate	Power	N (per arm)	N (total)
1%	70%	90%	43660	87319
		80%	32653	65306
7.5%	70%	90%	717	1435
		80%	536	1073
13.8%*	70%	90%	191	382
		80%	143	286
15%	70%	90%	157	315
		80%	118	236
22.5%	70%	90%	58	116
		80%	43	87
30%	70%	90%	24	49
		80%	18	37

**Effect size required to change practice*

4.6 RANDOMISATION

Participants were randomised to receive either a PDF-PIS or be directed to the IIS website.

Randomisation could have led to a chance imbalance in prognostic characteristics and biased results. In order to balance known prognostics between groups, randomisation was stratified by age and gender. Randomisation was stratified to three age groups: (1) those under 50 years, as previous literature showed response rate was likely to differ between those below and above the age of 50¹⁸⁰; (2) those over 65, since 'The Office for National Statistics Statistical' Bulletin "Internet Access Households and Individuals 2009" stated that Internet usage was low in this age group¹⁸¹; and, (3) those aged between 50 and 65. One inclusion criteria for the parent study was being aged 40 to 74, so these three age groups used for stratification also split the IIS RCT participants into approximately equal groups spanning between 10 and 15 years.

Blocking is a method of preventing unequal group sizes in randomised trials and guarantees that at any point in study recruitment, the imbalance in numbers between the study arms will be small (dependant on block size)¹⁸². Blocks of four were used for the IIS RCT, meaning that at any one time there could be a maximum difference of two participants per subgroup. A blocking group of four was chosen because a larger blocking size would potentially create a bigger difference between subgroup sizes. Since this study relied on participants choosing to enter themselves,

recruitment could stop at any time. If this happened before the end of the parent study blocking would ensure that the resulting groups were of equal size.

Blocks were assigned in random groups of four. There were, therefore, six sequences to which participants could have been allocated to group A (PDF-PIS) or B (IIS). The possible blocks were:

AABB

ABAB

ABBA

BAAB

BABA

BBAA

Each of these blocks was given a number from one to six and the random number generator function in Excel generated a random list using only these six numbers. Each random number in this list was replaced with the corresponding blocking sequence and a random list of allocations blocked in groups of four was produced.

4.7 INTERVENTIONS

PDF-PIS

The PDF-PIS was an electronic copy of the parent study paper PIS.

IIS

The IIS was the intervention in the IIS RCT and is described fully in Chapter 5. The IIS was developed based on the unfolding PIS intervention described by Antoniou et al⁶.

The IIS presented the reader with a screen containing a list of frequently asked questions (FAQ) about the parent study that corresponded to NRES suggested titles for a PIS. Behind each FAQ were up to four levels of information accessed by clicking on hyperlinks embedded in each level. Level one contained less detailed information than the parent study paper PIS (minimal information), level two an exact copy of the paper PIS (standard information), level three was more detailed than it (extended information) and level four contained links to external sources, for example scientific papers evidencing the information provided (external information).

Understanding and satisfaction questionnaire

Participant understanding and satisfaction were captured online or by postal questionnaire.

Since some participants would take part in at least two phases of the parent study it was undesirable to burden them with an additional lengthy questionnaire to answer,

so the questionnaire to determine understanding and satisfaction was designed to be completed in less than ten minutes.

There is no standardised measure of level of understanding of participants¹ but 'Quality of Informed Consent tool' (QuIC)¹, was adapted for use in this study. The QuIC was appropriate since it is a validated self-administered questionnaire that takes less than 10 minutes to complete¹⁸³. It tests participants on their knowledge of research and questions could be easily adapted to include specific aspects of the parent study without altering the questionnaire and, therefore, its validity. The final questionnaire is included as Figure 8.

Antoniou et al⁶ asked participants about their satisfaction with the way in which their study information was provided. Their questions were adapted to determine satisfaction for this study. Figures 9 shows the satisfaction questionnaire sent to those randomised to IIS, and Figure 10 shows the satisfaction questionnaire sent to those randomised to PDS-PIS or paper PIS.

Figure 8 - Questionnaire to determine understanding

Part A

Below you will find several statements about the blood pressure monitoring study. Thinking about the study, please read each statement carefully. Then tell us whether you agree with the statement, you disagree with the statement, or you are unsure about the statement by marking in the appropriate response box. Please respond to each statement as best you can. We are interested in your opinions.

- | | | | |
|--|--|---|--|
| 1. You have been asked to measure blood pressure with different machines. Do you think this is for a piece of medical research? | Yes ₁
<input type="checkbox"/> | No
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 2. Is this study to see if differences between blood pressure measured at home and blood pressure measured at the GP surgery are the same for different ethnic groups? | Yes ₁
<input type="checkbox"/> | No
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 3. Have you been chosen to take part in this study because you have high blood pressure? | Yes
<input type="checkbox"/> | No ₁
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 4. Do you have to take part in this study? | Yes
<input type="checkbox"/> | No ₁
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 5. If you take part in this study will you be involved in the study for 8 days? | Yes ₁
<input type="checkbox"/> | No
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 6. If you take part in this study, will you have to measure your blood pressure yourself at home? | Yes ₁
<input type="checkbox"/> | No
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 7. Will your GP be told you are taking part in this study? | Yes ₁
<input type="checkbox"/> | No
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 8. Will the research nurse for this study offer you treatment for high blood pressure? | Yes
<input type="checkbox"/> | No ₁
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 9. Will we keep information about you confidential if you agree to take part in this study? | Yes ₁
<input type="checkbox"/> | No
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |

- | | | | |
|--|--|---|--|
| 10. If you decide to pull out from the study, will it affect your care from your GP? | Yes
<input type="checkbox"/> | No ₁
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 11. Will statisticians involved in this study be able to see your name, address and other personal details? | Yes
<input type="checkbox"/> | No ₁
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 12. If you don't want your GP to know you are taking part in this study will you still be able to take part? | Yes
<input type="checkbox"/> | No ₁
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 13. Is this study is being organized by professional researchers at the University Of Birmingham? | Yes ₁
<input type="checkbox"/> | No
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 14. When we publish the results of this study, will we identify you in any report? | Yes
<input type="checkbox"/> | No ₁
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |
| 15. Has this study been looked at and approved by a research ethics committee? | Yes ₁
<input type="checkbox"/> | No
<input type="checkbox"/> | Don't know
<input type="checkbox"/> |

Figure 9 - Questionnaire to determine satisfaction for those randomised to IIS

We would like your comments about the information you read about the Blood Pressure Monitoring Study. Please tick any of the following statements that apply.

- I did not click on any of the (+) signs.
- I found the information under the (+) signs useful and it influenced my decision to take part in this study.
- I clicked on the (+) signs to see what was there but did not read the information.
- I clicked on the (+) signs and skimmed through the information. I did not read it fully.
- I clicked on the (+) signs and skimmed through the information. I picked out and read only parts which were important to me.
- I found the information under the (+) signs interesting but it didn't influence my decision to participate in the Blood Pressure Monitoring study.
- I would have been happy with just the first piece of information from each section. I did not need to read any of the information under the (+) signs to make a decision about whether I wanted to take part in the Blood Pressure Monitoring study.
- I would not have agreed to take part in the Blood Pressure Monitoring study without being able to read the information under the (+) signs.
- I would have liked more information about the study.
- I didn't need as much information about the study as I was given.
- I would prefer to have information provided electronically if I took part in research again.
- I would prefer to have information provided on paper if I took part in research again.

Figure 10 - Questionnaire to determine satisfaction for those randomised to PDF-PIS or paper PIS

We would like your comments about the information you read in the information sheet you were given about the blood pressure monitoring study. Please tick any of the following statements that apply.

- I read all of the information sheet I was given about the Blood Pressure Monitoring study.
- I read some of the information in the information sheet I was given about the Blood Pressure Monitoring study.
- I skimmed through the information in the information sheet I was given about the Blood Pressure Monitoring study and read only the bits that were important to me.
- I did not read any of the information in the information sheet I was given about the Blood Pressure Monitoring study.
- I read some of the information in the information sheet but it did not help me to decide whether or not I wanted to take part in the Blood pressure Monitoring study.
- The information sheet was important to read and helped me to decide whether or not I wanted to take part in the Blood Pressure Monitoring Study
- I found the information in the information sheet about the Blood Pressure Monitoring Study interesting but it did not influence my decision to take part.
- I would not have agreed to take part in the Blood Pressure Monitoring study without being able to read the information in the information sheet
- I would have liked more information about the study.
- I did not need as much information about the study as I was given.
- I would prefer to have information provided electronically if I took part in research again.
- I would prefer to have information provided on paper if I took part in research again.

4.8 OUTCOMES

Primary outcomes

The primary outcome measure for the feasibility component was the proportion of participants that provided an email address. The primary outcome measure for the IIS RCT was consent rate to the parent study.

The primary outcome measure for the observational study was the amount and type of information accessed. The proportion of people clicking on each link within levels of the IIS FAQ was used as the proxy for determining what information potential study participants accessed when they were deciding whether to participate.

Secondary outcomes

Secondary outcome measures were email address provision and level of study understanding and satisfaction with the information provided.

Feasibility study and IIS RCT

Demographic information was collected by the parent study for all participants who expressed an interest in taking part. These data were anonymised to participant ID number, so they could be matched to the participant ID number of participants in the Information Provision study. Each participant was given an Index of Multiple Deprivation (IMD) score¹⁸⁴, based on postcode and calculated using the GeoConvert tool available through the official Census website¹⁸⁵. These data were used in conjunction with the other outcome measures to determine if informational

requirements, access to the Internet and acceptability of the IIS varied between subsets of the population.

The proportion of participants who provided an email address was used as a proxy measure of accessibility to the Internet, which was then used as a measure of feasibility of using an IIS.

A comparison of responses to the satisfaction and understanding questionnaire was made between those who received the IIS and those who received the standard PIS (electronic or paper) to determine if satisfaction or understanding were affected by method of information provision.

Observational study

The proportion of people clicking on each link within the levels of the IIS FAQ was also used in conjunction with the proportion that consented to participate in the parent study to determine if the type and amount of information accessed differed between those who consented and refused to participate in the parent study.

The time spent within each level of the IIS was used to judge whether participants had read the information presented when they accessed an area.

4.9 STATISTICAL ANALYSIS

All analyses were carried out using SAS version 9.2

Feasibility study

The relationship between subject characteristics (gender and age [<49, 50-65, >66]) and the variables presented below were evaluated using a non linear effect model (with practice as a random effect)¹⁸⁶. The relationship between patient demographics and the following outcomes were assessed:

- Provided/did not provide an email address
- Accessed/did not access information online
- Level of understanding

IIS RCT

The RCT analyses were based on intention to treat (ITT)¹⁸⁷. The primary analysis for the IIS RCT intended to assess the impact of IIS on consent rate using a mixed model with a logit link and binomial error accounting for baseline age and gender and with practice as random effects¹⁸⁶. Odds ratio 95% CI and p value were also presented¹⁸⁸.

Observational study

Each time a participant clicked on a link to request information about the study from the IIS it was recorded and used to produce a list of what information was accessed by each individual and the proportion of participants that accessed each level of

information¹⁸⁹. The proportion of people that clicked on each link was used to show which levels of information were commonly read and which were not. This, along with how much time was spent on each piece of information was used to determine what information was regarded as important to participants.

The number of words an average person can read in one minute was used to determine how long it would take the average person to read each piece of text on the IIS^{190;191}. This calculation was then used to make a best guess as to whether the participant had read the text, skimmed through it, or opened up the level of information without attempting to read it at all.

The proportion of people that accessed each level of information was used to determine if there were particular questions on the IIS where participants were more likely to read the extended information available. Exploratory analyses using frequency and proportion were undertaken to assess whether different socio-demographic groups were more likely to access and read each piece of information. Frequencies and proportions were examined to see if any clear patterns emerged.

4.10 ETHICAL APPROVALS AND CONSIDERATIONS

Ethical approval was sought from The Black Country REC as an amendment to the parent study before commencement of data collection (REC reference 09/H1202/114).

This study was an electronic version of an observational study. Observational research presents methodological challenges because telling participants they are being watched can alter behaviour thereby biasing the results^{192;193}. For this reason we did not inform participants of this IIS RCT that we would record the type and amount of information they accessed. Participants were told of all aims that were not likely to invite bias into the study, for example, that we wanted to evaluate and pilot a new way of providing study information to participants.

Based on the results reported by Antoniou et al, it was anticipated that some potential participants would not choose to read information on the website and that still more would not access all of the information provided on the paper PIS. They would not, therefore, be fully informed about the parent study when they made a decision regarding participation. Moreover, we would be able to identify those participants who had read little or no information. Given the ethical significance placed on information in decisions regarding research, this presented an ethical challenge for the research team. Our justification for continuing was as follows:

1. The parent study was a low risk study unlikely to result in any physical harm to participants. Thus the participants who did not choose to access information were not 'blindly' consenting to significant risk.

2. There is always a danger that participants will not read the PIS, even when it is presented to them in full and on paper. The consent interview acts as a safeguard against this danger. GCP suggests that the person gaining consent should go through the information provided and the opportunity for the potential participant to ask questions. We confirmed that this was indeed the practice on the parent study, and that consent would not be gained until the research nurse was sure that the participant understood what they were agreeing to before gaining consent. Accordingly, we judged that the risk of ill-informed consent being gained from our participants was in fact quite small.

3. We, as researchers, were aware that some individual participants had not accessed study information prior to the first appointment, although in terms of the participants' experience, this is no different to them not reading a PIS sent through the post. The first ethical issue of the research lies here since tracking participants online activities moved the boundary from uncertainty (in the case of traditional versions of PIS) to near certainty (in the case of IIS) that individuals did not read study information before the appointment. UK NRES guidelines²² do acknowledge that PIS are only one part of the consent process and suggests the platform for presenting information (for example, verbal/written information) should be considered for every study. In the parent study we regarded the reading through of the PIS at the first appointment as a sufficient safeguard if participants had not read any (or 'sufficient' levels of) information prior to the appointment. Given this safeguard and NRES guidance, the researchers involved in the IIS study did not fail in their duty to ensure informed participation.

Finally, we accessed demographic information (not names or addresses) about participants in the parent study who either did not choose to participate in the information provision study or who were ineligible to participate because they did not include an email address. The PIS for the parent study stated that: “personal data will be kept separately from study results. Anonymised data from the study will be used in the main analysis and may be used in future work.” This meant that participants were informed that anonymised data may be made available for other research, such as this Information Provision Study. Demographic data anonymised by participant ID number for statistical analysis purposes in the parent study was made available for use in this Information Provision study. This information was then tied, by ID number, to participants in the Information Provision study. For this reason, we do not think that consent was exceeded.

4.11 CHANGES MADE TO THE PROTOCOL AFTER COMMENCEMENT OF THE STUDY

The parent pilot study (n=7) estimated a consent rate of 70% but the actual rate of recruitment was around 30%. Sample size calculations for the IIS RCT assumed a baseline consent rate of 70% and so were amended to take into account the lower rate. For a 30% baseline consent rate the required effect size was 27.0% (Section 4.5), so with 90% power the sample size estimation was n=132 (Table 8).

The proportion of parent study participants accessing the study website was much lower than anticipated, with only 29.7% (86/290) randomised. There were also an unexpectedly high number of people that participated in the parent study without accessing any study information (63/106; 59.3%). Based on results by Antoniou et al⁶ we anticipated that around 25% of our participants would not access any study data, but the actual figure was 59.3%. The lower than predicted parent study consent rate and high number of participants choosing to access no study information had an effect on uptake to the IIS RCT and so recruitment was slow. By the end of the recruitment period only 86 participants had been randomised in the IIS RCT.

Average recruitment to the IIS RCT for these 86 participants was 8.6 participants per month. Recruitment rate of ethnic minority groups to the IIS RCT was shown to be much lower than for White participants; 36% (62/172) White, 23.7% (14/59) Black Caribbean and 13.9% (6/43) South Asian were randomised to the IIS RCT. At the end of the IIS RCT planned recruitment period the parent study began to focus on

recruiting South Asian participants since they had recruited sufficient White participants. The recruitment of South Asian participants to the IIS RCT was 2.5 times slower than for White participants. It was expected that continuing the IIS RCT once the parent study began to focus on recruiting South Asian participants would only recruit 3.4 participants per month. It was estimated that the sample size would not be met in a timely manner if recruitment continued. For this reason, the trial was stopped on 12th December 2011 at the end of the planned recruitment period.

We also planned to compare the information accessed by participants using a logistic regression model to account for age and gender with GP practice as random effects. Due to the small numbers seen in each of the demographic groups, this model would have been overfitted¹⁹⁴, meaning results would not be reliable. Since this modelling work was not used to meet a primary aim, it did not need to be conducted to satisfy ICH Topic E 9 Statistical Principles for Clinical Trials Guidelines¹⁹⁵. Instead of this modelling work, exploratory subgroup analysis determined the proportion of participants in each demographic group that accessed each piece of information.

Estimate of costs

An exploratory retrospective analysis of costs was undertaken for the Information Provision study as described below.

Cost of invitations

Costs for electronic and postal invitations were calculated using a combination of actual and estimated costs. Stationery, printing, and phone call costs were accurately identified from invoices and used to calculate cost per item. Administrator's time was estimated, from the time it took to do the listed jobs in the Information Provision study (e.g. to print letters, fill envelopes, call participants, etc). The cost for administrator's time was then estimated using the middle of a band 400 salary grade at the University of Birmingham. For the postal invitations, the total cost per person was calculated by adding together the total cost for printing, stationery and administrator's time.

The estimated cost of sending electronic invitations was calculated using both the cost of administrator's time to send the invitations, and the cost of follow-up phone call to encourage participants to open the email. The cost of sending the email was calculated by estimating the administrator's time. The cost to call each participant who answered was calculated using the cost of the estimated average duration of the phone call, and estimated administrator's time to talk to participants and to call participants when they did not answer. The percentage of participants who answered was calculated from the actual percentage that did so in the Information Provision study. The cost to call each participant who did not answer was calculated using the estimated administrator's time to call participants when they did not answer. The percentage of participants who did not answer was calculated from the actual percentage that did so in the Information Provision study. The total average cost per invited participant was calculated by: (Total cost to send email to each participant) + ([cost to call participant when they answered] x 28.5% of total participants) + ([cost to call participants when they did not answer] x 16.9% of total participants)

Cost of developing the IIS

The cost to develop the IIS needs to be considered in relation to the costs associated with the standard PIS. The level two information was the REC favourably reviewed information and would have to be written for any research study involving humans anyway, so the costs in relation to this information would not increase for an IIS. The additional costs in developing the content of the IIS came with writing the information in levels one and three.

If an IIS was to be developed for a future low risk interventional study it is likely that the first draft would be written by a member of staff appointed at band 6 (i.e. research associate), it would be reviewed by a more senior member of the research team appointed at band 7 (i.e. research fellow) and then the principal investigator would undertake a final review of the information. The wages used in the cost estimate for the IIS were based on the average wage for the appointed band at the University of Birmingham.

Researchers involved in development of the IIS were asked to estimate how long it had taken them to review documents at each stage of the development process. The total cost of developing the IIS was then estimated with the calculation: ([Estimated total hours it took the Grade 6 staff member to develop the IIS] x [the approximate wage per hour for Grade 6 staff]) + ([estimated total hours it took the Grade 7 staff member to develop the IIS] x [the approximate wage per hour for Grade 7 staff]) + ([estimated total hours it took the Grade 9 staff member to develop the IIS] x [the approximate wage per hour for Grade 9 staff]).

5 DEVELOPMENT OF THE INTERACTIVE INFORMATION SHEET (IIS)

5.1 CONTRIBUTORSHIP OF CHAPTER 5

Antoniou et al⁶ developed an unfolding electronic PIS and used it in participants of a Internet questionnaire-based study, and this work formed the basis of the IIS intervention (Section 2.6).

Whilst the design and writing of the website used to host the IIS was carried out by the author, all programming of the website was undertaken by Christopher Withers who is part of the Education Technology Team at the University of Birmingham.

The information to be included in the IIS was drafted by the author of the thesis, but was reviewed and comments provided by Professor Heather Draper, Dr Melanie Calvert, Professor Sue Wilson and Professor Richard McManus.

5.2 DESIGN AND IMPLEMENTATION

Design of the IIS Website

Outline

The layout of the IIS website was consistent across each page and its basic design consisted of three parts:

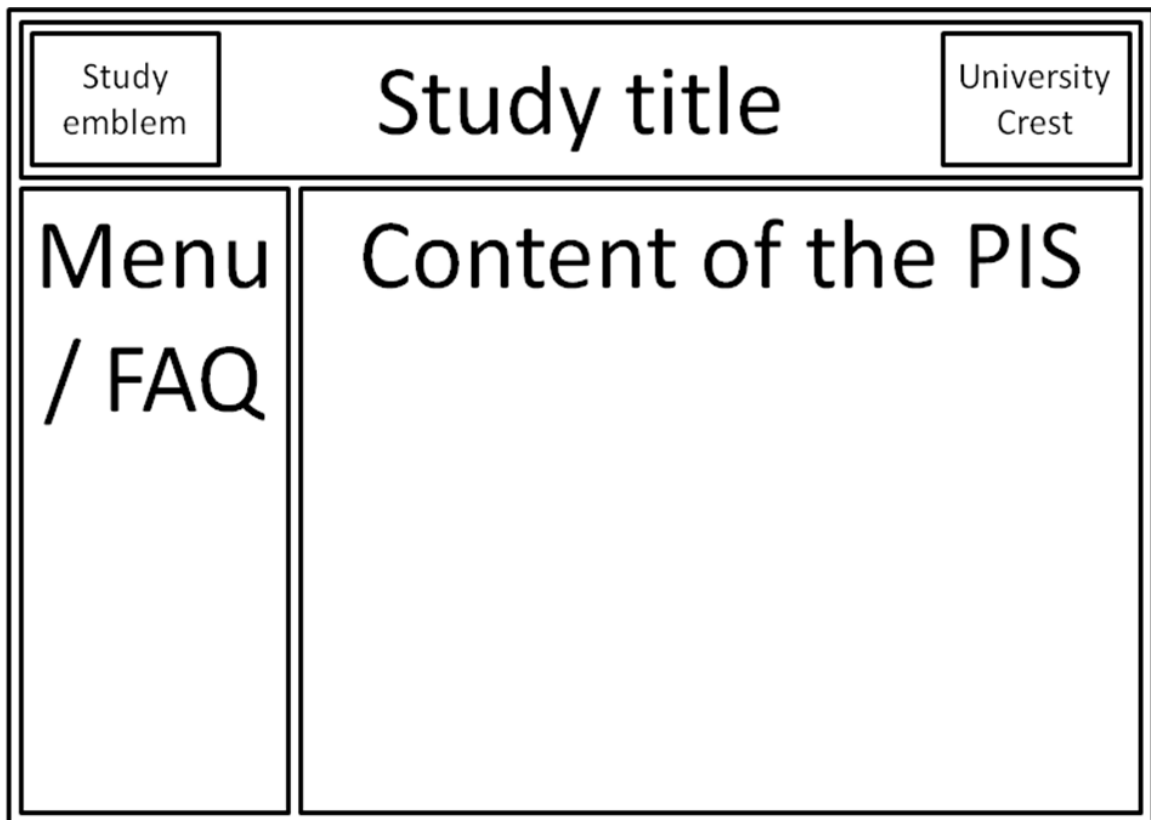
1. A header across the top of each page that provided participants with the name of the research study, the University logo and the parent study emblem. This allowed participants to identify that they had entered the correct URL.

2. A menu bar down the left side of each page contained a list of the FAQ's where participants were able to click to access information (Section 5.3 gives and explanation of how FAQ titles were chosen). When participants clicked on an FAQ, the initial information relating to that FAQ appeared in the 'content box' on the right hand side of the webpage.
3. At the bottom of this initial information was a 'button' they could click to access more information relating to that FAQ. Participants could access information relating to a different FAQ by clicking the hyperlink over the FAQ in the menu bar. When they did this, the information in the content box was replaced with information relating to the selected FAQ.

When designing the website the outline (Figure 11) of each page was written first using the master page function in ASP.net¹⁹⁶. The master page function allowed the same page design to be applied to each webpage and provided continuity and reading ease.

The menu bar formed a site navigation pane that provided access to all parts of the website containing study information. It included links to all of the FAQ's and enabled participants to click on the FAQ in which they were interested and access information relating to it. Participants were able to click on as many questions, in any order, as many times as they required. This allowed participants to access only the types of information they needed to meet their individual informational requirements.

Figure 11 – Outline of the IIS website



The website was written using a variety of computer languages¹⁹⁷. The layout of the pages used HTML (Hypertext Markup Language), the standard language for writing Internet pages. The design aspects were written using CSS (Cascading Style Sheets), which allowed a level of design detail greater than is achievable using HTML alone. Master pages cannot currently be written using HTML and CSS alone so this function was coded using ASP.net¹⁹⁶ (Active Server Pages language for Microsoft). Christopher Withers programmed the website and linked it to a database to collect study data using his preferred languages (C+ [C plus] and MySQL [My Structure Query Language]).

Allowing the information to 'unfold'

ASP.net language, specifically 'Asp.Panel' and 'Asp.Button' tags and the 'OnClick' functions¹⁹⁸, allowed the website to be written in such a way that each page could be programmed to unfold. Visual Basic (VB) programming code¹⁹⁹ linked these 'buttons' and 'panels' and added functionality to allow the information to unfold as buttons were clicked by participants.

Each level of information was written in a different 'Panel' and 'Panels' of text could be hidden or shown depending on code linked to it. Level one information was included in 'Panel 1', level two information in 'Panel 2' and level three information in 'Panel 3'.

Under the first level of information was 'button 1', that, when clicked, allowed the level two information to be seen. VB code added meant that when this button was clicked, Panel 1 (level one information) and Panel 2 (level two information) were visible, but Panel 3 (level three information) and Button 1 were hidden. A new

Button, 'Button 2', also appeared at the bottom of the level two information once 'Button 1' had been clicked.

When button 2 was clicked, the VB code told the website that Panel 1, Panel 2 and Panel 3 should be visible, but Buttons 1 and 2 should be hidden (see Figures 12 and 13 for pictorial representation of this process).

Figure 12 – Unfolding content of the IIS website

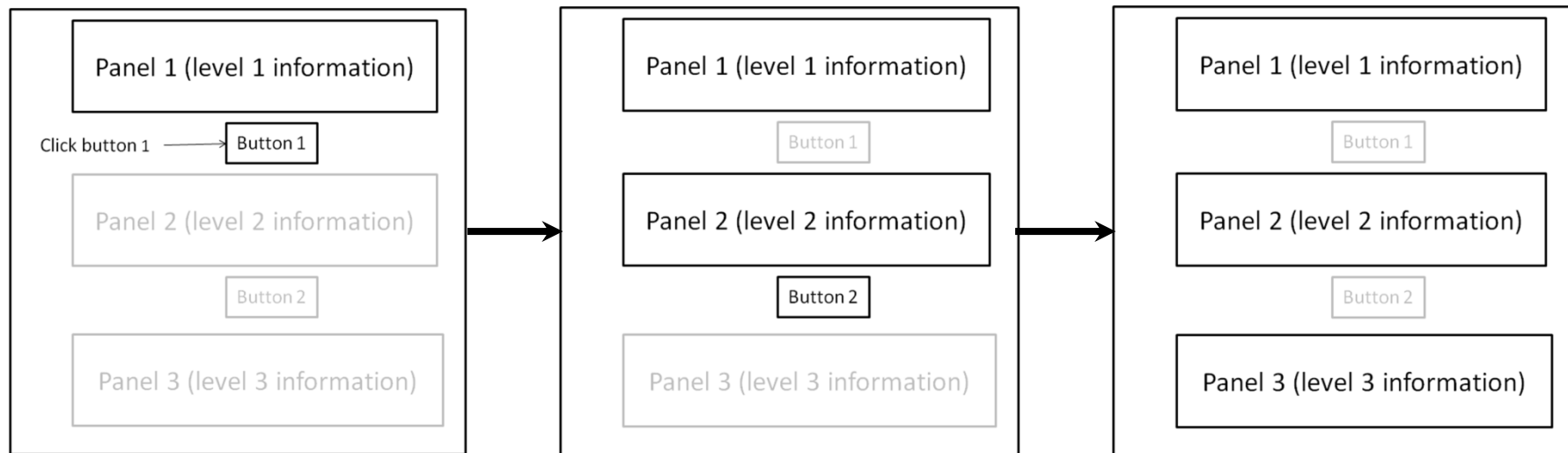
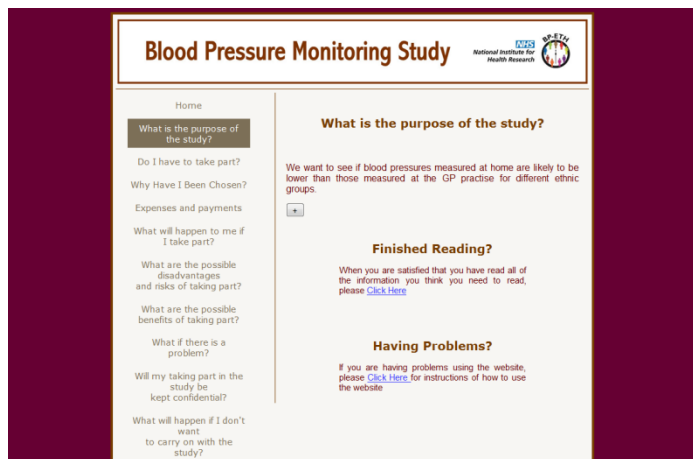
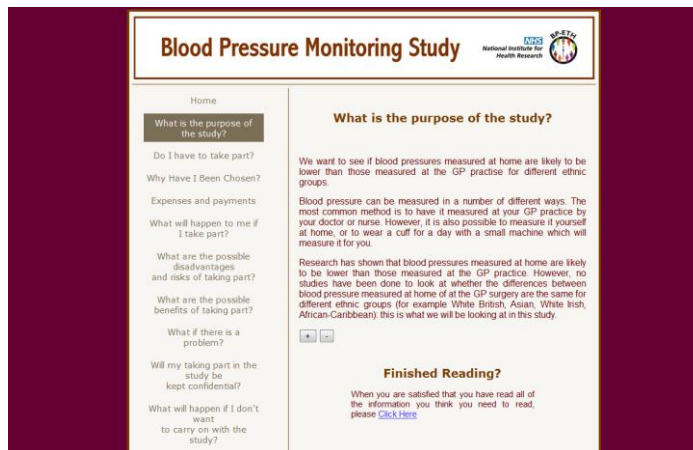


Figure 13 – Images of the unfolding content of the IIS website

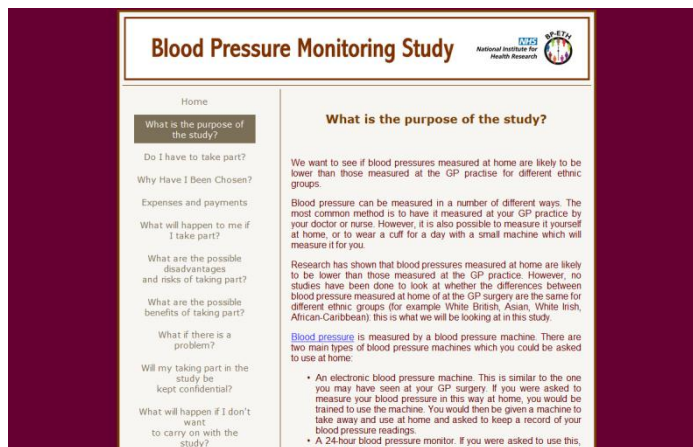
Level one



Level two



Level three



Hosting

The IIS was hosted on the University of Birmingham website under the study title URL (<http://medweb4.bham.ac.uk/bloodpressurestudy>). Participants randomised to receive the IIS were provided with access to the IIS part of the website and could use their participant ID number (provided when they were invited to participate) to log onto the website as frequently as they liked.

How participants accessed the website

Potential parent study participants who provided their email address when they returned their questionnaire were invited to take part by an email invitation. Included in this email was a link to the study website where, they were told, they would find information that would help them to decide whether or not to take part. If they chose to access parent study information online, the link took them to the login page of the study website where they were prompted to enter their participant ID provided on the email. On successful login a webpage explained that providing information online was a departure from standard paper-based practice and was being evaluated as an alternative and novel way of providing study information to potential participants. Participants were given the choice of opting into or out of the IIS RCT at this point. If they did not wish to participate they were automatically sent a paper PIS in the post and were not contacted electronically again. If they agreed to participate in the IIS RCT they were directed to a webpage that asked them for their age and gender (used for stratification during randomisation). Once participants clicked on the submit button at the bottom of this page they were randomised, automatically by the database connected to the website, to receive either the PDF-PIS (control arm) or the IIS (intervention arm). The information provided in the PDF-PIS was identical to

the paper PIS already approved for the parent study and could be saved and/or printed.

How information accessed by each participant was recorded

Christopher Withers programmed the website to allow information about the following participant actions to be stored in a database:

1. If they logged onto the website
2. If they agreed to participate in the IIS RCT
3. Age and gender
4. The arm randomised to
5. For those participants randomised to the IIS, the levels of information accessed and the time spent on each
6. If they were interested in participating in the parent study. Responses to the understanding and satisfaction questionnaire

5.3 DEVELOPMENT OF CONTENT

How titles for the FAQ were chosen

The parent study already had a PIS approved by the local REC (REC reference 09/H1202/114). The titles used in the paper PIS were also used as the titles in the IIS to ensure consistency between the two. Clicking on the links over the FAQ's allowed participants to choose what types of information they accessed. The FAQ titles used were:

1. What is the purpose of the study?
2. Do I have to take part?
3. Why have I been chosen?
4. Expenses and payments
5. What will happen to me if I take part?
6. What are the possible disadvantages and risks of taking part?
7. What are the possible benefits of taking part?
8. What if there is a problem?
9. Will my taking part in the study be kept confidential?
10. What will happen if I don't want to carry on with the study?
11. Involvements of the General Practitioner/Family doctor (GP) What will happen to samples I give?
12. Will any genetic tests be done?
13. What will happen to the results of the research study?
14. Who is organising and funding the research?
15. Who has reviewed the study?
16. Further information and contact details

Explanation of the type of information included in each level

The information in the IIS was split into three levels: level one contained less detailed information than in the parent study PIS (minimal information), level two contained an exact copy of the information in the parent study PIS (standard information) and level three contained more detailed information than the parent study PIS (extended information) (Figure 13). The objective was to determine if potential participants chose to access less detail, the same detail, or more detail about the study than was provided in the standard PIS.

Level one contained a short, easily digestible piece of study information. For example, if a participant clicked on the FAQ “Will my taking part in this study be kept confidential?”, they would simply have received information that stated “Yes, your taking part in this study will be kept confidential”.

Level two provided the same information as the paper PIS.

Those who wanted more information were invited to click a second button at the bottom of this level two information to access more detailed information (level three). This third level of information was the most detailed available on the IIS website, although it sometimes contained hyperlinks directing participants to external information sources, for example, to websites that explained terms used in the explanation, or linked to scientific papers evidencing information provided. All external links opened in a new window so participants could easily navigate back to the study website.

How content was decided

Parent study PIS

The information in the paper PIS was split into two parts as suggested in NRES guidance²² - part one gave basic information, and part two provided further information. All of the information in the parent study paper PIS was included in the IIS, generally in level two. Exceptions occurred when information topics were included in both parts of the paper PIS. An example of this is the FAQ 'What if there is a problem?' Part one stated:

“Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.”

Part two then stated:

“If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions: Dr Richard McManus (T: 0800 234 6 432). If you remain unhappy and wish to complain formally, you can do this by contacting Ms Sarah Bathers, Primary Care Clinical Trials Unit Manager, Primary Care Clinical Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT (T: 0121 414 3323).

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have

grounds for a legal action for compensation against The University of Birmingham but you may have to pay your legal costs.”

Information on the same FAQ was sometimes included in both parts of the PIS. In these cases, part 1 information from the parent PIS was included in level two of the IIS and part 2 information from the parent PIS was included in level three of the IIS.

Interviews with parent study pilot participants and research nurses to inform the IIS

The parent study conducted some pilot work on phase II of their study that involved seven participants, each of whom made three appointments with the research nurse. After appointment two, all seven participants were asked if they would be willing to take part in a short interview about their experiences of the consent process to help inform the design of the IIS RCT. Three participants agreed to be interviewed. All were provided with written information about the pilot work to describe what would be required of them (Appendix 9.6).

This pilot interview study did not require NHS permission because it was pilot work intended to inform the design of the main Information Provision study (which would be reviewed by NRES). This small IIS design pilot study did require further University review and was given favourable opinion prior to commencing (reference number RG_10-119).

Interviews were conducted with three parent study participants. A research nurse who was not involved in the parent study but had extensive experience in blood pressure monitoring research also agreed to be interviewed. Interviews lasted around 40 minutes each, during which participants were asked questions about each

section of the parent study PIS. Participants were asked to indicate which part of the information provided they thought was the most important to know. The data collected were used to inform what information would be included in level one of the IIS (Table 10).

Interviewees were also asked to describe what further information they would like to have for each FAQ in the PIS. For the most part, participants were unable to provide an answer to this question and simply stated that the information provided was already comprehensive.

Level three information was based on the information that participants from interviews wanted to know or thought that others might want to know (Table 11).

Table 10 - The minimal information participants thought should be included in a PIS

Question	Pt1	Pt2	Pt3	Nurse 1
What is the purpose of the Study	None I think the measurement at home which gives you, probably gives you a more accurate reading, er as long as you do it	Right, but what interested me was the fact that erm you get differences with home measurements than when you come to the doctors	None
Why Have I been chosen?	None	None	None	None
Do I have to take part?	We'll ask for permission to look at your records.	None	I would think perhaps to someone, some people, they may not be too willing to give permission for you to delve into their medical records	None
What will happen to me if I take part?	Er, you'll be involved in it for 8 days, erm, and in that time you'll be asked to have a 24 hour monitor, and, er to take your own blood pressure for a week	I wouldn't want to see it reduced I don't think	None	I think probably, the less that's inclusive the better, because the more information you give sometimes the less it's too overpowering isn't it?
Expenses and payments	None	None	None	None

What are the possible benefits of taking part?	I suppose that they're going to pass it onto your GP would, perhaps impress you	I just think the results basically are the most important	None	None
What are the risks of taking part?	None	None	None	None
What if there is a problem?	None	That you've got a telephone contact number if you've got a problem	None	None
Will my taking part in the study be kept confidential?	Just the fact that it's being kept er private really	I think the, the probably the telephone number and contact is, is probably the probably the most important	None	None
Involvement of your General Practitioner/Family doctor (GP)	We will ask your permission to inform to your GP regarding the results of this study?	None	None	None
Who is organising and funding the research?	None	No I, I would, the research is all gonna happen at Birmingham..... [pause] I don't know on this one. I really I think you only need to put the National Institute of Health Research or just the department, is funded by the Department of Health	None	None

What will happen to the results of the study?	None	Just the fact that you, you're going to publish the results of the study in medical journals	None	None
Who has reviewed the study?	I suppose the last sentence, 'this studies been reviewed and given favourable opinion by the research ethics committee'	I think that all research in the NHS is looked at by an independent group	None	None

Table 11 - Extended information participants thought should be included in the PIS

Question	Participant 1	Participant 2	Participant 3	Nurse
What is the purpose of the Study	None	None	Why the measurement at home is lower? I'm not really into why you're studying British, Asian, White, Irish. The sort of technical details of how it [blood pressure] works	The most common method is to have your blood pressure measured at the GP practice by a doctor or nurse, but that you can also have it measured at a pharmacy. Substantiate why you're looking at the differences between ethnic minority groups
Why Have I been chosen?	I think if it came out the blue, and I, I'd think well who's giving out my information?	I did want to know why I'd been chosen but I took it that erm I'd been chosen because I'd had problems before	None	None
Do I have to take part?	None	None	None	This will not affect the care that you receive from your GP. I'm just wondering if you need to say where they will sign that consent form

What will happen to me if I take part?	you see they said if you shower or anything erm, you could unplug it, but they didn't mention going to the toilet or anything like that	There's a phone number for queries, it might be worth putting erm the times that that phone I think they need to know why their blood pressure is unstable	None	To say where you write them down, are you going to give them a book, or write them down, are you going to provide that? Details of what the, the kinds of things that the questionnaire will be asking them How much teaching they will have about how to take their own blood pressure because it may seem like a big thing to some people to take their own blood pressure. Say why it's good to have an acceptable blood pressure reading in terms of prevention, of the illness, yeah, and preventing problems in the long term. I think it's important to mention actually that if your bp is over the NICE guidelines or the accepted limits, you feel probably very well. Right, so you might need to elaborate on that, will they be able to shower, will they be able to sleep? I think you will need to give a bit more information on that
Expenses and payments	None	None	None	You might want to ask if they'll bring a receipt if they use a taxi

What are the possible benefits of taking part?	None	None	Information about what high blood pressure does and what it can lead to and all that	None
What are the risk of taking part?	None	None	None	So it might be useful to just say, what uncomfortable is
What if there is a problem?	None	None	None	
Will my taking part in the study be kept confidential?	What's R&D audit?	None	None	Well I think it's worth mentioning that, that they will be assigned an ID number Stored securely, yes you could elaborate on stored securely, either in locked cabinets or a password protected database, something like that
Involvement of your General Practitioner/Family doctor (GP)	None	None	None	None

Who is organizing and funding your research?	None	None	None	None
What will happen to the results of the study?	Yeah, in a sort of simplified form, I mean I don't want to know all the official stuff would ya I think you'll have probably people who are really interested or people who want to know all the details	None	None	Some might want to know what the function of a research ethics committee is
Who has reviewed the study?	None	None	None	None

Results from systematic review

It was expected that the systematic review (Chapter 3) of existing literature would inform the development of the IIS. The review, however, identified no studies that looked in detail at what participants wanted to know, so could not be used to determine what further information to include in level three of the IIS.

Expanding on the information in the paper PIS

The pilot interviews and the systematic review did not provide sufficiently detailed information about areas that could be usefully expanded, so each sentence of level two information under each FAQ was read to identify places where further information could be included. Detailed information was collected from scientific papers, credible websites and lay publications/leaflets for this level.

The level three information was then re-searched to identify key words that could be used to link to external sources for further explanation. An example of this was the key word 'blood pressure' that was externally linked to the British Heart Foundation website where participants could find an explanation of what blood pressure is. This was done for as many key words as possible and only websites published by expert groups such as NHS Direct, scientific papers where appropriate and electronic lay information leaflets produced by credible sources were used as hyperlinks.

The readability of the first draft of level three information was assessed using the Flesch Reading Ease and the Flesch-Kincaid Grade Level²⁰⁰⁻²⁰². The wording of the information was adjusted until it was below Grade 8 level (i.e. comprehensible by the average 13 year old) and had a reading ease greater than 60%.

Review and comments from supervisors

The first draft of the IIS was assessed and discussed by all three academic supervisors - Professor Heather Draper, Professor Sue Wilson and Dr. Melanie Calvert - and the PI of the parent study (Professor Richard McManus), all of whom are senior academics at the University of Birmingham and experienced in the design of PIS. They ensured the information was scientifically and ethically sound and easy to understand and suggested appropriate places to add further information. The draft was updated to take into account their feedback and then included in website coding to allow it to be uploaded to the server and made available online.

The full information from the IIS is included as Appendix 9.2.

Testing of the content

Once the content of the IIS had been developed it was loaded onto the website and made live, which allowed the website to be de-bugged and user tested.

De-bugging and content testing with competent computer users

The website was first checked for errors by competent Internet users. Five volunteers were asked to log on to the website, navigate around it and report any problems they found and attempt to 'break' the website using methods such as pressing the back button on the Internet browser. Errors reported included CSS coding not working on some pages (meaning the page did not display properly), broken external website links, links to some external websites not being brought up in a parent window and the ability to 'trick' the website into allowing a user to be randomised twice. All errors were fixed and the same five volunteers re-reviewed the website and identified no further problems.

User testing with low computer users

Once the de-bugging of the website had been completed, it was then tested with low computer users (defined as using the Internet less than twice a week). It was expected that if potential participants provided an email address they would have at least some computer literacy. Three users (one male, aged 68; one female aged 45; and one female aged 54) were asked to log onto the website and follow the online instructions. All were able to follow the instructions correctly and successfully navigate the website. When asked how the website could be improved they suggested making text larger and darker. They also suggested that a link to the 'how to use this website' page should be

included at the bottom of each page. All three suggestions were incorporated into the website and the updated version was uploaded to the server.

6 RESULTS

This chapter provides detailed results of the Information Provision study. It begins by providing recruitment numbers for both the parent study and Information Provision study, and key results from the study. It then presents demographic data for participants, information accessed by participants and the time spent reading it, the effect of the IIS on consent rates, the level of participant understanding and satisfaction with the way information was provided, and finally, an estimation of costs. A streamlined PIS for the parent study is then presented, which was developed using the information accessed by participants in the Information Provision study and the information that guidelines states participants ought to know. The results of the Information Provision study and streamlined PIS were presented to the NRES expert panel, and so the chapter concludes with their feedback of this work.

6.1 PARTICIPANT RECRUITMENT

Data were collected for the Information Provision study between 5th February and 12th December 2011. Table 12 gives the number of participants included at each stage.

1160 participants returning the parent study questionnaire (phase I) were happy to be contacted about taking part in phase II of the parent study (63% response rate) (Figure 14). Of these, only 290/1160 (25%) provided an email address. All 290 participants were sent electronic invitations to participate in the parent study. Of these, 14/290 (4.8%) provided an incorrect email address and could not be contacted by telephone for the correct information (7 did not provide a valid telephone number and 7 did not answer the telephone after ten attempts). These 14 participants were sent a standard postal invitation letter and paper PIS to the parent study but remained in the electronic information arm for Intention To Treat (ITT) analysis. In total, 276/290 (95.1%) emails were assumed to have been delivered to the correct participants.

Of the 146/290 (50.3%) participants who were assumed not to have opened the email within 3 days, 83/146 (56.8%) were successfully contacted by telephone and resent the electronic invitation (Figure 15). Of the 83 participants successfully contacted by telephone, 61/83 (73.5%) responded to the email that was resent

following the telephone conversation, so a total of 191/290 (65.7%) of participants were known to have opened the email invitation to participate in the parent study.

A total of 85/290 (29.3%) participants were assumed not to have opened the email (although they may also have opened, read and deleted the email and so not responded). 22 of these (25.9%) were contacted by telephone, 13 (15.3%) had no valid telephone number and 50 (58.8%) did not answer the telephone.

Of the 290 IIS study participants, 101/290 (34.8%) accessed the website and 86/290 (29.7%) entered their age and gender into the website and were randomised to IIS or PDF-PIS (Figure 16). 86 participants were randomised and included in the Intention To Treat analysis for calculations of consent rate to trial arms IIS and PDF-PIS information.

99/290 (34.1%) Information Provision study participants booked a parent study appointment. A contact number to book a consent appointment for the parent study was provided in the invitation email and 63/106 (59.4%) participants booked a parent study appointment without first accessing any study information. Of those randomised in the IIS RCT (and, therefore, receiving study information), 36/86 (41.9%) participants booked a consent appointment.

Participants were divided into five study groups for analysis purposes; 'IIS' includes those randomised to IIS and 'PDF-PIS' includes those randomised to the PDF PIS; 'No PIS' is where participants opened the invitation email but did not access the study website and, therefore, received no PIS. The 'email address' group are those that provided an email address on the parent study phase I questionnaire and, therefore, were eligible for electronic communication, and the 'No email address' group were those that did not provide an email address and were sent a standard postal invitation and paper PIS.

Table 12 – Participants included at each stage of recruitment

	N	%
Eligible from parent study	1160	
Provided an email address	290/1160	25%
Opened invitation email	191/290	65.7%
Booked parent study appointment	99/290	34.1%
<u>Participants in each analysis group</u>		
Randomised to IIS	44	
Randomised to PDF	42	
No PIS	106	
Paper PIS	870	

Figure 14 - Distribution of participants through the Information Provision study

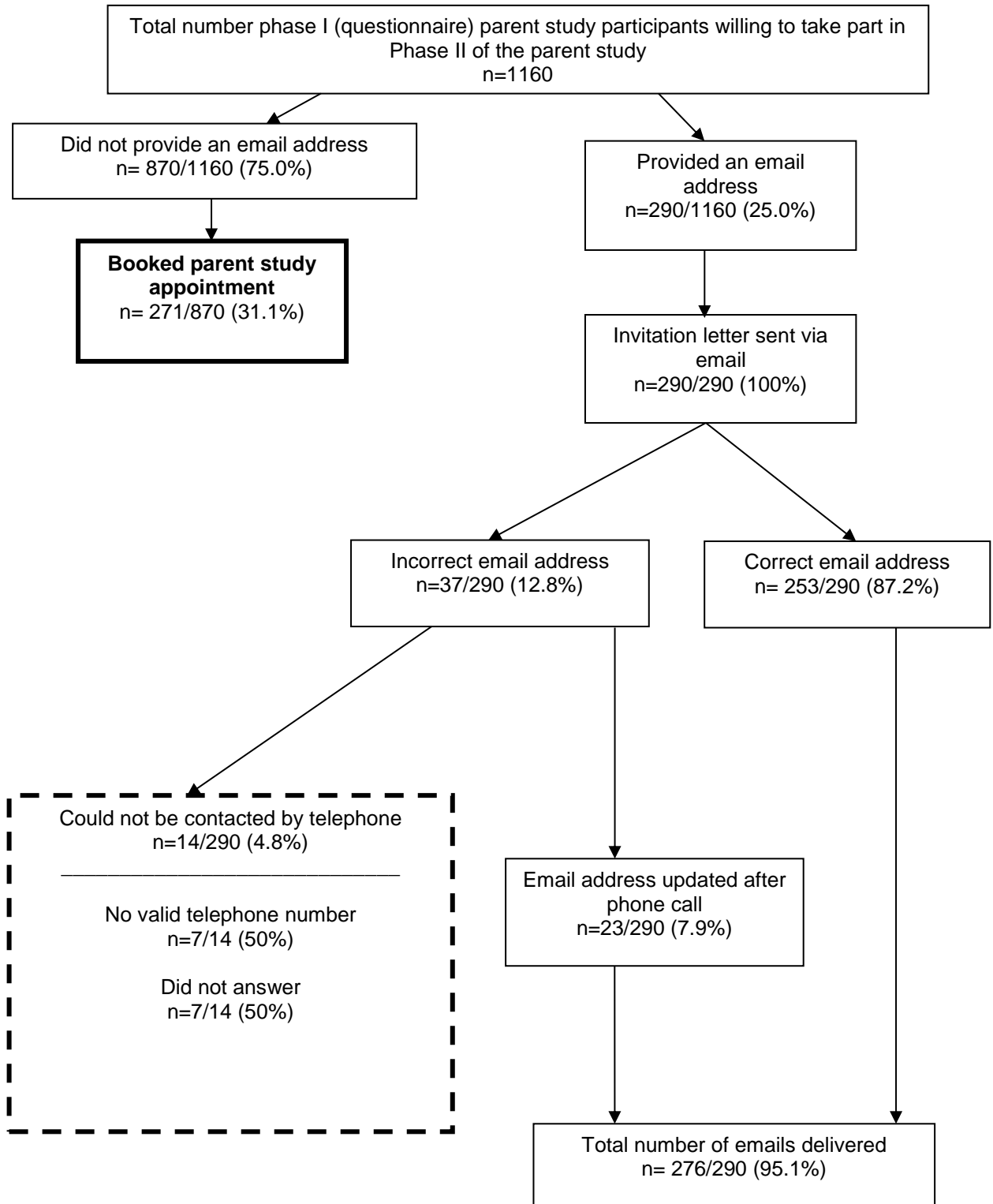


Figure 15 – Proportion of participants that opened the email.

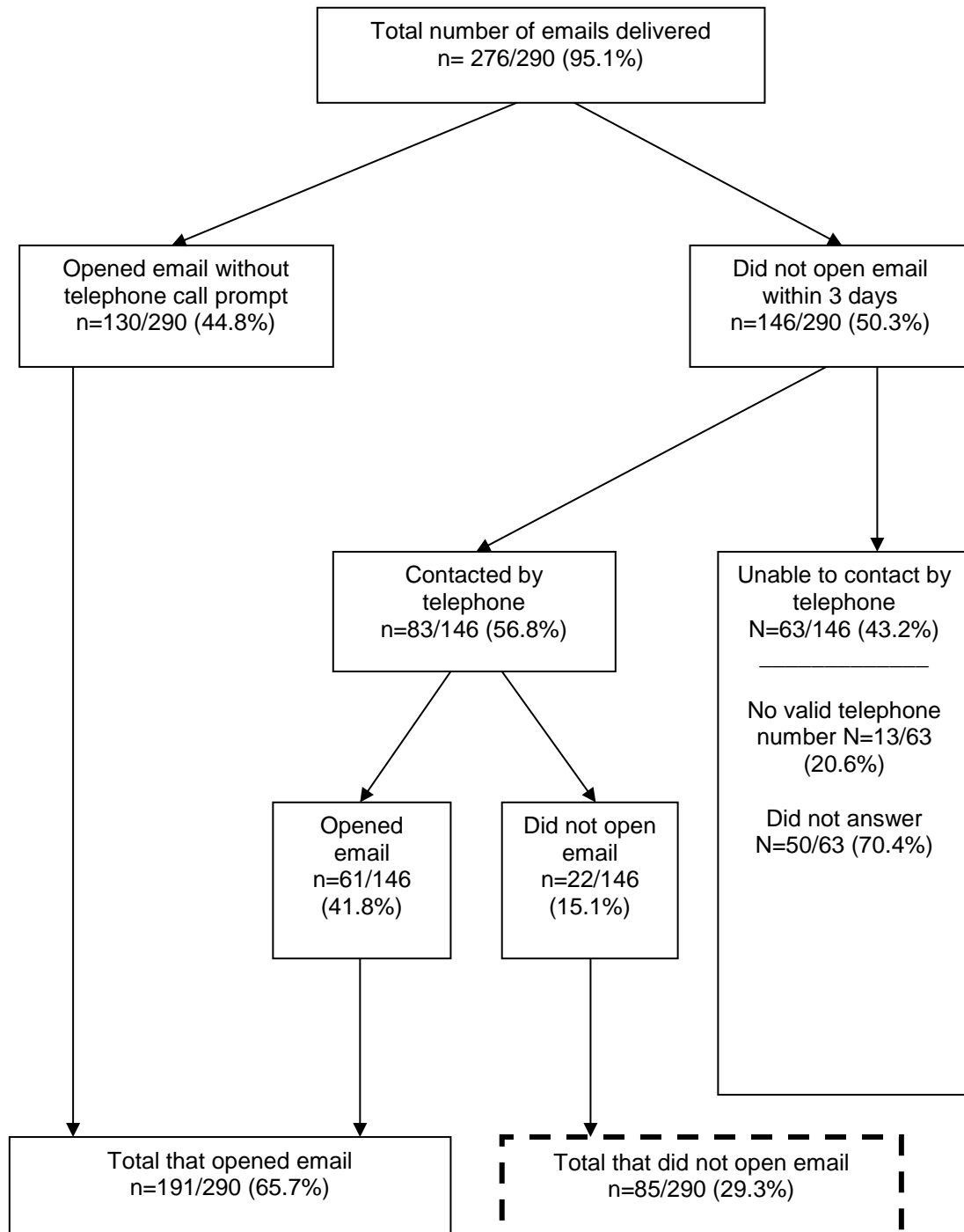
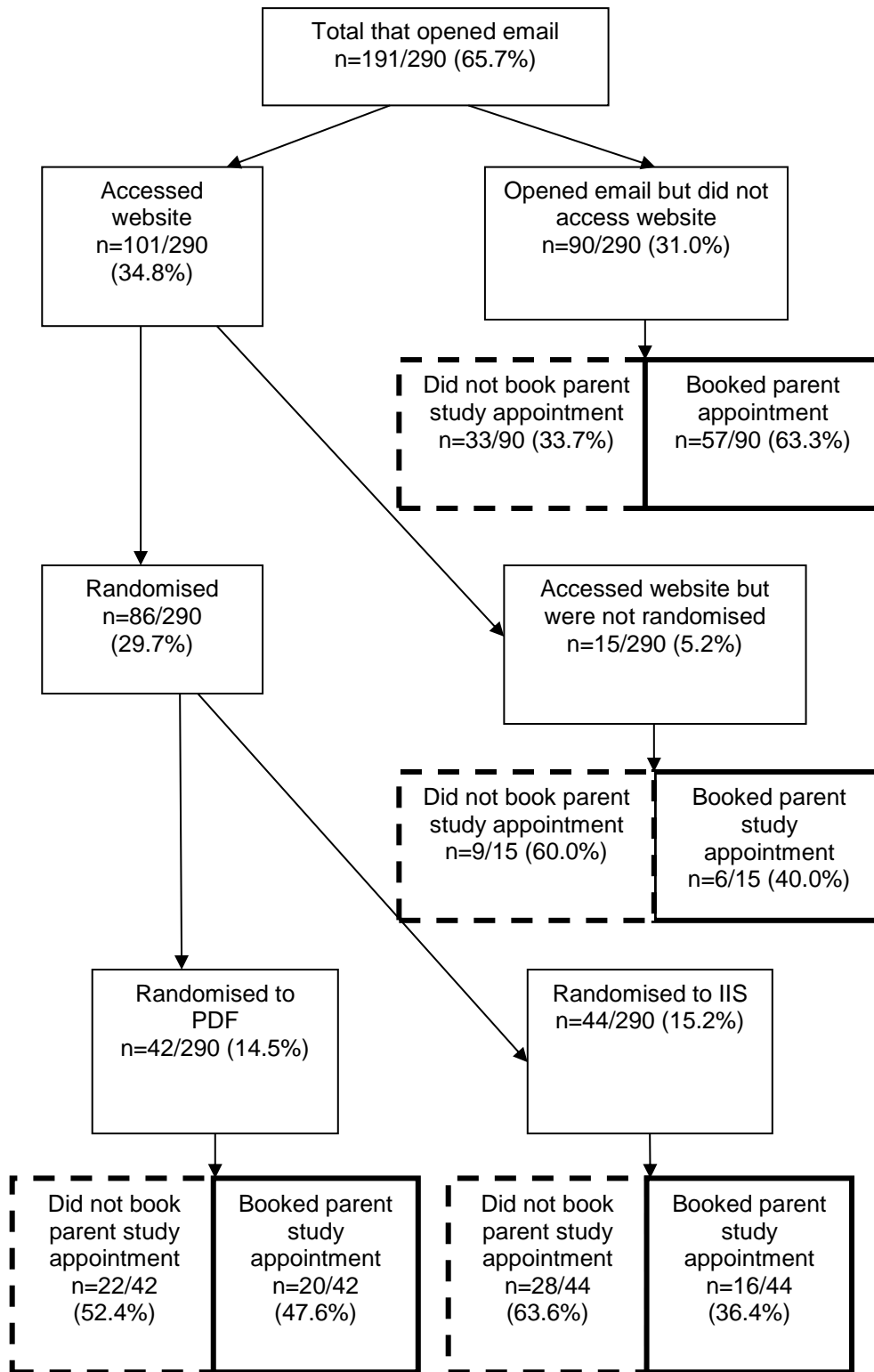


Figure 16 – Number of participants that took part in the IIS RCT



6.2 KEY RESULTS

An executive summary of findings is provided here and the following sections will provide detailed results of the Information Provision study.

The consent rate to the parent study was similar for all participants, whether they received information electronically or through the post. For parent study participants who did not provide an email address (and received information through the post) 271/870 (31.1%) booked a consent appointment. Of those that did provide an email address and so took part in the Information Provision study, 99/290 (34.1%) booked a consent appointment. A large proportion of participants consented to the parent study without accessing any study information (59.3% [63/106]).

11.4% of study participants randomised to IIS accessed the level of detail of information provided in the paper PIS for the parent study. 9.1% read more information than the paper PIS provided and 79.5% of participants read less than was provided in the paper PIS. Participants mostly accessed information about the practical aspects of taking part in the study, such as what they would have to do if they took part. Despite a high proportion of participants accessing no study information, the level of understanding was common across all study arms. Participants across all study groups were generally satisfied with the level of information they received, regardless of how much they chose to access. Those who

received information electronically were, however, less likely to want more information about the parent study.

6.3 DEMOGRAPHICS

Demographic data were collected for the study population and split by study groups (Table 13). Compared to those who did not provide an email address, those that did provide an email address were younger (email address=51 years and no email address=59 years), more commonly White (email address=172/290 [59%] and no email address=470/870 [54%]) and less deprived (email address=IMD 35.4 and no email address=IMD 38.6, where a higher IMD score indicates a higher level of deprivation). The three Information Provision study sub-groups (IIS, PDF-PIS and No PIS) were a similar age (median age 54.0, 53.5 and 50.5 respectively), but there were more males in the PDF-PIS group (24/44 [54.6%], 25/42 59.5% and 52/106 [49.1%] respectively). Of those with an email address, a higher proportion of Asian and Black participants chose not to access the study information (no PIS group) (White 57/172 [33.1%]; Asian 19/43 [44.2%]; Black 25/59 [42.4%]) and those in the 'no PIS' group were more deprived (IMD 34.6, 34.3 and 38.2 respectively).

Participants who consented to the parent study were more deprived (IMD 39.2 and 33.3 respectively) and more commonly Black (Black 33/256 [12.9%]; Asian 14/218 [6.4%]; White 54/642 [8.4%]) than those who did not participate in the parent study.

Table 13 – Baseline data for study population

	Information provision study groups			Electronic or paper		Consent status to parent study (those with an email address)	
	<u>IIS*</u>	<u>PDF-PIS*</u>	<u>No PIS</u>	<u>Email address</u>	<u>No email address (Paper PIS)</u>	<u>Consent</u>	<u>Did not consent</u>
Age							
Mean age (SD)	54.5 (9.3)	53.9 (9.8)	54.3 (9.7)	53.4 (9.28)	58.5 (9.5)	54.26	52.91
Median age (IQR)	54.0 (14)	53.5 (15)	50.5 (17.0)	51.0 (16)	59.0 (16)	52.5	51.0
Gender							
Male	24/44 54.6%	25/42 59.5%	52/106 49.1%	157/290 54.1%	430/870 49.4%	53/102 52.0%	104/188 55.3%
Female	20/44 45.5%	17/42 40.5%	54/106 50.9%	133/290 45.9%	440/870 50.6%	49/102 48.0%	84/188 44.7%

* denotes a randomised group in the IIS RCT

	<u>IIS</u>	<u>PDF-PIS</u>	<u>No PIS</u>	<u>Email address</u>	<u>No email address (Paper PIS)</u>	<u>Consent</u>	<u>Did not consent</u>
Ethnicity							
White	31/44 70.5%	31/42 73.8%	57/106 53.8%	172/290 59.3%	470/870 54.0%	54/102 52.9%	118/188 62.8%
Asian	2/44 4.5%	4/42 9.5%	19/106 17.9%	43/290 14.8%	175/870 20.1%	14/102 13.7%	29/188 15.4%
Black	5/44 11.4%	5/42 11.9%	25/106 23.6%	59/290 20.3%	197/870 22.6%	33/102 32.4%	26/188 13.8%
Deprivation							
Mean IMD Score (SD)	34.6 (17.8)	34.3 (17.8)	38.2 (16.6)	35.4 (16.9)	38.6 (17.2)	39.2 (18.3)	33.3 (15.8)
Median IMD Score (IQR)	32.0 (29.5)	30.1 (35.5)	36.0 (30.5)	32.1 (27.5)	37.2 (31.8)	36.7 (35.1)	31.2 (25.4)

Table 14 shows the proportion of the participants in phase II of the parent study that provided an email address, broken down into the demographic groups of age, gender and ethnicity. Younger, White participants were the most likely to provide an email address. As age increased, the proportion of participants with an email address decreased. South Asian participants were the least likely to provide an email address.

Table 14 – Proportion with an email address broken down into demographic groups (age, gender, ethnicity)

		Parent study participants that provided an email address	General population that use the Internet
Age	45-55	174/508 34.3%	89.5%
	55-65	69/303 22.8%	78.8%
	65+	47/350 13.4%	57.0%
Gender	Male	157/571 27.5%	84.6%
	Female	133/588 22.6%	79.8%
Ethnicity	White	172/639 27.0%	Unavailable
	Asian	43/218 19.7%	Unavailable
	Black	59/256 23%	Unavailable

6.4 INFORMATION ACCESSED BY PARTICIPANTS

One aim of this thesis was to determine what types and the level of detail of information potential study participants used to make a decision regarding participation in research. Only data from participants who were randomised to receive the IIS (n=44) in the IIS RCT contributed to this aim. This section describes what information participants accessed from the IIS.

The information in the IIS was available in an unfolding manner, meaning that participants could only access a higher level of information once they had accessed the previous level of information. Each time a participant clicked to access a piece of information; it was recorded in a database along with the amount of time they spent accessing it.

Table 15 shows the proportion of participants accessing (and not accessing) each piece of information. Where a higher level of information was not available, this is indicated by 'n/a'.

Table 15 – Proportion of participants accessing each level of information for each FAQ

	Level one		Level two		Level three		External information	
Purpose of the study	18/44	40.9%	4/44	9.1%	2/44	4.6%	2/44	4.6%
Have to take part	8/44	18.2%	0/44	0%	0/44	0%	0/44	0%
Why been chosen	18/44	40.9%	4/44	9.1%	1/44	2.3%	n/a*	
Expenses	22/44	50%	5/44	11.4%	2/44	4.6%	n/a*	
What will happen	22/44	50%	4/44	9.1%	2/44	4.6%	2/44	4.6%
Risks	22/44	50%	7/44	15.9%	2/44	4.6%	0/44	0%
Benefits	21/44	47.7%	5/44	11.4%	1/44	2.3%	0/44	0%
Problems	16/44	36.4%	1/44	2.3%	0/44	0%	n/a*	
Confidentiality	10/44	22.7%	1/44	2.3%	0/44	0%	0/44	0%
Don't want to carry on	7/44	15.9%	0/44	0%	0/44	0%	n/a*	
GP	14/44	31.8%	3/44	6.8%	1/44	2.3%	0/44	0%
Samples	15/44	34.1%	n/a*		n/a*		n/a*	
Genetic tests	10/44	22.7%	n/a*		n/a*		n/a*	

Results	11/44	25%	3/44	6.8%	2/44	4.6%	0/44	0%
Organising and funding	11/44	25%	4/44	9.1%	2/44	4.6%	0/44	0%
Reviewed study	11/44	25%	4/44	9.1%	2/44	4.6%	0/44	0%
Further info/contact	9/44	20.5%	n/a*		n/a*		n/a*	
Participants <u>not</u> accessing any information	18/44	40.9%	35/44	79.5%	40/44	90.1%	40/44	90.1%

* There was no information available for the FAQ under that level

Of those randomised to the IIS, 18 (n=44; 40.9%) participants did not read any study information. Seventeen participants (n=44; 38.6%) only accessed the minimal information provided in level one and 5 participants (n=44; 11.4%) only the information the REC favourably reviewed information (level two). Four participants (n=44; 9.9%) accessed more detailed information than provided in the paper PIS.

Twenty-six participants (n=44; 59.1%) accessed any one or more piece(s) of level one information. The most accessed pieces of information were about expenses (22/44; 50%), what would happen if one took part (22/44; 50%) and the risks of taking part (22/44; 50%). Slightly fewer accessed information about the benefits of taking part (21/44; 47.7%) and the purpose of the study (18/44; 40.9%). Fewer than a quarter of participants looked at any information concerning confidentiality (10/44; 22.7%), what would happen if they did not want to carry on with the study (14/44; 31.8%), genetic testing (10/44; 22.7%) and further information/contact details (9/44; 20.5%). The least accessed area of information related to what would happen if one did not want to carry on with the study (7/44; 15.9%). The remaining eight categories had access rates of between 25% (11/44) and 34% (15/44).

Only nine participants accessed any one or more piece(s) of level two information. The most viewed FAQ (risks of taking part) was accessed by only 7 (n=44; 15.9%) participants at this level. This reduced to 5 (n=44; 11.4%) for the expenses and benefits categories and to 4 (n=44; 9.1%) for the remaining FAQ's. No participants

accessed level two information about whether they had to take part or what would happen if they did not want to carry on with the study.

Only 4 participants (n=44; 9.1%) accessed any one or more piece(s) of level three information, and the most accessed pieces of information were accessed by only 2 participants. No participants accessed level three information on whether they had to take part, what would happen if there were any problems, confidentiality or what would happen if they did not want to carry on with the study. Only 1 participant (n=44; 2.3%) accessed level three information about why they had been chosen, what would happen during the study, the benefits of taking part and what their GP would be told about their participation. Only 2 participants (n=44; 4.6%) accessed level three information for the purpose of the study, expenses, risks of taking part, results of the study, who organised and funded the study and who had reviewed the study.

Only 4 participants (n=44; 9.1%) accessed any external information. Two participant's accessed external information for the purpose of the study (2/44; 4.6%) and what would happen if one took part (2/44; 4.6%).

6.5 TIME SPENT READING INFORMATION

A secondary aim of the Information Provision study was to determine how much time participants spent viewing each piece of information, with a view to determining if they had spent long enough on each piece to have read it.

The average time a participant spent viewing each piece of information was compared to the expected time it would take an average adult to read that piece of information, based on an average adult reading 200 words per minute¹⁹¹ (Table 16). No average viewing time could be recorded for the external information as it was accessed via an external link on the website.

For all level one FAQ's the average time participants spent viewing information was longer than the expected reading time so it is likely that where participants accessed this information they did read it.

For level two FAQ's the average time participants spent viewing information was usually much shorter than the expected reading time. The only category where the average and expected times were equal was the purpose of the study category (38s and 38.4s respectively). For all other categories it is likely that participants either skimmed through the information or clicked on the link just to see what was there. The increased reading time seen for the 'Purpose of the study' FAQ could have been

an artefact of it being the first FAQ offered by the IIS. Participants may have read through all of the information for this first FAQ in order to decide whether they were interested in the types of information included in levels two and three.

For level three FAQ information the average time participants spent viewing information exceeded the expected stay time in four categories (Why one had been chosen, expenses, risks, organising and funding) and took 75% of the expected time in five categories (purpose of the study, benefits, what their GP would be told, results, and who had reviewed the study). There was only one category where the average time spent viewing the information was not within 25% of the expected time (what will happen if one takes part). It is likely that although only small number of participants accessed level three information, those who did access it read it fully.

Table 16 – Average stay time measured in seconds for each level and expected time (in seconds) it would take the average adult to read each level of each question (based on average adult reading 200 words per minute)

	Level one		Level two		level three		Total time spent (seconds) <i>Mean (95% CI); median (IQR)</i>
	Time spent (seconds) <i>Mean (95% CI); Median (IQR)</i>	Expected time (seconds)	Time spent (seconds) <i>Mean (95% CI); Median (IQR)</i>	Expected time (seconds)	Time spent (seconds) <i>Mean (95% CI); Median (IQR)</i>	Expected time (seconds)	
Purpose of study	24 (13; 35) 14 (9; 34)	8	38 (-4; 81) 31 (21; 56)	38	116 (-1136; 1367) 116 (17; 214)	137	45 (17; 73) 28 (13; 49)
Have to take part	13 (-6; 32) 6 (4; 7)	6	No responses	27	No responses	156	13 (-6; 32) 6 (4; 7)
Why chosen	22 (15; 30) 17 (14; 22)	4	5 (0; 11) n/a	12	147 (n/a) 147 (n/a)	73	43 (18; 69) 22 (14; 68)
Expenses	21 (7; 36) 9 (5; 19)	2	<1 (0; 1) 0 (n/a)	3	73 (-379; 524) 73 (37; 108)	58	29 (4; 54) 10 (5; 25)
What will happen	12 (8; 16) 12 (6; 14)	11	2 (0; 3) 0 (n/a)	59	99 (n/a) 99 (n/a)	228	20 (9; 31) 13 (7; 23)
Risks	13 (10; 17) 12 (6; 19)	3	2 (0 5; 4) 0 (n/a)	6	106 (99; 112) 106 (105; 106)	61	122 (39; 204) 122 (115; 128)
Benefits	17 (11; 23) 14 (7; 23)	5	3 (0; 5) 0 (n/a)	23	46 (n/a) 46 (n/a)	62	99 (n/a) 99 (n/a)

Problems	15 (10; 21) 14 (6; 24)	2	<1 (0; 1) 0 (n/a)	6	n/a n/a	51	16 (11; 22) 15 (7; 24)
Confidentiality	11 (5; 18) 7 (6; 9)	<1	1 (-1; 4) 0 (n/a)	59	No responses	171 (570)	17 (3; 31) 8 (7; 25)
Don't want to carry on	9 (5; 14) 10 (5; 13)	4	No responses	11	No responses	55	9 (5; 14) 10 (5; 13)
GP	15 (9; 20) 13 (9; 17)	4	<1 (0; 1) 0 (n/a)	5	29 (n/a) 29 (n/a)	38	19 (11; 26) 13 (10; 24)
Samples	17 (9; 25) 10 (7; 28)	4	n/a	n/a	n/a	n/a	17 (9; 25) 10 (7; 28)
Genetic tests	3 (1; 5) 0 (n/a)	<1	n/a	n/a	n/a	n/a	3 (1; 5) 0 (n/a)
Results	11 (7; 15) 10 (5; 15)	4	1 (0; 2) 0 (n/a)	20	69 (-217; 354) 59 (46; 91)	72	27 (4; 51) 14 (10; 22)
Organising and funding	7 (4; 10) 6 (4; 13)	5	1 (0; 1) 0 (n/a)	11	80 (-206; 365) 80 (57; 102)	60	24 (1; 48) 13 (4; 16)
Reviewed study	8 (5; 11) 6 (4; 10)	3	9 (1; 17) 8 (4; 13)	11	22 (9; 35) 22 (21; 23)	26	42 (167; 67) 42 (40; 44)
Further info and contact	28 (11; 45) 22 (11; 41)	31	n/a n/a	n/a	n/a n/a	n/a	28 (11; 45) 22 (11; 41)
All FAQ							137 (76; 200) 57 (0; 195)

6.6 ADJUSTED ANALYSIS FOR INFORMATION ACCESSED

Participants spent a total median of 57 seconds (IQR 0-195 seconds) accessing information in the IIS (mean 137 [CI 76 to 200] seconds). Given this, it was hypothesised that participants may have sometimes clicked on information to see what was there without reading the information provided. For this reason, proportions of participants accessing each level of information were recalculated, including only those participants who spent long enough on the piece of information to have read it according to average reading times. To take into account variability in reading speed it was assumed that a participant had not read the information if they had the information open for less than 25% of the average reading time. Table 17 shows the proportion of participants who seemed to have spent long enough on each piece of information to have read it. The proportion of participants that accessed any information type for each level remained the same for unadjusted and adjusted results. Adjusted results were used as the principal analysis for the discussion chapter of this thesis, since they are more likely to accurately represent whether the information was read by potential participants.

The information provided to participants can be broken down into four types of information – information about practical aspects of the study, that participating was voluntary, scientific aspects/design of the study, legal aspects of the study. Based on the adjusted analysis, participants most often access information relating to study

aspects that could affect participants practically, including the risks and benefits of taking part, what would happen if they took part, what would happen if they had a problem whilst taking part, and any expenses they would received by participating. There were two types of information that very few participants were interested in knowing; that relating to the legal aspects of the study and that about the voluntary nature of participation. Participants accessed specific sub-categories of information relating to scientific aspects/design in varying proportions.

Table 17 - Adjusted proportion of participants accessing and time spent on each level of information (with all those who accessed no information taken out)

	Level one		Level two		Level three	
	Accessed	Did not access	Accessed	Did not access	Accessed	Not accessed
Purpose of the study	17/44 38.6%	27/44 61.4%	3/44 6.8%	41/44 93.2%	1/44 2.3%	43/44 97.7%
Have to take part	6/44 13.6%	38/44 86.4%	0/44 0%	44/44 100%	0/44 0%	44/44 100%
Why been chosen	18/44 40.9%	26/44 59.1%	4/44 9.1%	40/44 90.9%	1/44 2.3%	43/44 97.7
Expenses	22/44 50%	22/44 50%	5/44 11.4%	39/44 88.6%	1/44 2.3%	43/44 97.7%
What will happen	13/44 29.5%	31/44 70.5%	0/44 0%	44/44 100%	0/44 0%	44/44 100%
Risks	22/44 50%	22/44 50%	7/44 15.9%	37/44 84.1%	2/44 4.6%	42/44 95.5%
Benefits	20/44 45.5%	24/44 54.5%	3/44 6.8%	41/44 93.2%	0/44 0%	44/44 100%
Problems	16/44 36.4%	28/44 63.6%	1/44 2.3%	43/44 97.7	0/44 0%	44/44 100%
Confidentiality	10/44 22.7%	34/44 77.3%	1/44 2.3%	43/44 97.7	0/44 0%	44/44 100%
Don't want to carry on	6/44 13.6%	38/44 86.4%	0/44 0%	44/44 100%	0/44 0%	44/44 100%
GP	14/44 31.8%	30/44 68.2%	3/44 6.8%	41/44 93.2%	1/44 2.3%	43/44 97.7
Samples	15/44 34.1%	29/44 65.9%	n/a	n/a	n/a	n/a
Genetic tests	10/44 22.7%	34/44 77.3%	n/a	n/a	n/a	n/a
Results	11/44 25%	33/44 75%	1/44 2.3%	43/44 97.7%	1/44 2.3%	43/44 97.7%
Organising and funding	10/44 22.7%	34/44 77.3%	3/44 6.8%	41/44 93.2%	2/44 4.6%	42/44 95.5%
Reviewed study	11/44 26%	33/44 75%	2/44 4.5%	42/44 95.5%	2/44 4.6%	42/44 95.5%
Further info and contact	4/44 9.1%	40/44 9.1%	n/a	n/a	n/a	n/a
Accessing any information type	26/44 59.1%	18/44 40.9	8/44 18.2%	36/44 81.8%	4/44 9.1%	40/44 90.9%

6.7 PREDICTORS OF INFORMATION ACCESSED

Proportions of participants accessing each piece of information were conducted for each demographic group and between those that consented and did not consent to participate, to see if any clear patterns emerged. These data showed a trend towards participants accessing more information if they consented to the parent study, which is true for every FAQ (Table 18) although this was not tested by formal statistical methods due to small numbers and the associated risks of over fitting¹⁹⁴. These results must be interpreted with caution given the small numbers of participants in each group and may only be useful for hypothesis generation for future research. No other trends were seen for demographic groups, which can be found in Appendix 9.7.

Table 18 – Proportions of participants accessing each level of information for each FAQ by participation (did consent or did not consent)

	Accessed no levels		Level one		Level two		Level three	
	<u>Consent</u>	<u>Did not consent</u>	<u>Consent</u>	<u>Did not consent</u>	<u>Consent</u>	<u>Did not consent</u>	<u>Consent</u>	<u>Did not consent</u>
Purpose of the study	7/16 (43.7%)	19/28 (67.9%)	9/16 (56.3%)	9/28 (32.1%)	3/16 (18.8%)	1/28 (3.6%)	1/16 (6.3%)	1/28 (3.6%)
Have to take part	11/16 (68.7)	25/28 (89.3%)	5/16 (31.3%)	3/28 (10.7%)	0/16 (0%)	0/28 (0%)	0/16 (0%)	0/28 (0%)
Why been chosen	8/16 (50.0%)	18/2 (64.3%)	8/16 (50.0%)	10/28 (35.7%)	2/16 (12.5%)	2/28 (7.1%)	0/16 (0%)	1/28 (3.6%)
Expenses	7/16 (43.7%)	15/28 (53.6%)	9/16 (56.3%)	13/28 (46.4%)	3/16 (18.8%)	2/28 (7.1%)	1/16 (6.3%)	1/28 (3.6%)
What will happen	6/16 (37.5%)	16/28 (57.1%)	10/16 (62.5%)	12/28 (42.9%)	3/16 (18.8%)	1/28 (3.6%)	0/16 (0%)	1/28 (3.6%)
Risks	6/16 (37.5%)	16/28 (57.1%)	10/16 (62.5%)	12/28 (42.9%)	5/16 (31%)	2/28 (7.1%)	0/16 (0%)	2/28 (7.1%)
Benefits	7/16 (43.7%)	16/28 (57.1%)	9/16 (56.3%)	12/28 (42.9%)	4/16 (25.0%)	1/28 (3.6%)	1/16 (6.3%)	0/28 (0%)
Problems	9/16 (56.3%)	19/28 (67.9%)	7/16 (43.8%)	9/28 (32.1%)	0/16 (0%)	1/28 (3.6%)	0/16 (0%)	0/28 (0%)

Confidentiality	12/16 (75.0%)	22/28 (78.6%)	4/16 (25.0%)	6/28 (21.4%)	0/16 (0%)	1/28 (3.6%)	0/16 (0%)	0/28 (0%)
Don't want to carry on	12/16 (75.0%)	25/28 (89.3%)	4/16 (25.0%)	3/28 (10.7%)	0/16 (0%)	0/28 (0%)	0/16 (0%)	0/28 (0%)
GP	9/16 (56.3%)	21/28 (75%)	7/16 (43.8%)	7/28 (25.0%)	3/16 (18.8%)	0/28 (0%)	1/16 (6.3%)	0/28 (0%)
Samples	8/16 (50.0%)	21/28 (75%)	8/16 (50.0%)	7/28 (25.0%)	n/a	n/a	n/a	n/a
Genetic tests	10/16 (62.5%)	24/28 (85.7%)	6/16 (37.5%)	4/28 (14.3%)	n/a	n/a	n/a	n/a
Results	9/16 (56.3%)	24/28 (85.7%)	7/16 (43.8%)	4/28 (14.3%)	2/16 (12.5%)	1/28 (3.6%)	1/16 (6.3%)	1/28 (3.6%)
Organising and funding	9/16 (56.3%)	24/28 (85.7%)	7/16 (43.8%)	4/28 (14.3%)	3/16 (18.8%)	1/28 (3.6%)	1/16 (6.3%)	1/28 (3.6%)
Reviewed study	9/16 (56.3%)	24/28 (85.7%)	7/16 (43.8%)	4/28 (14.3%)	3/16 (18.8%)	1/28 (3.6%)	1/16 (6.3%)	1/28 (3.6%)
Further info and contact	11/16 (68.7%)	24/28 (85.7%)	5/16 (31%)	4/28 (14.3%)	n/a	n/a	n/a	n/a
Total participants accessing any information	5/16 (31.0%)	13/28 (46.2%)	11/16 (68.8%)	15/28 (53.6%)	6/16 (37.5%)	3/28 (10.7%)	2/16 (12.5%)	2/28 (7.1%)

Further exploratory analyses were then conducted to look at whether the average number of pieces of information accessed varied by demographics or consent decision. Table 19 shows the average number of pieces of information accessed per person split by age group, gender, ethnicity and participation decision. A 'piece' of information was considered to be an element (i.e. a level of information) within a FAQ. For example, a participant was deemed to have accessed one 'piece' of information if they looked at level one information for one FAQ and two 'pieces' of information if they looked at level one and level two information for one FAQ. A participant was deemed to have accessed four 'pieces' of information if they had looked at levels one, two and three for one FAQ and level one for a separate FAQ.

On average, participants looked at 6 pieces of information before deciding whether to participate in the parent study. The average number of pieces of information accessed increased with age (44-55=5.6; 55-65=6.5; 65+=8.5). For gender subgroups, there were no apparent differences in the total number of pieces of information accessed. Black Caribbean participants accessed the most pieces of information (7.2 pieces) and South Asian participants accessed the fewest (4.0 pieces). Those who eventually consented to take part in the parent study read more pieces of information than those who refused (9.2 and 4.6 respectively). Given the small numbers and exploratory nature of these analyses, these reported differences could be due to chance.

The exploratory analyses suggest that participants who accessed no information were likely to be: younger (45-55= 11/24 [45.8%]; 55-65= 5/14 [35.7%]; 65+= 2/6 [33.3%]); White (White= 14/31 [45.2%]; South Asian= 0/2 [0%]; Black Caribbean= 2/9 [22.2%]); and did not take part in the parent study (did not consent = 13/28 [46.4%]; consented= 5/16 [31.3%]) but this finding must be interpreted with caution given the small number of participants in groups, and used purely in hypothesis generation for future studies.

Table 19 – Demographics that predict the total number of levels accessed and total time spent

	N	Mean number of levels seen per person (95% CI)	Number people accessed no levels
<u>Total IIS study population</u>	44	7 (4; 10)	18/44 (40.9%)
<u>Age</u>			
45-55	24	6 (2; 10;)	11/24 (45.8%)
55-65	14	7 (3; 12;)	5/14 (35.7%)
65+	6	9 (1; 18;)	2/6 (33.3%)
<u>Gender</u>			
Male	24	7 (4; 10)	9/24 (37.5%)
Female	20	7 (3; 11)	9/20 (45.0%)
<u>Ethnicity</u>			
White	31	7 (4; 10)	14/31 (45.2%)
Asian	2	5 (-33; 43)	0/2 (0%)
Black	9	8 (2; 14)	2/9 (22.2%)
<u>Participation status for parent study</u>			
Consented	16	10 (5; 15)	5/16 (31.3%)
Did not consent	28	5 (2; 8)	13/28 (46.4%)

6.8 EFFECT OF IIS ON CONSENT RATE

Feasibility of electronic information provision

The highest consent rate was seen in the 'No PIS' group where 59.4% (63/106) of participants consented to the parent study (Table 20).

When both IIS and PDF-PIS methods of electronic communication are compared with the paper PIS there is an increase in consent rate to 41.9% and 31.1% respectively (OR=1.25 [95% CL 0.98; 1.75]) (Table 21).

When all methods of electronic communication are compared to paper PIS there is still a small increase in consent rate to 34.1% and 31.1% respectively (OR=1.25 [1; 1.7]) (Table 21).

IIS RCT

The primary outcome of the IIS RCT was whether using an IIS affected the consent rate to the parent study in comparison with the use of the PDF-PIS.

The consent rate for the parent study with the standard PIS was 31.1% (Table 20), so the effect size required to change practice was 27%, with a sample size of n=132 (90% power) (Section 4.5.2). The sample size was not met (IIS RCT sample size n=86).

Intention To Treat (ITT) analysis showed no statistically significant difference in consent rate for IIS when compared with a PDF-PIS; 36.4% and 47.6% respectively (OR=0.6 [95% CL 0.25; 1.4]) (Table 21). The effect size seen in the study was considerably less than the effect size required to change practice, so even if the sample size had been met the study would still have been underpowered.

Table 20 – Consent rate by study group

	Number consenting / n	Consent rate (95% CI)
Electronic recruitment		
PDF	20/42	47.6% (31.9; 63.3)
IIS	16/44	36.4% (21.6; 51.2)
No PIS	63/106	59.4% (44.3; 74.5)
All electronic	99/290	34.1% (28.6; 39.6)
Postal recruitment		
Paper	271/870	31.1% (25.8; 36.4)

Table 21 – Comparison of consent rate between groups

Comparison between groups*	Number consenting / n	Consent rate	OR (95% Confidence Limits)
IIS vs. PDF	16/44 vs. 20/42	36.4% vs. 47.6%	0.6 (0.25; 1.4)
PDF/IIS vs. Paper	36/86 vs. 271/870	41.9% vs. 31.1%	1.25 (0.98; 1.75)
Electronic vs. Postal recruitment	99/290 vs. 271/870	34.1% vs. 31.1%	1.25 (1.0; 1.7)
Opened email (PDF/IIS/None) vs. Postal recruitment	99/192 vs. 271/870	51.6% vs. 31.1%	1.5 (1.1; 2.1)

*Logistic regression with variables gender and age

6.9 UNDERSTANDING AND SATISFACTION

Participants were asked to complete questionnaires to determine what effect the method of information provision had on participant understanding and satisfaction. Figure 17 shows the number of understanding and satisfaction questionnaires that were sent and returned by each group of participants.

Questionnaires were not sent to all study participants. There were expected demographic differences between participants who did and did not provide an email address, and these differences mean responses from the two groups may have differed by a factor other than the format of information provision. We were only interested in ensuring the adequacy of understanding by those who took part in the parent study, to help ensure valid consent was taken. Given that electronic information provision is a new methodology, it was important that levels of understanding and satisfaction were not reduced because information was provided electronically. This means that even though those with and without an email address were likely to differ demographically, we needed to collect levels of understanding from both groups so we could compare results.

There were four distinct study groups that received understanding and satisfaction questionnaires:

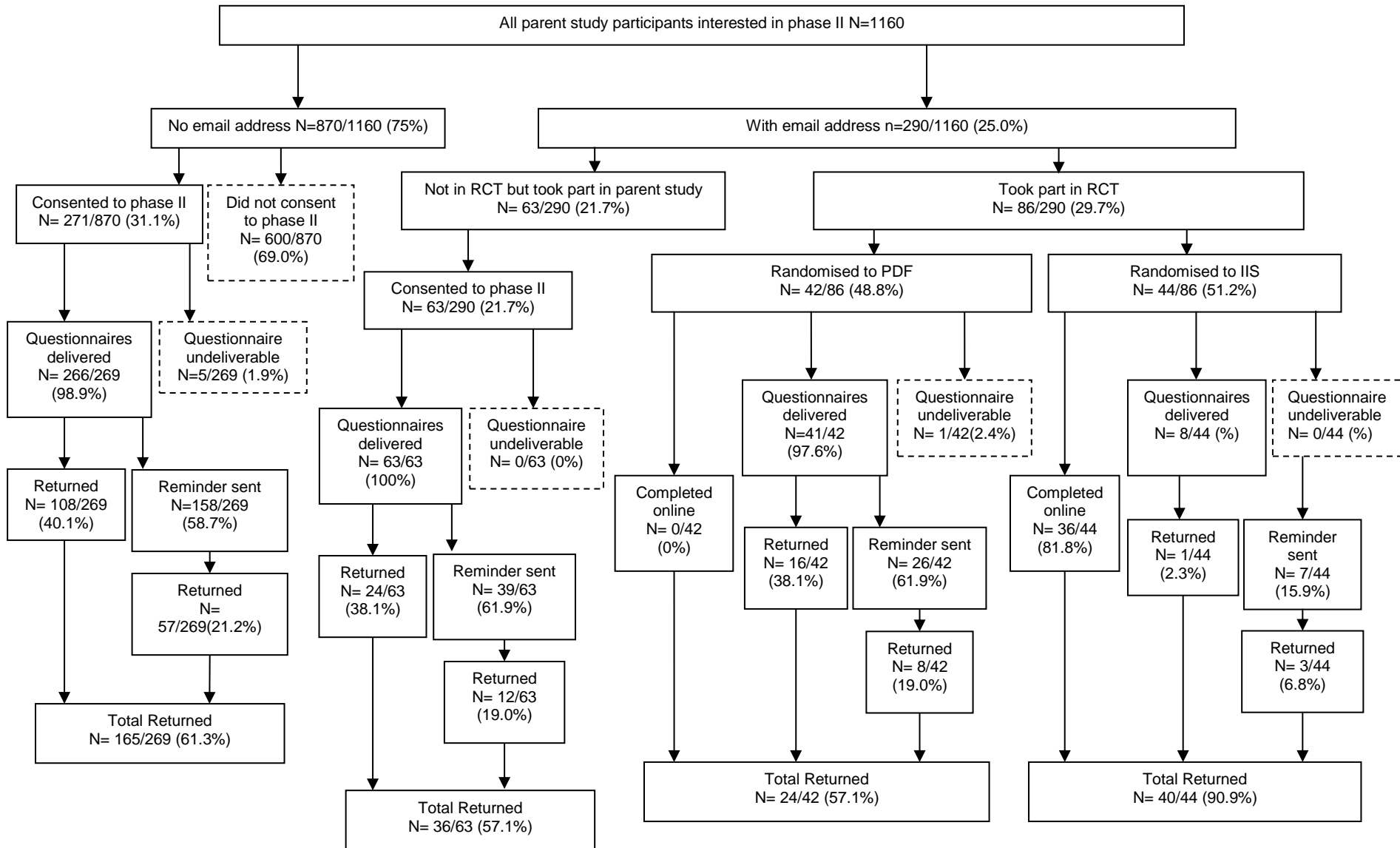
1. Those who did not provide an email address but participated in the parent study (n=870). These participants are the 'paper PIS' group
2. Those who did provide an email address and were randomised to PDF-PIS (n=42) regardless of consent status to parent study
3. Those who did provide an email address and were randomised to IIS (n=44) regardless of consent status to parent study
4. Those who provided an email address but were not randomised in the IIS RCT and, therefore, did not receive and study information, but who booked a consent appointment (n=63). These participants are the 'no PIS' group

Two groups of participants did not receive understanding and satisfaction questionnaires:

1. Those who did not provide an email address and did not participate in the parent study (n=290)
2. Those who did provide an email address but were not randomised in the IIS RCT and did not book a parent study appointment (n=600)

Response rate to the understanding and satisfaction questionnaire for the 'paper PIS' and 'no PIS' groups were similar (61.3% and 57.1% respectively). Response rate for participants receiving a PDF-PIS (n=42) was similar to the 'paper PIS' and 'no PIS' groups (57.1%) but the response rate for IIS randomised participants (n=44) was much higher (90.9%).

Figure 17 - Number of satisfaction and understanding questionnaires returned



Understanding

Table 22 presents participants' scores on the understanding questionnaire by study group. The overall score on the understanding questionnaire is similar across groups, including those we know to have received no study information prior to agreeing to take part.

Almost all participants across all groups correctly answered that they were being asked to take part in a piece of medical research rather than being asked to make a treatment decision. The question with the most incorrect answers across all groups concerned why they had been chosen to participate. The majority of participants believed they had been chosen to participate because they had high blood pressure when, in fact, the study was actually trying to recruit equal numbers of both normotensive and hypertensive participants. The proportion of correct answers across the other thirteen questions varied and no consistent pattern emerged from the data. For example, there were two groups of participants that accessed no information – those in the 'no PIS' group and those in the IIS group that accessed no levels of information. When asked what would happen to them if they took part, 83.8% in the 'no PIS' group but only 35.3% in the IIS group answered the question correctly, even though participants in both groups had accessed no information. The numbers in study groups were too small to test for statistically significant differences in the proportion answering correctly across individual questions.

The score on the understanding questionnaire was also presented by demographic group's age, gender and ethnicity (Table 23). The IIS participants were not split into different level groups for this analysis since numbers were already very small. No pattern emerged for the average score on the understanding questionnaire-based on participant's age group, gender or ethnicity, and should be interpreted with caution due to the small numbers in individual groups.

Table 22 – Participant score on the understanding questionnaire split by study group

	No PIS	IIS					PDF-PIS	Paper PIS
		No levels	Level one	Level two	Level three	Overall		
Overall scores								
Mean score (95% CI)	11.1 (10.3; 11.8) n=37	10.4 (9.2; 11.6) n=17	11.7 (10.6; 12.7) n=15	12.0 (11.1; 12.9) n=5	9.8 (5.8; 13.8) n=4	11.00 (10.3; 11.7) n=41	11.2 (10.0; 10.9) n=26	10.4 (10.0; 10.9) n=165
Scores for each question								
Is this treatment or research?	35/37 94.6%	14/17 82%	15/15 100%	5/5 100%	4/4 100%	38/41 92.3%	24/26 92%	147/165 89.1
Purpose of the study - Is it to test for differences between methods of BP measurement and ethnic groups?	28/37 75.7%	10/17 58.8%	12/15 80%	5/5 100%	4/4 100%	31/41 75.6%	18/26 69.2%	125/165 75.8%
Why have I been chosen? – Have you been chosen because you have high blood pressure?	12/37 32.4%	9/17 52.9%	7/15 46.7%	2/5 40%	2/4 50%	20/41 48.8%	13/26 50%	59/165 35.8%
Do I have to take part? – Do you have to	31/37	16/17	15/15	5/5	3/4	39/41	23/26	132/165

take part in this study?	83.8%	94.1%	100%	100%	75.0%	95.1%	88.5%	80.0%
What will happen to me if I take part? – if you take part in this study will you be involved for 8 days?	31/37 83.8%	6/17 35.3%	12/15 80%	4/5 80.0%	4/4 100.0 %	26/41 63.4%	20/26 76.9%	123/165 74.6%
What will happen to me if I take part? – Will you have to measure your BP yourself at home?	37/37 100%	11/17 64.7%	12/15 80.0%	4/5 80.0%	3/4 100%	30/41 73.2%	23/26 88.5%	148/165 89.7%
GP involvement – Will your GP be told you are taking part?	26/37 70.3%	9/17 52.9%	12/15 80.0%	4/5 80.0%	3/4 100%	28/41 68.3%	17/26 65.4%	122/165 73.9%
GP involvement – Will the research nurse offer you treatment?	25/37 67.6%	11/17 64.7%	5/15 33.3%	2/5 40.0%	1/4 25.0%	19/41 46.3%	17/26 65.4%	107/165 64.9%
Confidentiality – Will we keep information about you confidential?	36/37 97.3%	15/17 88.2%	15/15 100%	5/5 100%	2/4 50%	37/41 90.2%	25/26 96.2%	145/165 87.9%
Don't want to carry on – If you decide to pull out, will it affect your care from your GP?	36/37 97.3%	16/17 94.1%	15/15 100%	5/5 100%	4/4 100%	40/41 97.6%	24/26 92.3%	148/165 89.7%
Confidentiality – Will statisticians involved in the study be able to see your name, address and other personal details?	27/37 73.0%	13/17 76.5%	14/15 93.3%	5/5 100%	3/4 75.5	33/41 80.5%	16/26 61.5%	86/165 52.1%

GP - If you do not want your GP to know you are taking part will you still be able to take part?	4/37 10.8%	3/17 17.7%	2/15 13.3%	5/5 100%	4/4 100%	5/41 12.2%	5/26 19.2%	24/165 14.6%
Organising and funding – Is this study being organised by professional researchers at the University of Birmingham?	34/37 91.9%	16/17 94.1%	13/15 86.7%	5/5 100%	4/4 100%	38/41 92.7%	25/26 96.2%	149/165 90.3%
Results – When we publish the results of this study, will we identify you in any report?	28/37 75.7%	15/17 88.2%	15/15 100%	5/5 100%	2/4 50.0%	37/41 90.2%	22/26 84.6%	113/165 68.5%
Reviewed the study – Has this study been looked at and approved by a REC?	20/37 54.1%	13/17 76.5%	10/15 66.7%	4/5 80%	2/4 50.0%	29/41 70.7%	18/26 69.2%	94/165 57.0%

Table 23 – The average score on the understanding questionnaire, split by method of information provision and demographics

		All participants Mean score (n)	IIS Mean Score (n)	PDF-PIS Mean Score (n)	Paper PIS Mean Score (n)
All participants		10.8 (265)	11.00 (40)	11.15 (24)	10.8 (201)
<u>Age</u>	45-55	10.66 (75)	10.9 (21)	10.8 (12)	10.5 (42)
	55-65	11.0 (73)	10.8 (14)	10.6 (8)	11.1 (51)
	65+	10.8 (77)	11.8 (6)	12.5 (6)	10.5 (65)
<u>Gender</u>	Male	10.5 (114)	10.8 (24)	10.9 (14)	10.4 (76)
	Female	11.0 (114)	11.2 (17)	11.5 (12)	10.9 (85)
<u>Ethnicity</u>	WB	11.3 (130)	11.0 (29)	11.8 (19)	11.4 (82)
	SA	9.9 (28)	13 (1)	8.3 (3)	10.0 (24)
	BC	10.1 (67)	10.9 (9)	9 (3)	10.0 (55)

Satisfaction

Participant satisfaction was assessed to determine if providing information electronically affected whether participants were happy with the method of information provision (Table 24). Questionnaires were delivered to the same groups and at the same time as the understanding questionnaires.

Overall, 32/265 (12.1%) participants stated that they would have liked more information about the study. Participants were less likely to want more information about the parent study if they received study information electronically - only 1/40 (2.5%) of those in the IIS and 2/24 (8.3%) in the PDF-PIS group wanted to know more information about the study compared with 28/137 (20.4%) in the paper PIS group. One person (1/36; 2.8%) who received no PIS before booking a parent appointment stated that they would have liked more information about the study.

One person randomised to IIS but who accessed no information stated that they would have liked more information about the study. It is possible that this participant was unable to get the information they required because they were unable to use the website, which is a concern of providing electronic information. This participant did, however, complete the understanding and satisfaction questionnaire online. In order to do this s/he had to navigate through the website successfully to access the questionnaire pages. If they

were able to do this, it is likely they did have an understanding of how to use the Internet, and they were not unable to access information because they could not use the website. This may be an example of participants not using the information provided to make a decision but still requesting more information when asked.

9.1% (24/265) of all participants stated that they did not need as much information about the study as they were given, which increases to 22.5% (9/40) when only IIS participants are considered (PDF= 3/24 [12.5%]), no PIS= 2/36 [5.6%], paper PIS= 28/137 [20.4%]).

Overall, 20.4% (54/265) participants stated that they would prefer to have information provided electronically if they took part in research again. This figure rises to between 45% and 50% when considering only responses from participants who received electronic information (IIS= 18/40 [45%]; PDS-PIS=12/24 [50%]) and falls to 10.2% when considering responses from participants who received paper information (Paper PIS= 14/137). Comparable results were seen for those stating that they would prefer to have information provided on paper if they took part in research again.

12/40 (30%) participants who returned the questionnaire stated they did not click on any of the (+) signs. Results, however, showed that 40.9% (18/44) of

those that accessed the IIS did not click on any of the + signs. A high proportion of participants stated that they found the information under the (+) signs useful, but it only influenced the decision to take part of 13/40 (32.5%). Sixteen participants (n=40; 40%) stated that the information under the (+) signs did not influence their decision to participate, and eleven (11/40; 27.5%) did not respond to the question. Of those that stated they did access information under the (+) signs, most participants either skimmed through the information (12/40; 30%) or picked out only the bits that were important to them (14/40; 35%). A high proportion of participants stated that they would have been happy without reading any information under the (+) signs (17/40; 42.5%) but 11/40 (27.5%) would not have agreed to take part in the study without being able to read the information under the (+) signs.

Almost all participants stated that they read all of the information sheet they were given about the parent study, including most of those that we know to have received no information sheet at all (No PIS= 34/36 [94.4%]; PDF-PIS=18/24 [75.0%]; Paper PIS=129/137 [94.2%]). Fewer participants stated that they only read some of the information they were given (No PIS=4/36 [11.1%]; IIS=14/40 [30.0%] PDF-PIS=8/24 [33.3%]; Paper PIS=30/137 [21.9%]) or skimmed through the information sheet (No PIS=4/36 [11.1%]; IIS=12/40 [30.0%]; PDF-PIS=4/24 [16.7%]; Paper PIS=18/137 [13.1%]) and less than 5% (excluding the IIS group) stated that they did not read any of the information

sheet (No PIS=1/36 [2.8%]; IIS=12/40 [30.0%] PDF-PIS=0/24 [0%]; Paper PIS=6/137 [4.4%]). Despite almost all participants stating that they had read the entire information sheet, proportions for the remaining questions do not tally. For example, for the Paper PIS group, 94.2% said they read the entire information sheet, 21.9% said they read some of it, 13.1% said they skimmed through it and 4.4% said they did not read any of it, which equals 133.6%, so participants often answered 'yes' to more than one discrete question.

When asked questions about the importance of the PIS to their decision-making, the majority stated that it was important to read and helped them to decide whether to participate (No PIS=24/36 [66.7%] IIS=11/40 [27.5%]; PDF-PIS=19/24 [79.2%]; Paper PIS=114/137 [83.2%]), around half found the information sheet interesting but it did not influence their decision to participate (No PIS=17/36 [47.2%]; IIS=17/40 [42.5%]; PDF-PIS=10/24 [41.7%]; Paper PIS=67/137 [48.9%]) and around half said they would not have agreed to take part without being able to read the information sheet (No PIS=17/36 [47.2%]; IIS=11/40 [27.5%]; PDF-PIS=9/24 [37.5%]; Paper PIS=73/137 [53.3%]). This is interesting because 17/36 (47.2%) of those in the 'No PIS' group, all of whom took part in the parent study, stated that they would not have agreed to take part in the study without being able to read the information in the information sheet, but we know that they did not receive one.

The trend of participants agreeing with conflicting statements or agreeing with statements known to be untrue (based on the information we know they actually accessed) was apparent throughout the results of this questionnaire.

Table 24 – Participants’ satisfaction with the method of information provision, split by method of information provision

	No PIS	IIS					PDF-PIS	Paper PIS
		No levels	Level one	Level two	Level three	Overall I		
I would have liked more information about the study	1/36 3%	1/17 6%	0/14 0%	0/5 0%	0/4 0%	1/40 3%	2/24 8%	28/137 20%
I did not need as much information about the study as I was given	2/36 6%	3/17 12%	3/14 21%	2/5 40%	1/4 25%	9/40 23%	3/24 13%	10/137 7%
I would prefer to have information provided electronically if I took part in research again	10/36 28%	5/17 29%	5/14 36%	4/5 80%	4/4 100%	18/40 45%	12/24 50%	14/137 10%
I would prefer to have information provided on paper if I took part in research again	16/36 44.4%	5/17 29.4%	0/14 0%	0/5 0%	0/4 0%	5/40 13%	8/24 33%	116/137 85%
I did not click on any of the (+) signs		4/17 12%	7/14 50%	1/5 20%	1/4 25%	12/40 30%		
I found the information under the (+) signs useful and it influenced my decision to take part in this study		4/17 24%	6/14 43%	1/5 20%	2/4 50%	13/40 33%		
I found the information under the (+) signs interesting but it didn’t influence my decision to participate in the Blood Pressure Monitoring study		2/17 12%	3/14 21%	0/5 0%	0/4 25%	16/40 40%		
I clicked on the (+) signs to see what was there but did not read the information		6/17 35%	4/14 29%	2/5 40%	1/4 25%	5/40 13%		

I clicked on the (+) signs and skimmed through the information. I did not read it fully		2/17 12%	6/14 43%	3/5 60%	2/4 50%	12/40 30%	
I clicked on the (+) signs and skimmed through the information. I picked out and read only parts which were important to me		5/17 29%	8/14 57%	1/5 20%	1/4 25%	14/40 35%	
I would have been happy with just the first piece of information from each section. I did not need to read any of the information under the (+) signs to make a decision about whether I wanted to take part in the Blood Pressure Monitoring study		10/17 59%	5/14 36%	1/5 20%	1/4 25%	17/40 43%	
I would not have agreed to take part in the Blood pressure Monitoring study without being able to read the information under the (+) signs		1/17 6%	5/14 36%	3/5 60%	2/4 50%	11/40 28%	
I read all of the information sheet I was given about the Blood Pressure Monitoring study	34/36 94%					18/24 75%	129/137 94%
I read some of the information in the information sheet I was given about the study	4/36 11%					8/24 33%	30/137 22%
I skimmed through the information in the information sheet I was given about the study and read only the bits that were important to me	4/36 11%					4/24 17%	18/137 13%
I did not read any of the information in the	1/36					0/24	6/137

information sheet I was given about the study	3%		0%	4%
I read some of the information in the information sheet but it did not help me to decide whether or not I wanted to take part in the study	2/36 6%		1/24 4%	18/137 13%
The information sheet was important to read and helped me to decide whether or not I wanted to take part in the study	24/36 67%		19/24 79%	114/137 83%
I found the information in the information sheet interesting but it did not influence my decision to take part	17/36 47%		10/24 42%	67/137 49%
I would not have agreed to take part in the study without being able to read the information in the information sheet	17/36 47%		9/24 38%	73/137 53%

6.10 ESTIMATION OF COSTS

The cost analysis performed suggested that it was more expensive per participant to send electronic invitations than it was to send postal ones (Table 25).

It is estimated that it would cost £1173 in researcher's time (Table 26) to develop the content for the IIS, in addition to the time spent writing the 'standard' level two information.

Table 25 – Estimate of cost for electronic and postal invitations

<u>Postal invitations</u>		
<u>Type of cost</u>	<u>Reason for cost</u>	<u>Estimate of total cost for item</u>
Printing	Invitation letter	£0.05
	PIS	£0.05
Stationery	A4 envelope	£0.10
	2 nd Class stamp, large letter	£0.69
Administrator time	Printing and sorting invitation letters and PIS - 15 seconds per letter	£0.039
	Filling envelopes - 15 seconds per envelope	£0.039
<u>Total cost per person</u>		<u>£1.07</u>
<u>Electronic invitations</u>		
All participants		
Administrators time	Compiling email and sending, assuming mailing list rather than per person - 15 seconds	£0.039
<u>Total cost to send email to each participant</u>		<u>£0.039</u>
Costs to call participants - in 28.6% that answered		
Phone call	10 minutes	£0.50
Administrators time	On the phone talking to participants - 10 minutes	£1.56
	Calling participants when they did not answer - 1 minute x 10 phone calls	£1.56
<u>Total cost to call each participant that answered</u>		<u>£3.62</u>
Costs to call participants - in 16.9% that did not answer		
Administrators time	Calling participants when they did not answer - 1 minute x 10 phone calls	£1.56
<u>Total cost to call each participant that did not answer</u>		<u>£1.56</u>
<u>Total average cost per invited participant</u>		<u>£1.34</u>

Table 26 – Estimate of cost to develop the content for the IIS

	Research associate (Grade 6)	Research fellow (Grade 7)	Principal investigator (Grade 9)	Total cost of IIS
Number of hours	67	7	4	
Approx wage per hour	£14	£17	£29	
Total cost	£938	£119	£116	£1173

Key results

Consent rate:

Electronic communication did not affect consent rate, although the study was not powered to detect this.

Encouraging participants to open emails improved recruitment rate.

Highest consent rate seen in the group that accessed no PIS.

Information accessed:

High proportion accessed little or no study information.

The paper PIS matched the reading patterns of only 11.4%: 9.1% read more and 79.5% less than the information in the paper PIS.

Understanding and satisfaction:

Understanding consistent across groups, including those accessing no information.

Participants generally happy with the level of information received.

Participants were unable to accurately recall what information they had accessed.

6.12 LIMITATIONS OF THE INFORMATION PROVISION STUDY

The consent rate for electronic recruitment was shown to be higher than that for postal recruitment but not to statistical significance. Participants were also not randomised to the postal recruitment group because it was not feasible using the selected parent study. A further RCT would be needed to ascertain whether the improvement in consent rate was due to electronic recruitment or whether participants that provided an email addresses differed in some other way that made them more likely to participate.

Where participants were prompted to open their emails with a telephone call, the consent rate was shown to be higher in the electronic group. It is not known whether this was due to the electronic method of communication itself or whether calling participants influenced participation rates.

The highest consent rate was seen in the group that accessed no PIS. It is not known what proportion of those who received postal information read it and whether there was a similar correlation in the postal group. We know from the results of the questionnaire that what participants say they did does not reflect actual practice, so asking potential participant whether they read the information provided may not yield an accurate result.

The older average age of parent study participants may have been a limitation to this research. The study required participants to be competent Internet users, and ONS data¹⁰¹ showed that Internet use declines with increasing age. The majority of the study population did not provide an email address and so we assumed they were not able to access information electronically. We cannot be certain that this is the case though, since some participants may have chosen to not provide their email address, or they may have been able to access a study website with the help of a relative, for example, if they had been provided with the website details.

An exploratory retrospective analysis of costs was undertaken for the Information Provision study, but the costs and resource use could not be accurately calculated as they were not collected during the study. In future studies, a full cost-effectiveness analysis needs to be conducted comparing postal and electronic communication.

The sample size was lower than anticipated, with only 86 participants randomised in the IIS RCT by the end of recruitment. This was due to the proportion of parent study participants accessing the study website being much lower than expected, and an unexpectedly high number of people participating in the parent study without accessing any study information.

6.13 A STREAMLINED PIS

The results of the observational study were used to produce a streamlined PIS for the parent study because we wanted to see what an information sheet would look like that contained only that information which the majority participants (who accessed information) used to make a decision to participate. The resulting PIS can be found at the end of this section. The section justifies the length of this streamlined PIS, the information included and how it is structured.

Length

The median time spent reading the IIS was 57 seconds (IQR 0 to 195 seconds). The median and mean times differed due to a high proportion of potential participants reading no information and a few people spending a long time reading information. In order to account for the skew in the data caused by the few people that spent a long time reading, the median rather than the mean was used. For a streamlined PIS to be read in 57 seconds, it should be around 190 words long (assuming the average person reads 200 words per minute).

Information to be included

There are two reasons for including information in a PIS: 1) to ensure potential participants are sufficiently informed; 2) to ensure participants are provided with the information that meets international guidelines, which protects the researcher from the claim that adequate information was not provided.

Information participants want to know

Included here was the information most commonly accessed by participants randomised to IIS - the level one information for expenses, risks and benefits, purpose of the study, what would happen if they took part, what would happen if they had any problems, if their GP would be told of the results and what would happen to any samples they gave. Based on the access patterns, we can hypothesise that these were the sections of most interest to potential participants and should, therefore, be included in a PIS.

Around 20% of participants accessed more than the minimal level of information. Providing a streamlined PIS to these participants may not provide them with the information they need to make an informed decision. In order to meet the informational needs of this minority, greater access to information is needed. A streamlined PIS should include information about how more information can be found. This could include contact with researchers, or the opportunity to request a lengthier paper PIS or access more information on an IIS placed on the study website.

Information participants ought to know

There are some pieces of information that are specified by the ICH and the statutory instrument that reflects the EU directive (Section 2.2). The guidelines do not include the detail in which these pieces of information should be provided, so a brief and accurate summary may be all that is required to satisfy these regulations. The ICH states that⁴:

“Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:

- a) That the trial involves research.
- b) The purpose of the trial.
- c) The trial treatment(s) and the probability for random assignment to each treatment.
- d) The trial procedures to be followed, including all invasive procedures.
- e) The subject’s responsibilities.
- f) Those aspects of the trial that are experimental.
- g) The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
- h) The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
- i) The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.
- j) The compensation and/or treatment available to the subject in the event of trial-related injury.
- k) The anticipated prorated payment, if any, to the subject for participating in the trial.
- l) The anticipated expenses, if any, to the subject for participating in the trial.
- m) That the subject’s participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
- n) That the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority(ies) will be granted direct access to the

⁴ Section 4.8.10 of the ICH Topic E6(R1) Guideline for Good Clinical Practice

subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.

- o) That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.
- p) That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.
- q) The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
- r) The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
- s) The expected duration of the subject's participation in the trial.
- t) The approximate number of subjects involved in the trial.

Nine of these areas reflect the information that the majority of our potential participants accessed: risks and benefits (g, h), expenses (l), purpose of the study (b), what would happen if they took part (d, e, r, s), what would happen if they had any problems (q).

Four sections of the guidelines are not applicable to this piece of low risk interventional research and were therefore excluded: those aspects of the trial that are experimental (f), the trial treatment(s) and the probability for random assignment to each treatment (c), the alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential

benefits and risks (i), the anticipated prorated payment, if any, to the subject for participating in the trial (k)

This left seven pieces of information required by ICH guidelines that were incorporated into the streamlined PIS using simple sentences as follows:

a) That the trial involves research: “You are being invited to take part in a research study about x.”

j) The compensation available: “If something does go wrong and you are harmed during the research and this is due to someone’s negligence then you may have grounds for a legal action for compensation against The University of Birmingham.”

m) That participation is voluntary: “It is up to you to decide whether or not to take part and your decision will not affect your healthcare. If you decide to take part you are able to withdraw your consent to participate at any time and this will not affect your healthcare.”

n) Who will have access to their confidential information: “Personal data (names and addresses) will be only accessible by authorised persons such as researchers and regulatory authorities.”

o) That participant's information will be kept confidential: "your taking part in this study will be kept confidential and will not be made publically available. If the results of the trial are published, your identity will remain confidential."

u) The approximate number of subjects involved in the trial: "The study will involve x participants."

p) Informing participants of changes to the study: "You will be informed in a timely manner if information becomes available that may be relevant to your willingness to continue in the study."

Structure

As our results demonstrate, most participants read very little of the information available to them. When considering what the PIS might look like, the information participants are likely to want to know, and, therefore, is likely to influence their decision-making, was included first. The PIS begins by informing participants that they are being invited to participate in research. Participants are then made aware that reading the information provided is important and that they should ask the researchers if they have any questions. The rationale here is to encourage participants to read all of the PIS and to inform them that more information is available if they want it. Following this is the information that we hypothesised that participants want to know.

Finally, the information required by international guidelines was added. This information may not be decisive to participant's decision-making since it was not accessed in the Information Provision study. Accordingly, the rationale for placing it last was that putting it first may deter potential participants from reading on.

The resulting streamlined PIS (Appendix 9.8) was thereby generated for the parent study:



UNIVERSITY OF BIRMINGHAM
College of Medical and Dental Sciences
School of Health and Population Sciences
Primary Care Clinical Sciences
Professor of Primary Care Cardiovascular Research
Richard McManus PhD FRCGP

Bp-Eth
Participant Invitation Sheet

You are being invited to take part in a research study about the different ways of measuring blood pressure. Please take time to read the following information carefully and discuss it with your friends and relatives if you wish. Ask us if there is anything that is not clear or if you would like more information.

If you decide to take part you will make three visits to your GP surgery over 10 days. During that time you will be asked to have a 24 hour blood pressure monitor and take your own blood pressure for a week. The possible benefits of taking part are that your GP will be given the blood pressure measurements and offer you treatment if you need it. The possible risks of taking part are that some people find it uncomfortable to have their blood pressure measured. Any travel expenses you incur during this study will be refunded. We would like to let your GP know that you are taking part. Any problems you have during the study will be addressed.

The study will involve 800 participants. It is up to you to decide whether or not to take part and your decision will not affect your healthcare. If you decide to take part you are able to withdraw your consent to participate at any time and this will not affect your healthcare. You will be informed in a timely manner if information becomes available that may be relevant to your willingness to continue in the study.

Your taking part in this study will be kept confidential and will not be made publically available. If the results of the trial are published, your identity will remain confidential. Personal data (names and addresses) will be only accessible by authorised persons such as researchers and regulatory authorities.

You can get more information about this study by:

- o Accessing the study website at www.studywebsite.co.uk
- o Contacting Professor Richard McManus's study team on 0800 234 6 432 to request a more detailed information sheet or to ask any specific questions that you have

▶ Introduction

- o Aim of study
- o Advice to read info

▶ Information participants wanted

- o Expenses
- o Risks and benefits
- o Purpose
- o What will

▶ ICH required

- o Compensation
- o Voluntariness
- o Confidentiality
- o Number participants

▶ Where to access more information

- o Study website
- o Researchers
- o Detailed patient PIS

6.14 FUTURE OF THE STREAMLINED PIS

In order to seek feedback on the study results and resulting streamlined PIS, a meeting was arranged with the NRES expert panel on the 13th June 2012. This meeting discussed the results of this PhD, the panels opinions on the use of a streamlined PIS for low risk interventional research, and their advice on how to take the research further. The account of this interaction taken from the official, published minutes of the meeting can be found in Appendix 9.9.

The NRES expert panel exists to “help with the strategy, quality assurance and service development of RECs and improve the research environment in the UK”²⁰³. The panel is made up of the NRES Ethics Advisor, Dr. Hugh Davies, 12 other members with expertise in different areas of research and a secretary, Clive Collet. As quoted from the NRES website²⁰⁴, members of the panel present and areas of expertise at the time of the meeting included:

- The chair, Professor Andrew George, who has extensive experience of clinical research and holds a number of key positions, for example being a member of the Clinical Trials Expert Advisory Group for the MHRA.
- Caroline Harrison, who is a Barrister and lecturer with a special interest in legal aspects of medical research.
- Professor Nalin Thakker, who is a Professor and Clinician in the field of Dentistry, has been a vice-chair of a REC for 10 years and advises NRES on issues of human tissues for research.

- Professor John Saunders, who is a Consultant Physician in Abergavenny, chairman of the Committee for Ethical Issues in Medicine at the Royal College of Physicians, and has been a member of RECs for 20 years.
- Dr. Richard Tiner, who is a GP and President-Elect of the Faculty of Pharmaceutical Medicine and has a strong interest in clinical research.
- Dr. Arthur Tucker, who is a clinical embryologist and Senior Lecturer in Clinical Pharmacology, with a special interest in research regulation and who is currently the chair of a REC.
- Dr. Frank Wells, who has held many key positions including Medical Director of the Association of the British Pharmaceutical Industry (ABPI).
- Dr. Simon Woods, who is a Senior Lecturer at PEALS, Newcastle University and is involved in teaching and public engagement of ethical and social implications of the life sciences and who has a special interest in the ethical and social implications of research.

Dr. Hugh Davies, the NRES ethics advisor, is leading a group to revise NRES guidance for writing a PIS. One of this group's principles is to take into account results of recent empirical research regarding information provision, such as that undertaken for this PhD, with an aim to improving the guidance provided.

There were a few key discussion points relating to this thesis that came from the meeting, which are presented below and picked up for further discussion in the next chapter.

The use of summary PIS

Providing a summary of the PIS is something panel members in their REC roles frequently advise researchers to do, especially as a coversheet for complex studies. We commented that it would be useful for summary PISs to be advised throughout all REC's for all studies. The panel also compared the streamlined PIS to a recruitment document such as a poster or invitation letter, provided in addition to an existing lengthier PIS.

Distinguishing between what participants want and ought to know

There was a discussion of whether what potential participants want to know may be different from what they ought to know. The streamlined PIS was designed to take this into account, since it included both the information that participants had accessed and the information that ICH guidelines require. The ICH and related statutory instrument only list the topics required and not the level of detail and this proved something of a sticking point. The panel seemed to think that on balance, there was some information that participants must be given, even if they appeared not to want it, though there was not sufficient time to pin down the precise content for each at this meeting. One suggestion offered by Dr Calvert was that REC's could provide researchers with a list of important things that participants ought to know. Patient groups, researchers and the NRES expert panel were considered as other 'experts' that may make decisions on the level of detail to be included.

The PIS is a legal document

The NRES panel agreed that the PIS as a legal document, provided to potential participants protect researchers. They were concerned that scaling down the PIS information would diminish the legal protection it affords to researchers.

The PIS is a reference document

The panel reiterated that people have to have something to refer back to, and in research, this is the PIS. They made a comparison to reading the Patient Information Leaflet (PIL) in drug packets where people do not read the information until they have a side effect, for example, and then refer back to the PIL for advice. In the Information Provision study no one logged back onto the study website at a later date to refer to the information, but this was a low intervention study with no expected adverse effects.

Consent interviews

If the PIS is not read by potential participants, the consent interview was considered as an alternative platform on which to inform participants. There was a discussion of how the process of informing potential participants could be implemented if information provision was to fall more heavily on the verbal consent interviews. Suggestions were for consent interview scripts to be written and approved by REC's with researchers testing understanding of the information, rather than just providing the information. But again, this seemed to be preferred as an adjunct to rather than replacement for the traditional PIS.

The guidelines for information provision suggest that participants should be given sufficient time to consider the information, which is generally taken by researchers to mean 24 hours¹⁷⁻¹⁹. If consent interviews are used to impart information then participants may not be given sufficient time to make a considered decision. This concern was discussed by the panel and they were happy this should not prevent participants from taking part if they do not wish to consider verbal information for longer. There was not sufficient time for the panel to consider what sufficient time for consideration would mean if all the weight fell on the consent interview. If participants are presented with the information for the first time at the consent interview and not given any time to consider the information, it has implications for guidelines that says participants should have 'sufficient' time to consider the information.

Taking the research further

There was concern that electronic PIS would not suit all studies, especially those involving the elderly, who are the least likely to have access to a study website.

The panel were confident that similar research to the Information Provision study would be given favourable opinion by a REC, provided there were certain safeguards in place, for example, providing the standard lengthy PIS at some point during the study so that participants do have the PIS for future reference purposes.

Summary

In summary, the panel were interested in the work and broadly supportive of taking it further. They may be happy for PIS to be streamlined for low risk studies such as the parent study used in this PhD but were keen for this streamlined PIS to be used in addition to a full PIS, although the panel were not unanimous about this.

7 DISCUSSION – THE FUTURE OF INFORMATION PROVISION IN RESEARCH

The discussion to this thesis is split into three. The first section considers whether using electronic PIS would be feasible in research and looks at the practicalities of providing information electronically. The second section considers the ethical concerns of information provision in light of the results of the studies conducted for this PhD. The final section explores the future of information provision in research and considers ways this research could be taken further.

7.1 THE FEASIBILITY OF ELECTRONIC INFORMATION PROVISION

Internet access

When considering the feasibility of electronic methods of communication, future use depends on the proportion of potential participants willing and able to use the Internet. One aim of the Information Provision study was to determine the proportion of potential participants that had Internet access and were willing to access study information online. If participants provided an email address it was assumed they had Internet access and were willing to access study information electronically.

The proportion of participants that provided an email address in this study was lower (290/1160; 25%) and the average age higher (mean age 57 years) than the general population (80% of households in the UK have an Internet connection¹⁰¹⁻¹⁰³; average age 40²⁰⁵). When the participants who provided an email address were broken down into age groups (Table 14), younger participants were more likely to provide an email address (45-55=174/508 [34.3%]; 55-65=69/303 [22.8%]; 65+=47/350 [13.4%]). Since it is known that younger people are much more likely to use the Internet for everyday tasks^{102;206-210}, it can be anticipated that a much higher proportion would provide an email address as a method of communication if invited to participate in research. Antoniou et al⁶ used the IIS successfully in a study with younger participants (20-50 years) and previous research has also shown that the frequency of Internet use and the types of Internet activity engaged in may also increase as number of years of Internet use increases²¹⁰. As today's younger generation

become tomorrow's older generation, the proportion of research participants willing to access study information electronically is likely to increase²¹¹.

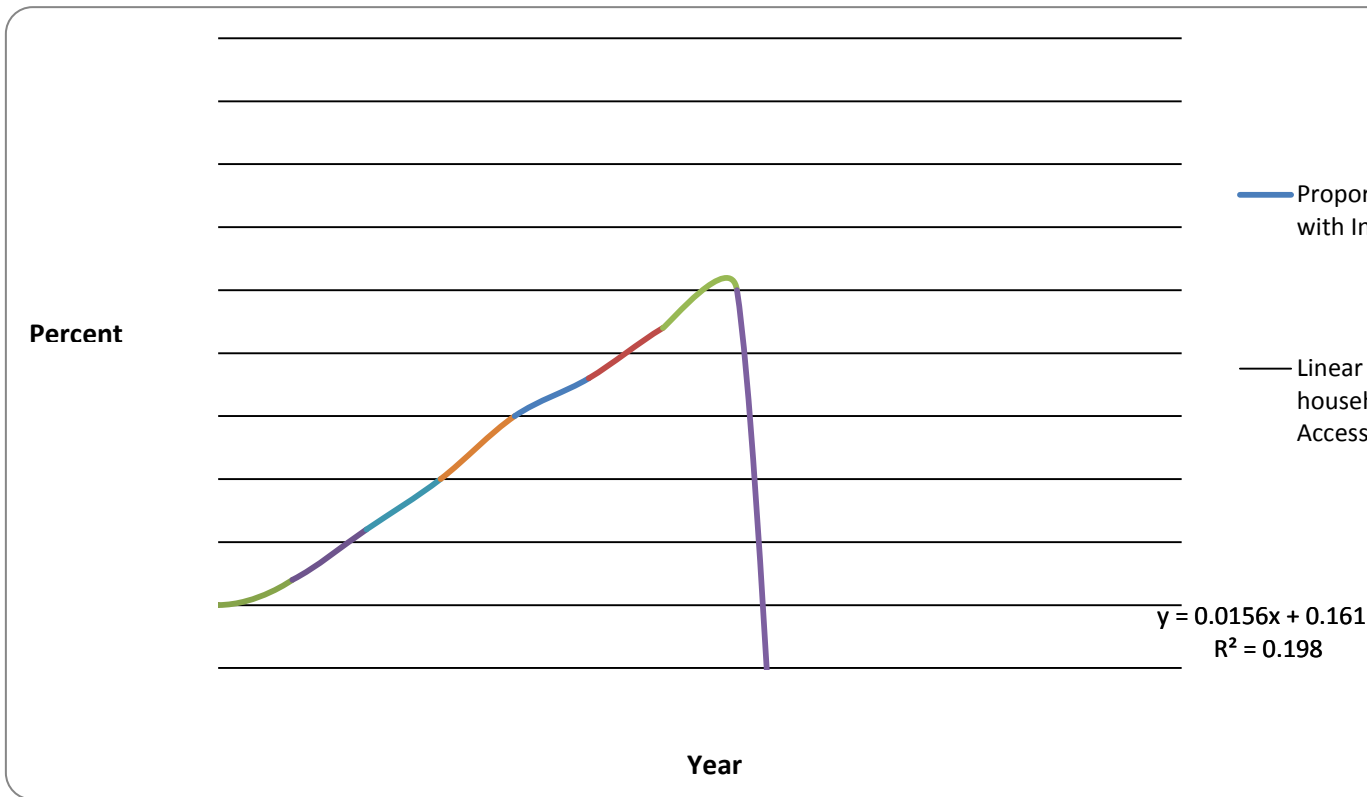
The participants of this study had a higher deprivation level (median IMD score 37.8) than the general population (average IMD score 19.0²¹²). The level of deprivation of participants also adversely affects whether they have Internet access²⁰⁸, since having access to the Internet requires both an Internet connection (or access to a free Internet connection) and a device to connect to it with. Mobile phones and Smartphones, which are likened to a hand-held computers, provide a more cost-effective method to access the Internet²¹³. As their popularity has increased over recent years, the link between deprivation and Internet access has lessened²¹⁴. It may be that in time, access to the Internet does become as common and accessible as the telephone, and even the more deprived areas will have Internet access²¹³.

The Information Provision study showed that White participants were the most likely (172/639; 27.0%) and South Asian the least likely (43/218; 19.7%) to provide an email address, and previous research has shown that Internet users are predominantly White²¹⁰. Whilst not a demographic collected in the Information Provision study, previous research has also found level of education to be strongly correlated with Internet use^{208;210;211}.

Electronic communication is commonly used in other aspects of life^{215;216} and there are already a large proportion of the population that use the Internet to do everyday

tasks, such as banking, that would previously have been done either in person or over the telephone²¹⁵. It is expected that people of the future will generally conduct relationships electronically as the Internet becomes more accessible. The most prevalent and convenient communications methods need to be reflected in research if we are to continue to encourage people to participate in research. According to 2012 ONS data¹⁰², 80% of households currently have Internet access and this has been rising steadily for the past 8 years. Figure 18 shows that based on a linear forecast of this rise, it is expected that all households will have Internet access by 2018. As more households are able to access the Internet, research using the Internet is likely to become more generalisable to the UK population.

Figure 18 – Household Internet access with linear future predictions, adapted from ONS data¹⁰²



Although only 25% of participants in the Information Provision study provided an email address, around half of those who did provide an email address said they would prefer to have information provided electronically if they took part in research again. This suggests that electronic information provision methodology could be readily developed in populations where the proportion of participants willing to use the Internet for communication is likely to be higher, for example in studies that recruit mostly younger people in less deprived areas.

Problems contacting potential participants electronically

Two problems were encountered during the study that meant additional work was needed to maximise recruitment to the Information Provision study. These problems were: 1) incorrect email addresses provided and 2) ensuring emails were delivered to the inbox rather than the 'spam' box and read by the recipient.

Inaccurate email addresses were provided by 37 (N=290, 12.8%) potential participants and these then had to be rectified with a telephone call, which increased the number of potential participants eligible for the study (23/37; 62.1% addresses were rectified). This added costs to the study that would need to be taken into account in studies using electronic recruitment.

The second problem encountered with contacting potential participants electronically was ensuring that the invitation emails were not filtered into 'spam' boxes. The initial response rate to the email was much lower than the response rate to the paper invitation, which suggested that emails were either not being received or not being read. Although a read receipt was requested, these are not automatically issued when an email is opened and recipients were free to choose not to send one, and not all email servers allow read receipts to be sent. Emails could only be identified as having been opened if a read receipt was returned, the participant had logged into the study website using their unique username, or they had booked a consent appointment. To ensure that potential participants were aware that they had been

sent an invitation by email, we telephoned them if they had not responded within three days of the email being sent.

Around half of the potential participants (146/290; 50.3%) did not respond to the email within three days and attempts were made to contact all by telephone. If they could not be contacted or did not respond to the email within seven days of it being sent they were sent a postal invitation. In the parent study, potential participants were given two weeks to respond to the letter of invitation before a reminder was sent out. The shorter time frame for the Information Provision study was a condition of embedding into the parent study, as this time frame permitted a postal invitation to be issued in timely fashion so that recruitment was not adversely affected, even though it was not unreasonable for participants to have taken longer than three days to reply. Contacting participants via telephone increased the number of participants available to participate in the IIS RCT component of the Information Provision study. It is difficult to know, however, whether making the phone call itself increased the chance that they would take part, or whether participants would have accessed their emails eventually if given two weeks to respond and a further reminder. Further research is required to determine how comparatively reliable electronic communication methods are and how reliability can be improved.

Methods that are already used to maximise recruitment from postal invitations may be adapted to assist with electronic recruitment in the future. One such is to send out invitation letters from their GP surgery or hospital clinic, which encourages more

reliable responses and negates the need to further contact^{217;218}. This also ensures data protection as if the surgeries/clinics send out the letters the researchers are not given access to personal information without consent²¹⁹. Once GP surgeries and hospitals routinely use email to communicate with patients, not only will accurate email addresses be routinely collected by them, but hospital/GP email addresses are likely to be on patients' email 'safe' list so emails are not filtered into junk boxes. At this point, the practice of sending invitations from GPs surgeries and clinics will be readily adaptable to electronic research recruitment. This would combine all of the advantages of electronic communication with that of invitations sent from collaborators known to the potential participant.

Effect on consent rate

One of the aims of the study was to determine if using an IIS could improve consent rates to research when compared to a PDF-PIS. We found that it did not improve consent rates and actually decreased consent rates slightly, although not statistically significantly (PDF=20/44 [47.6%; IIS=16/44 [36.4%]; OR 0.6 [95% CL 0.25; 1.4]). The IIS RCT did not meet its target sample size and it emerged that the effect size used in sample size calculations was overly optimistic. The method used to determine the effect size¹⁷⁹ (set out and justified in Section 4.5) were hampered by the fact that no previous effect size was available. Future studies, however, could calculate a sample size using the 13.2% effect size seen in the Information Provision study. Given that the study was not powered to detect the effect size seen, no confident conclusions can be drawn from this study about the effect of using an IIS on consent rate.

When exploratory analyses were conducted between electronic and postal communication groups as a whole, electronic communication appeared to increase consent rate, although not statistically significantly (electronic=99/290 [34.1%]; postal=271/870 [31.1%]; $p=0.3$). Participants in this study were also not randomised to electronic or postal information provision and those with email addresses may be more likely to participate in research because of systematic differences to those without an email address. This finding could, however, be used as a hypothesis for a future equivalence study to determine the effect of electronic recruitment on consent rate.

Effect on understanding

As was discussed in Section 2.3, it is difficult to determine research participants' understanding of information provided at the time of recruitment since there are no standardised methods to measure understanding, and such methods tend to measure recall rather than understanding⁵⁸. The understanding questionnaire was based on the best current tool for assessing understanding, the Quality of Informed Consent Tool¹. It is likely, therefore, that this study also measured recall rather than understanding, and this remains a limitation to comments on understanding in this research.

The level of understanding was shown to be consistent across all study groups and there was no difference seen in understanding between participants that received electronic and those that received paper information. Interestingly, though, the level of understanding was similar in all groups including those that chose to access no information. There are several potential reasons for this.

First, some of the information participants were asked about was also contained in the invitation letter; for instance, that they were being invited to participate in a research study. To have booked an appointment, the participants must have read at least some of the invitation letter even if they did not read the PIS, and this was the source of their knowledge. Accordingly, it is also possible that designing the invitation letter along the lines of the suggested streamlined PIS might be an effective means

of ensuring that the basic study information is communicated to participants effectively. The ethics of proceeding to recruitment on the basis of limited information, and what the minimum information required might be, are discussed in the next sections.

Second, the understanding questionnaire included generic questions about research, in addition to questions specific to the study in hand. It is possible that participants who understood that they were being asked to participate in health research were therefore able to make valid assumptions based on their existing knowledge of healthcare and research; for example, they may assume their medical information is kept confidential because health care practitioners normally protect confidentiality²²⁰. If so, it is arguable that it is not necessary to provide information to research participants that reflect existing norms. In the case of confidentiality, for example, participants need only be informed when information will *not* be kept confidential. The most incorrectly answered question on the questionnaire related to why they had been chosen to participate: the participants assumed it was because they had high blood pressure. This was not the case and may be the reason why the parent study initially recruited more hypertensive than normotensive participants⁵. This again suggests that it is information that is contrary to what invitees might reasonably expect that needs to be emphasised in the invitation letter, because participants may make assumptions in place of reading the PIS.

⁵ The difficulties in recruiting normotensive participants were discussed during investigator meetings for the parent study.

Third, it is possible that the questionnaire was too simple and participants were able to take an educated guess at the answers by deduction or they selected the right answer by chance, since the questionnaire provided multiple choice answers. The questions reflected the information that statutory instruments require all research participants to be given. This suggests that even if the questions were too simple and generic to research rather than specific to the study, participants already had an adequate understanding of what being asked to participate in research means. If so, this is a further reason to suppose that generic information need not be included in a PIS, since our results suggest that reading the PIS did not improve understanding in the areas tested. The Information Provision study, however, used a low risk interventional study as the parent study and it may be that more information is needed for high risk studies²².

Effect on satisfaction

Level of information provided

Participants provided with an IIS were generally happy with the level of information they received, whether they received a small or large amount. This goes some way to showing that even though participants may have only accessed a small amount of information, it was enough to satisfy their own informational requirements. It also suggests that different potential participants do need different amounts and types of information about a study before they consent to participate.

The advantage of using an IIS is that participants can choose the type and level of detail of information they access. More information can be included in the IIS than is possible with a paper PIS, and it is easier for the user to pick out the specific pieces of information that interest them. If participants are able to access information more easily, it may be possible that they are more likely to read the information they are actually interested in. They may be deterred from accessing any information if they have to skim through a lengthy PIS to find the information they require for their decision making.

The detailed information provided in the IIS can be chosen by clinicians/researchers on the basis of their expert assessment of the existing evidence. This decreases the risk that participants who do want more information will research the topic themselves^{221;222} and, in the process, access unreliable information^{223;224}.

With a paper PIS participants are able to skim through all of the information and then pick out what is important. With an IIS they have to click on a specific topic of information to read and may miss information that is important to their own decision-making because they chose not to click on that topic of information. If a lengthy PIS was provided, however, they may have picked out additional information by skim reading the whole document that they would not have accessed (in the IIS) based on title alone. It is not known whether participants who received the paper PIS did skim the information provided, and they may have not read it at all. It would be useful to explore the information-seeking behaviours of potential research participants to

determine exactly what they do when they receive a paper PIS. Research in this area may be difficult to conduct, however, since we know from this study and that of Antoniou et al⁶ that what participants say they do when asked may not reflect what they actually do. Since it is generally held that hypothetical opinions may not reflect real opinions¹⁷⁰⁻¹⁷², asking potential participants to indicate what information they would access may also not reflect what they actually do. It may not, therefore, be sufficient to ask potential participants what they read, or what they want to read, and future research may achieve better results from observational techniques.

Method of communication

The majority of those who provided an email address said they would like to receive information electronically if they took part again. This may be because they found electronic communication more convenient than postal communication. In this case, electronic communication may have improved their research experience. They may also prefer electronic communication for other reasons; for example, a participant may find it less convenient to access information electronically if they have to go to the library to access it, for example, but they may prefer electronic communication because of a desire to reduce paper waste. Here the participant may prefer to receive information without it actually improving their research experience (since it was more inconvenient).

Equally, however, those who received postal information tended to prefer to receive paper information in the future. There may be no conflict between these two

preferences, provided researchers ask potential participants to give their email addresses as routinely as they ask them to give other contact details. It might then be safely assumed that participants who do provide an email address may prefer electronic communication. Invitation letters and PDF copies of PIS can easily be sent electronically, and the majority of participants were satisfied with the way in which they received information. This suggests that there are no disadvantages to receiving identical information electronically, but there may be advantages, such as not having to reply by post, which entails going to a post box. This is a particular advantage for questionnaire-based research since a link to an online questionnaire can be included in the email. Giving participants the option of electronic communication may be a relatively easy way to improve their level of satisfaction.

Consideration of cost

Electronic communication

In terms of cost, communicating electronically appears cheaper than by post since it avoids printing, stationery and postage costs, and there is no need to stuff envelopes, mail merge and print letters or send mail, all of which absorb staff time^{112;118;128;129;135;136}. As found in this study, however, having an email delivered quickly is no guarantee that it will be read, or responded to, quickly. This study incurred additional costs because of the telephone calls required to prompt participants to open and respond to the email invitation. A further driver of cost was the development of the IIS, which will be considered separately in the next section

The cost analysis performed on the Information Provision study suggested that it was more expensive per participant to send electronic invitations than it was to send postal ones (Table 25) primarily because of the additional costs involved in calling participants. Such costs may decrease if email becomes the main mode of written communication because potential participants would be more likely to access their emails regularly, and email addresses would be routinely collected as a communication method. Participants were only given three days to respond to the invitation email before being contacted by telephone, but they were given two weeks to respond to the postal invitation letter before being sent a reminder. Three days is a short a timeframe and our participants may not have accessed their emails frequently enough to respond this quickly, or may have accessed the email but not intended to respond immediately. If participants had been given longer to respond to the email, fewer telephone contacts may have been necessary, and, therefore the corresponding costs may have been lower.

Development of the content of the IIS

It was estimated that it would cost £1173 in researcher's time (Table 26) to develop the content for the IIS, in addition to the time spent writing the 'standard' level two information. There would also be costs associated with writing the website to host the study information. These costs would diminish with frequency of use since, once written, the system could be readily used for other studies with little or no additional cost.

It may be difficult for researchers to justify the additional cost to develop an IIS for small studies since, based on the costs outlined above, it would cost £11.70 per participant for a study with 100 participants. As the study size increases, however, the cost per participant will decrease, i.e. it would only cost 23p per participant for a study with 5,000 participants. The cost of developing the IIS may also be justified if there are other reasons for using it, for example, participants are more satisfied if they can easily tailor the information to their individual requirements. The next section will explore why an IIS, despite the associated development costs, may be justified for use in future research.

Key points

Internet access

It is likely that email communication will become routine for most people.

Current communications methods should be used in research – this will require a well developed methodology to be established in advance.

Difficulties communicating electronically

It is not clear whether emails have been received by participants.

If GP surgeries, for example, use email to communicate with patients, it may provide a reliable way to contact potential research participants electronically.

Consent rate

The effect size reported in the IIS RCT could be useful in similar future research.

Results suggest there may be no difference in consent rate between postal and electronic communication.

Understanding

Communication method and amount of information did not affect understanding. This may be because participants:

- Gathered information from the invitation letter.
- Applied common sense to respond to questions.

- Correctly guessed answers because the questions allowed educated guesses based on deduction or sheer guesses because of the multiple choice answer format.

Satisfaction

Making detailed information available to participants who want it allows accurate information to be provided, rather than further information be sourced by participants.

Future research on the informational requirements of research participants should rely on observational methods.

Providing a choice of communication method may improve satisfaction.

Consideration of cost

Additional costs of electronic communication may decrease as emails become the main source of written communication.

The IIS was expensive to develop in terms of additional researcher's time, but the cost may be justified if there are other reasons for using it.

7.2 INFLUENCES ON THE PARTICIPATION DECISION

Previous studies have shown that when asked directly, potential research participants will often say they want more information regardless of how much they have already received^{6;26;225-230}. In this study the IIS allowed the amount of information actively accessed by potential participants to be recorded when they were deciding whether to participate in a low risk interventional study. The integration of the technology in this study enabled us to show that when given the option to access more information than was provided in the paper PIS, the majority chose to read very little of the information available. Even more surprisingly, perhaps, are the 59% that booked a study appointment despite accessing no study PIS at all because they chose not to click the link to access it, and the 40.9% that were randomised to IIS but still chose not to access any information. These results reflect those of Antoniou et al⁶ who, for a questionnaire study, found that 88% of potential participants agreed to participate without reading the level of information pegged at the level of the standard PIS and between 28% and 30% chose not to access any information. These two studies are, as far as we know, the first to record the amount of information actively accessed by potential study participants.

It can reasonably be assumed that in the Information Provision study, participation decisions were based on something other than the information provided in the PIS, since the information was often not read. This section seeks to explore how

participant's decisions might have been made, if not based on the information provided.

Using common knowledge

Previously in this chapter, it was hypothesised that participants may have a 'common knowledge' about research and research practices that does not need to be repeated in a PIS. One way to reduce the length of future PISs without compromising participant understanding may be to only include information contrary to the norm. Extra care may need to be taken when a study deviates from the norm, to ensure that participants really do understand what they are consenting to. It may also be useful to have a central point of information that states what the norms of research are, so potential participants are able to check their knowledge.

Preferred communication

In order to measure the effect of the PIS on consent, this study took the decision to book a consent interview, rather than actual consent at interview, as the outcome against which to measure the consent rate. The aim of the Information Provision study was to determine the effect of written (rather than verbal) information on participation decision. Using the decision to book a consent interview as the measure of consent discounted the impact of information provided during the consent interview on actual consent rates.

Kreiger et al²³¹ found that participants may be more likely to participate in research if they are able to establish a rapport between themselves and researchers and results from Townsend et al¹¹⁹ suggest that electronic communication may be an effective way to establish that rapport, since 76% (29/38) of participants used email as the main form of communication with researchers. Townsend et al¹¹⁹ also used a found there to be a high level of communication between researchers and potential participants concerning aspects of recruitment and consent before the consent decision was made. Taken together with results from Townsend and Kreiger, the results reported in the Information Provision study may suggest that participants did not access information in the PIS because they preferred to communicate directly with researchers. Participants may have contacted researchers to discuss the study and only after this discussion decided to book a consent interview. If participants do use information communicated verbal and/or via email to make participation decisions, inviting participants to communicate with researchers prior to booking a consent interview, for example, may be one way to inform study participants. Study invitations usually include a contact number for researchers²², so it may be that proactive communication from the researchers is key to providing verbal information before the consent interview. This would be another way of tailoring information to individual requirements, but would be labour intensive and, therefore, costly.

Most evidence of preference for method of information delivery is limited to patients rather than potential research participants^{66;67;232-234}. As outlined in Section 2.2, in the routine clinical setting, the decision of how much information to provide to

patients is left with the treating physician^{2;37}, whilst information provision in research has to meet requirements of statutory instruments for GCP^{22;26;35;42-45}. Guidelines for information provision are different for patients in routine care and research participants, but the reasons for providing the information remain the same – information allows patients and potential participants to make an informed and voluntary decision regarding participation. Since the reasons for information provision are the same, it may be that research concerning information provision preferences will apply to both patients and potential research participants alike. Prior evidence suggests that verbal communication is well received by patients and that discussion with research staff can improve understanding of study information^{66;234}. Recent studies have also shown a mix of verbal and written communication to be preferred^{67;232;233}, and so the consent interview may be important in providing verbal information to potential participants and satisfying informational requirements. If this is the case, in addition to written information, verbal communication needs to be offered to potential participants, in order to inform them about the study. If potential participants do prefer a mix of written and verbal communication, the results of the Information Provision study suggest that they may only want basic written information, with further information provided verbally.

In addition to individual potential participants wanting different levels of written information, then, they may also want that information communicated in different ways. In order to further tailor information provision to individual participants, they could be provided with access to both verbal and written communication. An IIS that

incorporates a streamlined PIS could be provided to potential participants first, to attempt to tailor information to the individual and reduce the number of potential participants likely to want the information delivered verbally. In addition to written information, an offer of contacting researchers may satisfy participants who want a mix of communication types, or who prefer only verbal information provision. Challenges with providing verbal information include ensuring the consistency of verbal information and ensuring information is provided sufficiently to provide legal protection to researchers. These issues are considered in later sections.

Length of PIS

Smith et al²³³ randomised patients to a summarised participant information leaflet (PIL) and verbal information about a treatment, compared to verbal information alone. 90% of participants across both groups preferred to receive both written and verbal communication and providing a summarised PIL improved recall of risks. Since it is difficult to distinguish between a measure of recall and that of understanding (Section 2.3), it may be that providing a summarised PIL also improved understanding in Smith et al's study. The information in their summarised PIL contained the same information as provided verbally and comprised a summary of practical details of the treatment such as the diagnosis, proposed treatment, possible risks, postoperative care and rehabilitation. This equates to the types of practical information that participants in the Information Provision study wanted to know. If study information summarised only the practical information that potential participants wanted to know, as in the study by Smith et al, participants may use that

summary to aid their decision making⁶⁶. This summary information could be provided as a streamlined PIS rather than a standard (often lengthy) PIS, with the same information provided verbally at the consent interview. An IIS could also be provided as a back-up for those who do need to access more information to satisfy their informational requirements.

Participants may not have wanted to know the information

The lines of discussion so far have focussed on other ways participants may have accessed information, either by using their common sense to make assumptions or by extracting the information from verbal discussion with researchers. It may be, of course, that participants did not access very much information because they did not want or need to know the information to make a participation decision. If this is the case, then there must be other factors influencing their decision-making. Three possibilities to consider are: altruism, trust and external influences unrelated to the study.

Participants often take part in medical research for altruistic reasons²³⁵⁻²³⁷ and it is healthy patients, such as the ones in this study, who are more likely to suggest that they are altruistically motivated²³⁸. It is not surprising that healthy patients are the most likely to be motivated altruistically, since participation is unlikely to be of benefit in terms of their health. There may, however, be limits to their willingness to help others, and the extent of risks and inconveniences of participating may be a consideration when making a participation decision. In addition to this, they may also

consider the extent to which the research is likely to help the wider community. If participants were taking part purely for altruistic reasons, this may help to explain why certain topics were accessed more often. Information accessed most frequently concerned expenses, what would happen if they took part, the risks of taking part and the purpose of the study. These topics of information may have helped participants weigh up the costs and inconveniences of taking part against the benefits of the study to the wider community, to decide if they did want to make an altruistic participation decision.

Another influence on the potential participant's participation decision may be that of trust in the person inviting them. The invitation for the first phase of the parent study (the questionnaire-based phase) was from a University researcher. The invitation, however, came via the potential participants' GP surgery rather than directly from the University. This may have meant that the potential participant believed their GP, rather than a University researcher, was inviting them to take part. This is common practice in primary care research, both for data protection purposes and as a way to improve recruitment. There are data protection issues surrounding accessing patient's names and addresses unless they have consented for researchers see that information²¹⁹, and so one common way around this is to send the invitation directly from the GP surgery and ask potential participants to return their contact details to researchers, as happened in the parent study²³⁹.

Patients can often trust doctor's opinions explicitly²⁴⁰⁻²⁴⁴, and sending an invitation as if from a patient's GP plays on that trust, in order to improve recruitment rates. Kraetschmer et al²⁴⁰ found a strong correlation between the level of trust a patient had in their doctor and their desired level of participation in decision-making. The higher the level of trust the patient had in their doctor, the less likely they were to want to be involved in decision-making (between 81.1% and 97.3% [depending on the type of decision] with very high levels of trust wanted their doctor to make the treatment decision). As the level of trust in their doctor decreased, patients were more likely to want to share the decision-making role or make the decision for themselves (between 14.8% and 26.4% with low levels of trust wanted their doctor to make the treatment decision). In addition to the results found by Kraetschmer et al, the Information Provision study also found potential participants accessed very little information. This relation of trust to the level of information accessed was consistent with views expressed at the NRES expert panel meeting, where one member quoted (Appendix 9.9):

“He felt that patients in this country particularly are still very trusting of their healthcare professionals.....this culture of trust was still very important factor in a patient's decision to take part or not in research as they will tend to trust an invitation coming from their doctor or other healthcare professional.”

Manson and O'Neill's¹⁵ thoughts are useful when defining trust in the doctor-patient relationship. Since patients have a limit to their capabilities in terms of their medical

knowledge, they rely on their doctor's knowledge and expertise to provide information on their medical condition and appropriate treatments. Having trust in another means relying on what they say. One may also make a judgment of trustworthiness of a person based on previous episodes of trust. If a patient has previously been able to rely on what their doctor has told them they are more likely to trust that they can rely on what they say in the future. Over time, this builds a relationship of trust between doctors and their patients, and patients come to the conclusion that their doctor is trustworthy. If participants of the parent study believed that the invitation was from their GP, they may have believed their GP would not invite them to participate in something that was not safe or of no benefit to them; evidence of their trust in their doctor. If the potential participant believed the study to be safe and appropriate for them to participate in, they may have neglected to read the information provided.

In clinical trials, the first study discussion about participation is often between a doctor and patient in clinic³⁹⁻⁴¹. In this situation, the doctor could meet all of the consent criteria by telling the participant about the study and ensuring they understood the information, but the participant could still disregard everything they have been told and continue to base their decision on trust in their doctor's judgement and the belief that the doctor would protect their best interests by, for example, not exposing them to unnecessary harm. Patients often do not want to make an independent decision regarding their treatment, and actually want to share the decision-making with their doctor²⁴². Salkeld et al²⁴³ found, however, that even

when patients expressed that they preferred a less active role in decision-making, the information provided by their doctor still had an impact on their decision-making. This means that if information provision preferences are consistent between patients and potential research participants, any study information provided may still influence decision-making for potential participants, even for those that usually prefer the doctor to make decisions for them.

There may be other factors, completely unrelated to any medical situation, which influence a decision to take part in the research^{245:246}. Cohen²⁴⁵, describes four thought experiments where patients used something other than the information in hand on which to base their decision. He refers to these cases as 'Gettier' type cases. One example²⁴⁵ is of a patient who had understood all of the information about a treatment and decided against it. She then had a dream that resulted in a belief that the doctor was her 'god sent saviour' and later agreed to the treatment on the basis of that dream. If this situation is applied to research settings, the participants would have been given all of the information, understood that information and been capable of making a participation decision, but based their decision on something entirely unrelated. Or, the participant could have chosen not to even read any of the information provided because they had already made the decision to participate based on the external influence alone.

The question Cohen raises is whether providing information and giving free consent are dependant or independent. The current informed consent model suggests

dependency, since the term 'informed' would not be used if information did not play a causal role in the consent decision. In practice, this dependence would be impossible to ensure, since ulterior motives for consent could never be ruled out. The current consent model uses autonomous deliberation of the information provided as the grounds for free consent to be given¹²⁻¹⁴. If the provision of information and giving free consent were to be acknowledged as independent from each other, there would need to be a revised consent model that took this into account. This revised consent model would still allow potential participants the option of autonomous deliberation when making a consent decision, i.e. the potential participant is able to use the information provided to make a consent decision. It would, however, also respect an idea of free choice of whether the potential participant acts autonomously or not, i.e. it would allow potential participants to choose to make a participation decision based on something other than study information.

Key points

Participants may use their common knowledge to assume things about research. If this is the case, care must be taken to ensure participants are informed when a research protocol deviates from normal expectation.

Participants may prefer a mix of verbal and written communication. Potential participants may prefer a summarised PIS with additional verbal information.

Participants may not have been interested in study information at all and based their decision on an influence other than the information provided. An altruistic desire to participate, trust in their GP, or another influence completely unrelated to the research may explain why little information was accessed. The current consent model may need to be revised in order for these influences to conform to meet consent requirements.

7.3 CONSENT WHEN PARTICIPANTS CHOOSE TO READ LITTLE INFORMATION

For consent to be valid it has to fulfil three criteria: 1) the participant is given specific detailed information about the study; 2) the participant is capable of understanding the information provided and using it to make a decision regarding participation; 3) the decision is made voluntarily^{2;3;15;16}. In the previous section it was suggested that when potential participants read little or no study information, they base their participation decision on common knowledge, preferred other forms of communication, were deterred by the length of the PIS or based their decision on an influence other than the information provided, such as an altruistic desire to take part, trust in their doctor, or an alternative external influence unrelated to the study. In all of these suggestions, criterion one for consent was met since all participants were given access to detailed study information (the IIS), even though they often chose not to read it. Criterion three was also met since, although the decision may have been based on something other than the information in hand, all decisions were voluntary. The uncertainty lies in whether criterion two was met by participants. All study participants were deemed competent by their GP to understand the information provided and use it to make a decision regarding participation, but they often did not use the information provided to make the decision. The criterion states that participants should have the capacity to use the information to make the decision. The problem, however, is that the formulation infers the information provided should be used to make the decision. This is a different issue to that of capacity, since a participant can have the capacity to use the information to make a decision without

basing their decision on that information, and a participant can have the capacity to understand the information but still choose not to read it. This section considers whether valid consent can be given if a participant chooses not to access all of the information provided.

It was suggested in the previous section that participants may not read study information because they used their common sense to assume things about the research based on information provided in the invitation letter. In a sense, participants were using information about the study to make a decision, although this was assumed rather than given knowledge. It is reasonable for participants to make assumptions about research, assuming these beliefs match the facts, i.e. they believe their information is going to be kept confidential, and it is. A problem arises when their beliefs do not match facts about the study, i.e. their information is not going to be kept confidential but they assume it will be. In this situation, the participant may have decided not to participate if they had known that their medical information was not going to be kept confidential, but they would not know this to be the case unless they read or were told that information. It is in this situation that their consent may not be valid; not because they lack capacity, but because they lack the relevant information. In order for their consent to be valid, then, their misunderstanding would need to be corrected. One way to do this would be to make it explicit to potential participants when protocols deviate from the norm, although doing this assumes that everyone has the same norm. Since participants may not

read the PIS, this information would need to be imparted in some other way, for example, verbally during the consent interview.

Participants may not have read the PIS because they obtained the information they needed from research staff instead. If so, the participants used the verbal information to make a participation decision. There may be a concern that where verbal information was given at consent interviews, participants were not given sufficient time to consider the information before giving their consent and may have only been given the information they wanted rather than ought to know, or vice versa. The NRES expert panel confirmed that there is no requirement to give participants 24 hours to consider their decision, though this is often the period of time allocated in custom and practice¹⁷⁻¹⁹. The validity of the consent would only be affected if participants were not given *sufficient* time to consider the information. Fulfilling this requirement would mean allowing each participant the time they personally needed to consider the information before being asked to make a participation decision. This may vary considerably between participants, and for some participants may mean they have to come back for a further consent interview at a later date. The implications of this would need to be considered, since it may have resource and cost implications and may not be feasible for participants to be offered an additional consent interview in all studies.

The final hypothesis as to why potential participants accessed little of the information provided was that an influence unrelated to the study affected the decision to

participate. As outlined in the previous section, these types of participation decisions do not fit with the current consent model that does not allow a potential participant the free choice to make a participation decision based on an influence other than the study information. Providing potential participants with an IIS would provide them with a free choice to choose what information they access. There are difficulties in allowing potential participants the free choice of what information to access, since even if they chose not to access any study information, there still may be parts of the PIS that if read, may have been important to their decision making. They would not know this, however, if they made the decision not to use the information provided to inform their decision-making. There are also adverse legal implications to allowing potential participants to enter into research without adequate understanding of the information provided⁵. As the consent model currently stands, participants that chose to access no study information because they made their decision on a completely external influence, would not have given their valid consent to participate.

In this study and that by Antoniou et al⁶, we were in the unique position of knowing what information potential participants had accessed. In the Information Provision study 59% of participants booked a study appointment despite accessing no study PIS at all because they chose not to click the link to access it, and 40.9% of those randomised to the IIS still chose not to access any information. Antoniou et al found that between 28% and 30% of participants chose to take part without accessing any information. These findings should be a concern to other studies, since one of the consent criteria is that the participant must be given specific information about the

study. The way in which the information is provided to potential participants should, therefore, be a consideration in, and for, future research.

Key points

When research protocol deviates from the norm, participants may use incorrect beliefs (using common knowledge) to assume things about research.

When research deviates from the norm, this should be made explicit to potential participants - if they do not read the PIS, this needs to be imparted verbally.

Participants may base their decision on information provided at the consent interview. It is not necessary to give potential participants 24 hours to consider information provided at the consent interview, but they must be given the sufficient time they personally need to consider the information.

If participants use a reason unrelated to the study to make a decision, their consent would not be taken in accordance with the current consent model.

7.4 AUTONOMY, PATERNALISM AND CONSENT

As outlined in Section 2.1, the requirement for consent prior to research participation comes from a respect for autonomy. When the research community use 'respect for autonomy' in terms of consent it is generally understood to mean that potential participants make a choice based on their own values, for their own reasons and should have that choice respected¹²⁻¹⁴. Providing potential participants with study information allows them to decide if participating in the research is consistent with their values, interests and preferences and contributes to autonomous decision-making^{2;3;14;21-23;247}. Buchanan²⁴⁸ describes paternalism as "interference with a person's liberty of action, where the alleged justification of the interference is that it is for the good of the person whose liberty of action is thus restricted" (p.371). There are at least two ways in which paternalism can manifest itself in information provision. The first is where the doctor-researcher acts in the patient's best's interests to make a decision on their behalf. This takes the decision away from the participant, who is no longer able to exercise their autonomy to make the decision. The second is where the doctor-researcher withholds information. This does not interfere with the potential participant's freedom to make a decision. It does interfere with their autonomy, however, since they are not provided with all of the information pertinent to their decision making.

When researchers decide what information to provide this can be described as paternalistic since researchers are deciding what potential participants need to know

in order to be able to make a decision. Researchers may be described as acting paternalistically by making the decision about how much information potential participants need to know, since it takes the decision of how much information is required away from the potential participant. They may also be described as acting paternalistically if they do not include every aspect of the research in the PIS, since this would mean they were withholding information from the potential participant. Someone has to decide what information to provide, because the alternative would be to provide potential participants with every piece of information relating to the study, which may itself hinder decision-making. Researchers act in the potential participants best interests to provide the information they think will have an effect on decision-making. Deciding what information to provide may be paternalistic, but it is a justified paternalism since someone has to make a decision of what and how much to provide. It may be, however, that researchers alone are not best placed to make the decision of how much information to provide.

It is reasonable to expect that individual potential participants may want different levels of study information and that for some this may mean they autonomously choose not to receive any study information at all, trusting perhaps in their doctors judgement, whilst others want much greater information provision^{6;25;225;249}. Helgesson et al²⁵⁰ discuss that the current formulation of consent assumes that if participants ask for more information they should get as much detail as they need until they are satisfied with what they have been given. Participants may not be given all of the information that researchers decided to leave out, but the paternalism

here is weak, since allowing participants to ask further questions concerning the research allows them to gather any further information they require for their own decision-making. Weak paternalism is often justified because it has a positive effect on the person, in this case, improving the information provision process for the potential participant.

What Helgesson et al²⁵⁰ do not consider the current consent model to do, however, is to cater for those who wish to access less information, a topic they believe had been ignored in the literature. The results of the Information Provision study showed that a large proportion of participants accessed little or no information before deciding to participate. If we accept that different people will want to know different information, and for some this may mean not knowing anything, then a different model of consent would be required. A problem with allowing participants to choose to access no or little study information is that a potential participant cannot possibly know how much or what types of information would be important to their own decision-making until they had read that information. A participant may make an autonomous decision to access no information before making a consent decision, but when a researcher paternalistically insists she reads it, she may decide she does not want to participate on the basis of the information she reads. In this case, insisting that the potential participant reads the information neither affected her freedom to make a consent decision, nor did it mislead her by omitting information, but it gave her the information she required to make a consent decision. It follows then, that some acts of weak

paternalism can be beneficial to decision making, without restricting the potential participants freedom to make an autonomous decision.

Allowing potential participants to access no information about a study would also bring about a tension for researchers, since in order to comply with statutory instruments for GCP there is a certain amount of information that must be provided to potential participants; although guidance is silent concerning what to do if a potential participant does not want that information^{7;42-45;50}. Researchers may also consider informing participants to be part of their moral duty, regardless of the law²⁵¹.

Previous research has suggested that research participants often get better care, which may be due to additional tests being carried out and care being monitored in order to adhere to strict research protocols^{192;252-254}. A recent Cochrane review by Vist²⁵⁵ et al, however, suggests that the outcomes of research participants are often similar, rather than superior, to those of patients receiving similar treatments outside of the trial. It may not be an ethical problem if participants choose not to access any study information, if their care is unaffected by participating in research, or if the study benefits them in some other way, for example, a new treatment in a clinical trial proves to be of benefit. The concern, however, is that there will always be some known and unknown risks that mean participating in research of new therapies may lead to harm. Although potential participants cannot be told about unknown risks because they are unknown, they could be told about the potential for unknown risks. The knowledge that they are putting themselves at unknown risk may be sufficient to

prevent some participants from giving their consent. Information about risk, including the potential for unknown risks, then, is likely to be one topic of information that if made mandatory, may affect a potential participant's participation decision, even if they had previously decided they did not need to access any study information. This means that in addition to providing mandatory information to meet statutory requirements, there is some information that potential participant's *ought* to know because it is likely to affect their participation decision.

A final problem with accessing no/little information lies in the different types of participants doing this. One can imagine a participant who understands they are being asked to take part in research and wants to take part regardless, so makes a decision to access very little information (for one of the motivations outlined in the previous sections). This participant is choosing to access little information for a reason based on their own beliefs. They may, for example, trust researchers to act ethically and may only want to know what they would have to do in order to participate, to ensure that taking part would not inconvenience them substantially^{256;257}. Imagine a second type of participant, one who does not read the information because they do not understand what is being asked of them. An example would be a participant who believed the decision being sought related to treatment rather than research and confused the invitation to participate in a clinical trial with a recommendation to take a certain treatment. It is this latter participant who is of concern, because they may, after actually reading the PIS, realise the true nature of what is being asked and be unwilling to participate. Mill²⁵⁸ uses the

example of a person attempting to cross a dangerous bridge, to argue that it is not paternalistic to stop a person from making a decision when they do not have all of the necessary information before them. Preventing him from crossing whilst bringing to his attention the danger of doing so would not infringe his autonomy, since he can use that information to decide whether he still wishes to cross the bridge. Although he can be prevented from crossing whilst the information is given, he cannot be detained if he still decides to cross. If the dangerous bridge analogy is applied to the research setting, it would not be deemed paternalistic or an infringement on autonomy to verbally force study information on potential participants who chose not to read the PIS. It would, however, be paternalistic to prevent someone from entering a study if they chose not to listen to and demonstrate understanding of that information.

It seems then, that there is a requirement for some mandatory information to be provided to potential participants in order for them to be able to make an autonomous participation decision.

Key points

There are at least two ways in which paternalism can manifest itself in information provision - the researcher makes a decision on behalf of a potential participant, or withholds information pertinent to their decision making.

Weak acts of paternalism may be beneficial in research. A participant may make an autonomous decision to access no information before making a consent decision, but when a researcher paternalistically insists she reads it, she may decide she does not want to participate on the basis of the information she reads.

In order to comply with statutory instruments for GCP, potential participants must be provided with a certain amount of information.

Bringing important information to the attention of potential participants does not impact on their autonomy since they can still use that information to decide whether they want to take part. Preventing them from participating in the study because they chose not to listen and demonstrate understanding of that information would be paternalistic.

There is a requirement for some mandatory information to be provided to potential participants in order for them to make a participation decision.

7.5 MANDATORY INFORMATION

There is a risk that when researchers (and RECs) exercise their judgement on how much and what information to include in a PIS, some participants will not have enough information to make an autonomous decision and some will consider it too much information. The problem with standardised information is that it is impossible to know which piece of information is decisive, and therefore significant, for any given individual. Just as it is reasonable to expect that different people will want different amounts of information²⁵, it is reasonable to expect that different people will give differing significance to the same piece of information in their decision-making. Previous research has also shown that researchers and potential participants have different opinions on what information is important to potential participants^{70;259;260}. What we can do, is to conduct research, such as that done for this PhD, that enables us to produce a best guess of what the average potential participant regards as important when producing standard information sheets.

The consensus from the NRES expert panel was that PIS's are not only to provide information for consent purposes but also legal documents that protect researchers. General Medical Council (GMC) guidance² concerning consent to research also states that potential participants should be given the fullest possible information, and this is echoed in common law²⁶¹. Providing a lengthy PIS, then, provides legal protection for researchers since it allows full information to be provided. The NRES expert panel agreed that there may be a need to simplify PISs for low risk research

such as the parent study in this thesis, but felt that there are inevitably essential items that must be included in the PIS, in accordance with international statements^{7:35}. In addition, the PISs provide a reference of information for participants if they encounter problems during the study. If lengthy PISs must be provided to participants for legal reasons, then assuming researcher's responsibilities are to inform participants rather than simply provide information, the problem of how to inform participants still remains since our results suggest that the majority of research participants may not read the PIS.

On reviewing the suggested streamlined PIS for the parent study, the NRES expert panel draw a distinction between what participants *want* to know and what they *ought* to know. The first consideration to determining what potential participants *ought* to know, is who should decide on the list of key information to be provided; patient advocates, researchers, experts such as the NRES expert panel, by following statutory guidelines for medical research, or a combination of these?

This and research by Antoniou et al⁶ has shown that when asked, patients will often say they want to know more information even if they will not actually use it to make a decision, so providing patient groups with a PIS and asking them if they want to know more information is unlikely to provide results that reflect what they would do in practice. If a patient group were to be provided with a full PIS and then asked what they thought people needed to be told, however, they may decide differently. In designing the content for level one of the IIS for this PhD, participants were provided

with a PIS and asked to identify what they thought was the most important information to know in each section. Participants were able to identify what information they thought to be the most important, and this proved to be useful in determining what information to include in level one. Research has shown that the information patients want to know is likely to differ from what experts think they want to know⁷⁰, and so using user groups may be one way to ensure the information that patients want to know is provided.

Experienced researchers also seem well placed to form a judgement, since it is their obligation to gain valid consent and they often understand the study and its ramifications. Their experience in what participants ought to know is likely to come from the information they have included in PIS in the past. This may be advantageous if they have had contact with potential participants, since it may give them an idea of the types of information that those participants wanted to know. It may also be a disadvantage, however, since researchers currently design PIS that are often considered to be lengthy and complex²².

The streamlined PIS demonstrated that something more streamlined that still followed GCP guidelines could be produced. Providing information that met GCP guidelines would provide a defensive argument for researchers, since they would have told potential participants all of the information they need to know to meet legal guidelines. Experts within the area of research ethics, such as those on the NRES expert panel, could make the decision about what participants *ought* to know about

research in order to meet statutory requirements and provide this information in NRES guidelines for writing PIS²². The strength of the panel lies in the mix of backgrounds of individuals whose experiences cover a range of areas within research ethics²⁰⁴. Members of the panel are key stakeholders within the NHS, Clinical Trials units, REC's, and the pharmaceutical industry. As mentioned previously, there is likely to be a mismatch between what researchers and potential participants think, and so they may not be best placed to decide what potential participants *want* to know. Given their diverse and experienced backgrounds, however, the panel are likely to have expert opinions on the information that participants *ought* to know to participate. The NRES expert panel may be able to suggest (and provide guidance on) how information could be presented to potential participants in order to meet statutory requirements. RECs should then use this guidance to determine if there is any additional information they consider wise for potential participants to know before they consent.

NRES PIS guidance is currently being updated (led by Hugh Davies), and one update could be to provide a list of mandatory information that potential participants must be told about research, devised by experts within research ethics, such as the NRES expert panel. The guidance already covers information they recommend to be included in a PIS, but in order to produce a streamlined PIS, mandatory information specifications would need to be much more succinct. A paragraph of information could be included in the PIS guidance document, for example, that covers all the basic aspects of research, such as that used in the streamlined PIS example

provided in Section 6.12. This paragraph of information could be adapted to each study. It could also be expanded, for example in an attached lengthier PIS, but used to help ensure that basic mandatory information is provided to potential participants who otherwise would choose not to access any information about the research. In addition to this mandatory information required to meet statutory guidelines patient advocates, and evidence from empirical research such as this PhD and the study by Antoniou et al⁶, could be used to add information that potential participants are likely to *want* to know, to the information that potential participants *ought* to know, to produce a streamlined PIS for each research study. This is the process used to produce the streamlined PIS in Section 6.12, and it allows both the information that potential participants *want* (according to the information they are likely to access) and *ought* (according to the statutory instruments) to know to be presented in a succinct and accessible way.

These recommendations for future information provision and the resulting streamlined PIS are only appropriate for the low risk interventional study used in the Information Provision study. The focus may be different in low risk studies using a different disease area or participant group, and in higher risk studies. Further research should be conducted to determine if these recommendations can be translated to other types of research, and this research would need to be conducted before general guidance could be produced for the mandatory information to include in a PIS. Guidance on producing a streamlined PIS could be developed now and

used in addition to a lengthier PIS, but in the future it may be advantageous to provide just the reduced PIS.

The NRES expert panel suggested that the aim of lengthy PIS documents is not only to inform potential participants, but also to act as legal protection for researchers. In order to deal with this, the panel suggested that a streamlined PIS could be included at the beginning of the PIS as a summary of the information provided. If this streamlined PIS provided both the information that potential participants *ought* to know and the information that they *want* to know, it may be sufficient to inform a consent decision for the majority of potential participants. The streamlined PIS may also be more likely to be read by potential participants if they were previously deterred by the length of the document. If the information in the streamlined PIS was not sufficient, they could access the attached, lengthier PIS, for more information.

Key points

The PIS provides information for consent purposes and legal protection for researchers.

Mandatory information for research could take into account what potential participants both *want* and *ought* to know, with experts such as the NRES expert panel developing guidance for the basic information participants *ought* to know, and the information that potential participants *want* to know developed using research evidence with input from patient advocates.

A streamlined PIS providing mandatory information used in conjunction with an IIS or attached lengthier PIS could improve information provision in research.

7.6 PROVIDING VERBAL INFORMATION

The streamlined PIS developed for this PhD thesis was an attempt to provide mandatory information for participants whilst meeting the needs of those who need more information than this by including at the end of the streamlined PIS ways the participants could access more information. Even if a streamlined PIS does encourage potential participants to read the basic information, the results of the Information Provision study suggest that there will be some participants that still choose not to read it. If there is mandatory information for potential participants to know before taking part, then other ways to impart this information also need to be considered.

Previous research has shown that extended discussion with research staff is likely to improve understanding^{73;91-94}. In research, potential participants are not only provided with information in a PIS but also have a consent interview with a member of the research team. This interview gives the opportunity for researchers to check that potential participants understand the information they have been given, and to ask if there is more the potential participant wants to know. If there is mandatory information that potential participants should know before making a participation decision, providing it orally at this interview and checking understanding allows researchers to ensure the information has been given. Simply providing the information as a PIS is not sufficient, since the Information Provision study suggested that a significant proportion of potential participants may not be reading it.

Ensuring participants understand the information is difficult since there is a difference between participants being able to recall the information provided and understanding it sufficiently to use it to make a decision, and measuring actual understanding is not easy (Section 2.3). Ensuring participants have understood the information at the consent interview means more than simply reading the PIS to participants and a standard method to encourage understanding needs to be developed. In order to do this, the person gaining consent must check the level of understanding throughout the consent interview. If mandatory information was provided verbally, it is advocated that the interview scripts of consent interviews be reviewed by REC's, in a similar way to PIS. This would standardise the verbal information to ensure that mandatory information was both imparted and provided in an easily accessible way. Developing scripts through input with patient representatives may improve the accessibility of the information provided.

In addition to the review process, the information provided at the consent interview could be further standardised by providing additional training to consent receivers to ensure that consent is given in accordance with the study protocol. This additional training may have logistical issues and cost implications for research studies, however, particularly if there are a number of sites.

Key points

Since potential participants often do not read the PIS, mandatory information should be reinforced verbally.

Interview scripts of consent interviews should be reviewed by REC's and additional training provided to consent takers, to standardise verbal information provision and ensure consent is taken in accordance with the study protocol.

7.7 IS AN IIS A SOLUTION TO INFORMING THE MINORITY?

Researchers have a legal and moral obligation to ensure that valid consent is obtained from participants, and this means ensuring that participants understand what they have consented to. Given that this PhD has shown the majority of participants did not want to know very much information about the parent study, a streamlined PIS with information that participants both want and ought to know, such as the one presented in Section 6.12, may be one way to provide the majority of participants with enough information to make a participation decision and give their valid consent. If further research showed that these streamlined PISs were also not read, then the previous section has suggested that the consent interview may be an alternative way to impart key knowledge and check understanding. These recommendations would likely satisfy the majority of participants that did not want to know very much information.

The results reported above suggested that there was a minority of participants for whom this minimal level of information would not be sufficient to meet their informational requirements, even in low risk research such as the parent study in this thesis. These are the participants who accessed the higher levels of information and more than is included in the traditional paper PIS. In addition to this, the NRES expert panel suggested that lengthy PIS provide legal protection for researchers by providing full information and allow participants to refer back to information at a later

date. An IIS may meet both of these concerns since it allows a substantial amount of detailed information to be easily accessed by participants.

If an IIS was provided to inform potential participants in future studies, it could be designed to display the level one information rather than requiring users to select the information they wish to access from a list of FAQs. This would produce an electronic version of the streamlined PIS, but as a hybrid of the IIS since users would have the option to access more information on each topic if required.

Providing an IIS will not be feasible in all studies because not all potential participants will have access to the Internet. If an IIS could not be used, then lengthy paper PIS could be provided to participants for reference purposes. As suggested previously, a streamlined PIS could then be included as a cover page to this lengthier PIS as a summary of the information included. This would provide potential participants with a summary of information sufficient to inform the majority, whilst providing access to lengthier information to satisfy those participants who require more information. Given that there are likely to be a range of informational needs across all study participants, however, providing only a streamlined and current standard length PIS is not likely to satisfy those that want to know detailed information on only some study aspects. The IIS allows participants to easily choose the topics of information where they require more detail, rather than a lengthy paper PIS that requires participants to sift through detailed information for all topics. The IIS provides a

tailored approach to information provision in general that may satisfy the individual specific needs of participants.

As a final thought, the results of this study and the discussion above provided an ethical issue for future electronic research that is conducted remotely with no face-to-face contact between potential participants and researchers²⁶². As these types of e-trials become more popular, the results of the IIS study show there to be a certainty that many participants read little, if any, of the information provided to them and, therefore, would not be informed to give their valid consent in the way that UK GCP Guidelines currently require²². Further research is needed in this area, to ensure that e-trial participants do give their consent in such a way that meets requirements.

Key points

A minority of potential participants are likely to want more than the mandatory information. Their needs may be met by providing an IIS, since this allows a substantial amount of detailed information to be easily accessed by participants. Where an IIS is not feasible, a lengthy paper PIS could be provided in addition to mandatory information.

7.8 FUTURE OF INFORMATION PROVISION IN RESEARCH

This thesis has shown that electronic communication does have a place in the future of research and could be a mainstream form of communication if the right safeguards are in place. This final section of the chapter provides suggestions for future provision of information in research.

Other communication technologies

There are many other technologies available now that could be used to communicate electronically with research participants. These include text messaging²⁶³⁻²⁶⁶, mobile phone software called applications (apps)^{213;214;267-274} and interactive buttons on the TV²⁷⁵⁻²⁷⁷, which could all be used to invite potential participants to research studies or communicate with them throughout studies. Mobile phone apps are the most likely of these to be suitable for research and mobile phone technologies are already becoming widely used in the healthcare and research setting^{213;214;267-274}. Mobile phone apps have great scope for inclusion in research and could have multiple uses. Participants could, for example, download study software (an app) that alerted them when it was time to complete a study questionnaire, the questionnaire is completed using the app and sent straight to the researchers. In fact, all aspects of e-trials could be incorporated into a mobile phone app that the participant keeps with them all the time and so communication is not limited to when the participant is sat at the computer screen²⁷⁸.

The Internet and electronic recruitment at the moment is best suited to questionnaire-based studies because of the functionalities that can be added to online questionnaires, for example, automatic collating of information^{112;128;129}. In the future there may be scope for e-trials to use electronic consent forms when electronic signatures become more widely used and accepted¹²⁴⁻¹²⁶, and consent interviews could be conducted remotely via Skype type video conferencing^{279;280}. This could minimise disruption to potential participants who could do the meetings from their office or home and so may improve recruitment to trials. There may, however, be some confidentiality issues if the conversation could be overheard. The future use of the Internet in research could reduce costs and improve the effectiveness of them greatly^{112;118;128;129;135;136}, but requires further advancement of the technology.

Future of the IIS

This research has shown that the IIS may have a place in research, either as a first line method to provide information to potential research participants, or as a way for participants who want more than a minimum amount of information to access more information about a study. Now a web-based template has been written for the IIS, it would be easily adaptable to other studies. It could be set up in a user friendly manner that allows researchers to use it to input the information for their study. Instead of having to deal with code, administration pages could be set up that allow researchers to easily add their own information and logos.

Further to this, a central website could be set up where researchers can add their study specific information and participants can access it by logging in with a username and/or password unique to that study. If the website was managed centrally it would also include admin pages that mean researchers would not have to learn code to use web-based information sheets. These could be used in addition to short paper PIS and the minority of participants that wanted to know more information could access the IIS online. There are a lot of steps involved in hosting a website¹¹², and so a central user friendly website may promote online information and the use of an IIS because researchers would not have to work out the logistics of posting information online.

Other populations

The other point to consider in the future of the IIS is conducting similar studies to the one done for this PhD in other populations. It could be used with younger people to see if results were similar and to see if it was more acceptable with that cohort. It could be tested in a higher risk study to see if potential participant's informational requirements are different for studies of different risk. It may be that participants want to know more information when the risk is higher. There may be ethical implications of trying to conduct this research in higher risk trials if researchers knew that participants had not accessed any study information before agreeing to participate, since the risks of taking part are considered to be greater. In high risk research, particularly early phase cancer trials, there is often more of an emphasis on discussion of trials with patients than in low risk primary care research^{281;282}. This

may mean that high risk research is actually a safe environment in which to place further work because the verbal information may be more comprehensive than in low risk studies. The NRES expert panel noted that a lengthy PIS is required as a legal 'living document' that protects researchers and allows participants to refer back to information at a later date. The panel were happy for the work to be continued in a higher risk setting, providing that the standard lengthy PIS was provided at the time consent was received.

A discussion with the NRES expert panel about taking the research forward into riskier clinical trials was led by Professor Heather Draper. Prior to the meeting she, Dr Melanie Calvert and Dr Sarah Damery circulated a report to the panel that identified how clinical trials may entail greater risk for participants:

“The intervention itself may be riskier in terms of known or potential side-effects (such as in clinical trials of pharmacological interventions)

Different levels or types of risks for participants may be associated with different phase clinical trials (from those designed to determine treatment safety, through trials to assess treatment efficacy or the broader effectiveness of an intervention)

The trial may be conducted in a clinical area where the risks are greater due to the condition of interest itself being more serious, regardless of the study arm to which a participant may be allocated

The trial design may be complex (e.g. adaptive or cross-over designs), and/or comprise a multi-factorial intervention, so there may be a risk that participants will not understand the complexities of participation

The research may take place over a long period of time and there may be a risk that the participants may not remember what they have been told about it

There may be little time for a considered decision to be made (e.g. for trials being undertaken in an emergency medicine setting)”

Future work would be required in all of these different higher risk areas, in order to determine what information potential participants want when taking part in studies considered higher risk than that conducted for this PhD.

If a study in the higher risk population was not feasible, it could be conducted for a ‘sham’ study instead²⁸³. Healthy participants could be invited to take part in a high risk study, such as phase I clinical trial, and asked to read the information available before they consented to take part. They could then be asked online whether or not

they would still like to take part in this study, and the information they accessed would have been recorded. They would not actually be taking part in a study, but they would think they were and so their information seeking behaviours are likely to be consistent with what they would do if asked to participate in a real high risk study. This would also raise ethical issues though, for example, deception of participants²⁸³.

There is much research required before we can be sure that participants are properly informed about research and it is an area currently neglected by researchers. This PhD has advanced our knowledge and provides an evidence base for future research.

8 CONCLUSION

The overall aim of this thesis was to gather further evidence on the topics and level of detail of information potential research participants access when deciding whether to participate in a piece of low risk interventional research, and to determine the feasibility of electronic information provision. In relation to this aim, four important research questions have been addressed: 1. What does the current evidence suggest potential participants want to know when they are deciding whether to participate in research? 2. Is electronic information provision in research feasible? 3. What information did potential participants access when they made a decision about whether to participate in a piece of low risk interventional research? 4. What are the implications for the future of information provision given answers to research questions 2 and 3?

The first chapter of this thesis considered the background information required to put these research questions into context. Consent is a pre-requisite for participation in research, and participants understanding the study they are giving their consent to participate in is required for valid consent to be given⁸⁻¹¹. Information provision in research is tightly controlled by regulatory codes and overseen by ethics committees and institutional review boards^{22;26;35}, but although international GCP guidance states that participants should be 'adequately' informed of a study before making a consent decision, it does not detail what 'adequately' informed means.

There is a concern that current PIS are not readable and consequently participants' understanding of the study is not sufficient⁵⁵⁻⁶³. Previous research has shown that

study understanding can be improved by providing less detailed information^{88;89}, rearranging the information in a PIS to be more user friendly^{79;81;86;87} and allowing participants to have extended discussions with researchers^{73;91-94}. A problem with ensuring that participants have achieved a suitable level of understanding is that understanding is difficult to measure; recall is often measured, but being able to recall the information is different to being able to understand it^{23;58}. Measurement strategies for understanding are tailored towards individual trials and no standardised method to measure understanding exists¹. A final problem with ensuring the understanding of participants is that participants think themselves to be well informed but when tested are considered by researchers to have low levels of understanding. This may be because the information researchers think participants need may differ from what participants think they need^{60;67-69}.

A systematic review (Chapter 3) was the first study conducted for this PhD. In answering the first research question, the systematic review found limited evidence to suggest what information potential participants want to know at the time they are deciding whether to participate in research. This may be because the research is difficult to conduct accurately, since results from the Information Provision study and that by Antoniou et al⁶ suggest that asking participants what information they used to make a decision is unlikely to produce accurate results.

In answering the second and third research questions, the Information Provision study gathered evidence on the feasibility of electronic information provision and the

information that potential participants access when making a decision of whether to participate in a piece of low risk interventional research. The Information Provision study used an IIS that allowed participants to choose both the types of information and level of detail they accessed and also recorded the information accessed by each participant. The study also compared electronic recruitment and information provision to paper versions and assessed participants understanding of the study and satisfaction with the information provided. The study found that electronic communication did not affect consent rate, and the highest consent rate was actually seen in the group that accessed no study information. The study was underpowered to detect this, however.

The study information that had been favourably reviewed by the REC was found to satisfy only 11.4% of participants, undersupply 9.1% and oversupply 79.5% of participants. Understanding was consistent across groups, including those accessing no information, and participants were generally happy with the level of information they received, regardless of the mode of information delivery. The final important result was that participants were unable to accurately recall what information they had accessed.

Problems were encountered when trying to contact participants electronically; incorrect email addresses were provided and email invitations were often not opened and participants had to be contacted by telephone to prompt them to open their emails. Participants receiving electronic information, however, were often more

satisfied with the information provided than those receiving paper information and those that provided an email address were likely to prefer electronic communication in future research. 99% of young people¹⁰¹ use the Internet but the mean age of the Information Provision study population was higher than the general population, at 57 years. This presents difficulties in recruiting and providing information purely electronically since only 40% of the population over the age of 65 currently use the Internet¹⁰¹. As the younger generation of today become the research participants of tomorrow, it is likely that electronic communication and information provision will become more feasible. Given that recruitment rate and understanding were not compromised and satisfaction may have been improved by electronic information provision, this study, together with the results of that by Antoniou et al, suggest that electronic communication and information provision may be feasible and further research is warranted, particularly in higher risk studies.

The observational component of the Information Provision study found that little information was accessed by participants - 59% booked a study appointment despite accessing no study PIS at all because they chose not to click the link to access it, and 40.9% of those randomised to IIS also chose not to access any information. Understanding, however, remained consistent across all study groups, including those accessing no study information.

In answering the fourth and final research question, the final part of this PhD aimed to discuss the implications for the future of information provision given the results of

the studies conducted. A streamlined PIS was produced for the parent study that combined the information that most participants using the IIS wanted to know before participating with the information required by the ICH⁷. This streamlined PIS and the results of the PhD were presented to the NRES expert panel to gather their opinions on the work and seek advice on how to take the research further. The panel were interested in the work conducted for this PhD and broadly supportive of taking it further.

Participants did not base their consent decision on the information in the PIS, since results showed that they did not access the information. If they did not use this information, they may have based their decision on common knowledge about research in general, they preferred verbal communication from researchers^{67;119;231-233}, or they did not want to know they information because they based their decision on an influence such as an altruistic desire to take part²³⁵⁻²³⁷, their trust in their health care professional²⁴⁰⁻²⁴⁴, or an influence completely unrelated to the study^{245;246}.

In order for participants to be informed about a study, researchers (and RECs) have to decide what information to impart to potential participants, and this may be considered paternalistic, although only of a weak form if potential participants are able to gather further information about the research by asking questions. This information may be required for the potential participant to make an autonomous an informed decision, and so this type of weak paternalism may be beneficial to the potential participant. In addition to this, in order to comply with statutory instruments

for GCP, potential participants must be provided with certain information. Although there is mandatory information that must be provided to potential participants of all studies, this could be relayed to potential participants in the form of a streamlined PIS and/or verbally at the consent interview.

The final consideration was how to ensure that participants do understand the mandatory information. This is likely to be a challenge given that the results of the information study suggest that potential participants may not read information provided in a PIS. One way to do this may be to develop the verbal consent interview for studies. Mandatory information could be provided verbally at the consent interview to ensure participants have been given it, and the person gaining consent could check their understanding as the information is imparted. In this case, the content of these consent interviews may need to be reviewed by REC's just as the PIS is currently, in order to standardise the information imparted. Placing the burden of information giving on the consent interview may necessitate additional staff training, and further research would be required into ways to check the understanding of potential participants.

In the Information Provision study there was a minority of participants whose informational requirements may not have been met by a streamlined PIS plus verbal information at a consent interview. The traditional PIS also functions as a reference document for participants and provides legal protection for researchers. For both these reasons, it may not be desirable to make a complete move to a streamlined

PIS reinforced by a verbal consent interview. In research where electronic communication is feasible, access to an IIS would allow participants to access further information. A hybrid version of the IIS could also be developed that displayed information from the streamlined PIS with the option to access more information for each topic. Where access to an IIS is not appropriate, the streamlined PIS could be included as a cover summary sheet to the traditional, lengthier PIS.

In order to improve information provision in low risk interventional research, a few suggestions are made in conclusion of this PhD. A streamlined PIS may be a useful adjunct to the traditional PIS and improve understanding. Given that the results of the information study suggest that the majority of potential research participants may not read the traditional PIS, any information important enough to be included in a streamlined PIS should be reinforced verbally at the consent interview. Given that this study showed that a high proportion of potential participants do not read the written information provided, providing information verbally at the consent interview may be central to ensuring valid consent in future research.

8.1 CONSIDERATIONS FOR FUTURE RESEARCH

The results and discussion in this thesis are important to the future of research, and identify concern with the current informed consent process. Much more research needs to be conducted in this area, and in this final part, I outline considerations for future research.

The rise of the Internet in medical research¹⁰⁷⁻¹¹⁹ means a move towards online PIS and a consideration of ways for participants to give consent that fit with the remote nature of e-Trials. Given that the results of this thesis have shown that a verbal consent interview may be central to ensuring valid consent is given, it is important that this is considered in future research. It may, for example, be possible to conduct virtual 'face-to-face' consent interviews to ensure that researchers engage participants and assess understanding. The consent process in e-Trials should, therefore, be a consideration for future research to ensure that participants are adequately informed.

If IIS, or more structured consent interviews are to be used in future research, these may come with higher costs. There may also be other technologies that could be used to communicate with research participants, including text messaging²⁶³⁻²⁶⁶, and mobile phone software applications (apps)^{213;214;267-274}. Research is needed to identify the value of other methods of information provision, and full economic evaluations of each process are required.

This thesis considers information provision in only one group of patients, in a low risk interventional study. All interventions come with different levels of risk, and participants may want more information when considering participation in a study perceived to be of higher risk. The research methodology developed in this thesis needs to be replicated in higher risk interventional studies to determine patterns of

information access across a range of study types. Information requirements may differ between different sub groups of the population, both in terms of demographic groups and disease areas. Further research should also, therefore, be conducted with different sub groups of participants.

9 APPENDICES

9.1 - KIRKBY HM, CALVERT M, DRAPER H, KEELEY T, WILSON S. WHAT POTENTIAL RESEARCH PARTICIPANTS WANT TO KNOW ABOUT RESEARCH: A SYSTEMATIC REVIEW. *BMJ OPEN* 2012.

Open Access

Research



What potential research participants want to know about research: a systematic review

Helen Michelle Kirkby,¹ Melanie Calvert,¹ Heather Draper,² Thomas Keeley,¹ Sue Wilson¹

To cite: Kirkby HM, Calvert M, Draper H, *et al*. What potential research participants want to know about research: a systematic review. *BMJ Open* 2012;**2**:e000509. doi:10.1136/bmjopen-2011-000509

► Prepublication history and an additional appendix for this paper are available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2011-000509>).

Received 15 December 2011
Accepted 3 April 2012

This final article is available for use under the terms of the Creative Commons Attribution Non-Commercial 2.0 Licence; see <http://bmjopen.bmj.com>

¹MRC Midlands Hub for Trials Methodology Research (HTMR), University of Birmingham, Edgbaston, Birmingham, UK
²Medicine, Ethics, Society and History, Primary Care Clinical Sciences, School of Health and Population Science, University of Birmingham, Edgbaston, Birmingham, UK

Correspondence to
Helen Michelle Kirkby;
hmk592@bham.ac.uk

ABSTRACT

Objective: To establish the empirical evidence base for the information that participants want to know about medical research and to assess how this relates to current guidance from the National Research Ethics Service (NRES).

Data sources: Medline, Web of Science, Applied Social Sciences Index and Abstracts, Sociological abstracts, Health Management Information Consortium, Cochrane Library, thesis index's, grey literature databases, reference and cited article lists, key journals, Google Scholar and correspondence with expert authors.

Study selection: Original research studies published between 1950 and October 2010 that asked potential participants to indicate how much or what types of information they wanted to be told about a research study or asked them to rate the importance of a specific piece of information were included.

Study appraisal and synthesis methods: Studies were appraised based on the generalisability of results to the UK potential research participant population. A metadata analysis using basic thematic analysis was used to split results from papers into themes based on the sections of information that NRES recommends should be included in a participant information sheet.

Results: 14 studies were included. Of the 20 pieces of information that NRES recommend should be included in patient information sheets for research pooled proportions could be calculated for seven themes. Results showed that potential participants wanted to be offered information about result dissemination (91% (95% CI 85% to 95%)), investigator conflicts of interest (48% (95% CI 27% to 69%)), the purpose of the study (76% (95% CI 27% to 100%)), voluntariness (39% (95% CI 2% to 100%)), how long the research would last (61% (95% CI 16% to 97%)), potential benefits (57% (95% CI 7% to 98%)) and confidentiality (44% (95% CI 10% to 82%)). The level of detail participants wanted to know was not explored comprehensively in the studies. There was no empirical evidence to support the level of information provision required by participants on the remaining seven items.

Conclusions: There is limited empirical evidence on what potential participants want to know about research. The existing empirical evidence suggests that individuals may have very different needs and

ARTICLE SUMMARY

Article focus

- What information do potential participants want to know when they are deciding whether to take part in research?
- What is the established empirical evidence base?
- How does the current empirical evidence base relate to current guidance from the NRES?

Key messages

- There is little empirical evidence of what information potential participants want to know about research when they are making the decision to take part.
- The limited empirical evidence available suggests that potential participants may have very different information needs.
- Further research is required to determine what potential participants really want to know about research and how this can be delivered in a way that takes into account their different informational needs.

Strengths and limitations of this study

- An extensive search strategy ensured that the review was systematic in capturing all available empirical evidence.
- Papers included in the review differed in their methodologies and presentation of results, making comparisons between papers extremely difficult.

a more tailored evidence-based approach may be necessary.

INTRODUCTION

Medical research is central to the advancement of treatments, services and technology.^{1–3} Potential participants have the right to choose whether they participate in medical research,^{4 5} and individuals must give their consent prior to participating in research. As part of this ongoing process,

potential participants must be provided with sufficient information to make a voluntary and informed decision.^{2 6–11} In research settings, study information is usually conveyed to potential participants in the form of a written participant information sheet (PIS), which is later reinforced by a verbal consent interview with a member of the research team.¹²

In the UK, the National Research Ethics Service (NRES) provides extensive guidance on how a PIS should be written and presented. The guidance suggests that a PIS should be split into two parts where part one provides a brief and clear explanation of the essential elements of the specific study and allows participants to make an initial choice of whether the study is of interest. Part two should then contain additional information on matters such as confidentiality, indemnity and publication intentions.

There is some concern that PIS have become increasingly lengthy over recent years.^{10 13 14} Complex studies, for example, where the potential participant might, for example, on the basis of test results be invited to participate in a further phase of the study, often use detailed and lengthy PISs. This can lead to poor understanding by participants^{15–17} and a corresponding concern that consent criteria are not always met. The NRES guidance is not explicit in the level of detail to be included in a PIS, and there is disagreement among experts about how much information to include.¹⁸ If PISs become so complex that only the most confident and educated participants are able to digest all the information, this may result in selection bias meaning that research is less generalisable.¹⁹ Furthermore, there is a risk that healthcare researchers are becoming increasingly paternalistic in their information provision without recognising individual participant needs. In order to help address the problem of how much information to include in PIS, we conducted a systematic review that aimed to establish the empirical evidence base for the information that potential participants want to know when they are deciding about participation.

METHODS

Selection criteria and literature search

This systematic review included all studies that asked participants to indicate how much or what type of information they wanted to be told about a research study or asked them to rate the importance of a specific piece of information. We included studies published between 1950 and 27 October 2010 with no limit to language or participant group. We only included studies of participant opinion and excluded studies of healthcare professional or other expert opinion.

We combined Mesh terms Patient, Research Subjects, Consent forms, Informed Consent and Research ethics with terms relating to information provision (online appendix 1). We conducted searches in Medline, Web of Science, Applied Social Sciences Index and Abstracts, Sociological abstracts, Health Management Information

Consortium and the Cochrane Library electronic databases. We also searched thesis index's, grey Literature databases, reference and cited article lists, key journals and Google Scholar and we asked expert authors to identify relevant studies.

We did not conduct a formal quality assessment of included literature because there were both quantitative and qualitative studies, widely varied study methods and different types of results that were often not comparable between papers. Instead, we conducted a critical appraisal of each paper using five quality indicators (response rate, sample size, demographics, participant characteristics and strengths and limitations of study methods). The strengths and limitations of each study are presented in table 1.

Data extraction and synthesis

One researcher (HMK) extracted data from papers using a pre-defined data extraction sheet and a second researcher (TK) checked it for accuracy with disagreements resolved by discussion between these two authors (table 1). A metadata analysis using basic thematic analysis was used to analyse the data from the 14 papers. Themes were based on the sections of information that NRES recommends should be included in a PIS (table 2).¹⁰ Each paper was assessed to identify any further themes relating to what information research participants may want to know. A metadata analysis coded individual results based on their relevance to each theme and then themes were collated to report overall results. For themes where more than one quantitative study reported a proportion of participants wanting to know the information, pooled proportions with random effects were calculated using StatsDirect statistical software (StatsDirect Ltd).

RESULTS

The search yielded 11943 unique references. We discarded 11291 after reviewing the title, 620 after reviewing the abstract and a further 18 after reviewing the full paper (figure 1). HMK conducted the citation screening and TK independently validated approximately 10% of the references identified from electronic databases (96.0% κ agreement rate). All 14 included studies were identified from searches of Medline and Applied Social Sciences Index and Abstracts. Expert authors identified 37 unique references; 13 were duplicates from the electronic searches and 24 did not meet the inclusion criteria.

Of the 14 studies included in the review, three specifically considered the return of research results to participants and six considered only investigator conflicts of interest. Five studies looked broadly at what information potential research participants wanted to know.

Of the 20 sections of information NRES suggest should be included in a PIS, there were seven categories where no empirical evidence was identified that

Table 1 Summary of studies included in the systematic review

Lead author/ country/ year	Inclusion/ exclusion/ criteria	Participant illness	Participant demographics	Total number of participants (response rate)	Study design	Sampling strategy	Analysis	Key themes explored	Study strengths	Study limitations
Walkup, ²⁰ USA, 2009	None provided	None	Gender: not reported Age: not reported Education/ deprivation: not reported Ethnicity: not reported	57 (not provided)	Exploration of conversation and questionnaire	Convenience	Descriptive summary statistics	Study purpose, voluntariness, study method, risks, benefits, and confidentiality and review board approval	Participants approached in a public setting, and invited to complete a questionnaire and researcher recorded study information spontaneously requested Did not specify a disease group	No inclusion/ exclusion criteria Participant demographics not reported
Bento, ²¹ Brazil, 2008	Female participants aged 18–49 years who had taken part in a clinical trial of women's health in the previous 12 months and lived in Metropolitan Campinas, Sao Paulo, Brazil	Women's health	Gender: only female Age: 18–49 Education/ deprivation: 4 focus groups 8th grade or less, 4 focus groups above 8th grade education Ethnicity: not reported	51 participants 8 focus groups (not provided)	Focus groups	Convenience	Framework analysis	Study methods, risks and benefits	Participants of different ages and educational level likely to have different needs and opinions regarding topic Focus groups homogeneous for age and educational level; suitable to ensure they were comfortable expressing opinions Recruitment continued until data saturation point	Demographics not representative of the general population as the study only included women and was limited to participants from a trial of a contraceptive intervention

Continued

Table 1 Continued

Lead author/ country/ year	Inclusion/ exclusion criteria	Participant illness	Participant demographics	Total number of participants (response rate)	Study design	Sampling strategy	Analysis	Key themes explored	Study strengths	Study limitations
Hutchinson, ⁷ Australia, 1996	Participants of clinical trials of COPD, asthma, diabetes, osteoporosis, rheumatoid arthritis and the influenza vaccine. Excluded if clinical trial for acute, life-threatening or debilitating conditions with inadequate therapy	Chronic illness	Gender: 52% male Age: median age 70 (range not reported) Education/ deprivation: range of backgrounds Ethnicity: not reported	259/324 (80%)	Questionnaire	Convenience	Descriptive summary statistics and multivariate logistic regression	Conflicts of interest (Col)/ organisation and funding of the research		Demographics not representative of the general population as median age 70
Gray, ²² USA, 2007	Participants enrolled onto a phase I research trial, spoke English and were medically and mentally capable of participating	Phase I research trial	Gender: 52% male Age: median age 61 (range 26–82) Education/ deprivation: range of backgrounds Ethnicity: 81% white	102/119 (86%)	Questionnaire	Consecutive participants enrolling onto parent trial	Descriptive summary statistics, χ^2 tests and multivariate logistic regression	Col/ organisation and funding of the research	Same interviewer conducted all interviews	Demographics not representative of the general population as the median age was 61 and was limited to cancer patients participating in an early phase clinical trial

Continued

Table 1 Continued

Lead author/country/year	Inclusion/exclusion criteria	Participant illness	Participant demographics	Total number of participants (response rate)	Study design	Sampling strategy	Analysis	Key themes explored	Study strengths	Study limitations
Fernandez, ²³ Canada, 2007	English-speaking adolescent with cancer or parents of children with cancer. Excluded acutely unwell or recently relapsed	Cancer	Gender: adolescents not reported Parents mostly women (23/30; 77%) Age: adolescents median age 16 (range 13–20) Parents median age 40.9 (range 28–53) Education/ deprivation: adolescents predominantly in education (no figures reported) Parents 50% with post secondary education Ethnicity: 80% Caucasian Parents 100% Caucasian	40/43—10 adolescent, 30 parent participants (93%)	Questionnaire	Random	Descriptive summary statistics and χ^2 tests	Return of study results		Demographics not representative of general population as participants were well educated, mostly Caucasian and limited to adolescents with cancer/parents of children with cancer

Continued

Table 1 Continued

Lead author/ country/ year	Inclusion/ exclusion criteria	Participant illness	Participant demographics	Total number of participants (response rate)	Study design	Sampling strategy	Analysis	Key themes explored	Study strengths	Study limitations
Bento, ³³ USA, 2006	Participants of HIV, hepatitis, arthritis and surgical oncology trials who were >18 years and English speaking	Various	Gender: 61% male Age: not reported Education/ deprivation: range of backgrounds Ethnicity: 70% white	33 (not provided)	Face-to-face semi-structured interviews	Convenience	Transcripts coded and themes and major concepts identified	Col/ organisation and funding of the research	Open questions used during interviews Data collection continued to saturation point Two authors independently conducted analysis	Used hypothetical scenario Demographics not representative of general population as participants were more often men and limited to adults participating in HIV, hepatitis, arthritis or surgical oncology trials
Hampson, ²⁴ USA, 2006	Participants with cancer and enrolled in a clinical trial who were English speaking and >18 years	Cancer	Gender: 56% male Age: 24%, <50; 32%, 50–59; 26%, 60–69; 16%, >70 Education/ deprivation: well educated and financially secure Ethnicity: 92% white	252/272 (93%)	Structured face-to-face interviews	Not provided	Descriptive summary statistics and Fishers exact test/Kruskal–Wallis test	Col/ organisation and funding of the research	Validated interview questions	Demographics not representative of general population as the study population were well educated, financially secure and limited to adult participants of a clinical trial

Continued

Table 1 Continued

Lead author/ country/ year	Inclusion/ exclusion/ criteria	Participant illness	Participant demographics	Total number of participants (response rate)	Study design	Sampling strategy	Analysis	Key themes explored	Study strengths	Study limitations
Weinfurt, ²⁵ USA, 2006	Healthy adults or those with a mild chronic illness. Excluded if they had participated in another focus group within the previous 6 months or were working or had worked for an organisation involved in the conduct of clinical trials	Healthy	Gender: 42% male Age: 12%, 18–29; 51%, 30–49; 37%, >50 Education/ deprivation: well educated and financially secure Ethnicity: 56% white	16 focus groups (not provided)	Focus groups	Convenience	Initial content codes based on transcripts developed that were summarised and reviewed to identify main themes	COI/ organisation and funding of the research	Participants not limited to disease group	Only one moderator conducted focus groups Non-verbal communication not recorded Demographics not representative of general population as the study population were well educated, financially secure and the majority had previously shown interest in research
Partridge, ²⁶ USA, 2005	All participants of the parent trial (chemotherapy trial)	Cancer	Gender: only female Age: mean age 55 (range not reported) Education/ deprivation: range of backgrounds Ethnicity: 96% white	94/135 (69.6%)	Questionnaire	Convenience	Simple descriptive statistics	Return of study results	Participants that wanted to know study results Demographics not representative of general population as the study population were mostly Caucasian, only included females and was limited to participants of a breast cancer trial	Participants that wanted to know study results Demographics not representative of general population as the study population were mostly Caucasian, only included females and was limited to participants of a breast cancer trial

Continued

Table 1 Continued

Lead author/country/year	Inclusion/exclusion criteria	Participant illness	Participant demographics	Total number of participants (response rate)	Study design	Sampling strategy	Analysis	Key themes explored	Study strengths	Study limitations
Kim, ²⁷ USA, 2004	Potential research participants >18 years, diagnosed with heart disease, breast cancer or depression and listed on the Harris Interactive Chronic Illness Database	Various	Gender: 50% male Age: 4% 18–29, 16% 30–44, 61% 45–64, 19% 65+ Education/ deprivation: range of backgrounds Ethnicity: 92% white	5478/20205 (27%)	Online questionnaire	Random	Two-way ANOVA modified for ordinal data and multinomial logistic regression	Coll/ organisation and funding of the research	Validated questionnaire Participants chosen at random but from the subset of those registered on the Harris Interactive Chronic Illness Database	Demographics not representative of general population as it was limited to internet users
Partridge, ²⁸ USA, 2003	Any participant enrolled into the parent study (chemotherapy trial)	Breast cancer	Gender: not reported Age: median age 54 (range 29–82) Education/ deprivation: range of backgrounds Ethnicity: 84% white	51/55 (93%)	Questionnaire	Convenience	Simple descriptive statistics	Return of study results	Multicentre	Unvalidated questionnaire Demographics not representative of general population as the study was limited to participants of a breast cancer trial. Gender was not presented but expect most were women given disease area
Casarett, ²⁹ USA, 2001	Participants with a current telephone number, enrolled at a pain clinic, who had chronic non-malignant pain, were taking scheduled opioids and had experienced the pain for at least 6 months	Chronic pain	Gender: 40% male Age: mean age 47 (range 30–86) Education/ deprivation: range of backgrounds Ethnicity: 85% white	40/86 (46.5%)	Semi-structured telephone interviews	Convenience	Descriptive summary statistics and bivariate analysis with non-parametric tests	Voluntariness, study methods, expenses, risks and the drug/device/ procedure being tested	Validated interview topic guide Questions spontaneously asked by participants were recorded	Demographics not representative of general population as more often men and limited to chronic pain patients

Continued

Table 1 Continued

Lead author/country/year	Inclusion/exclusion criteria	Participant illness	Participant demographics	Total number of participants (response rate)	Study design	Sampling strategy	Analysis	Key themes explored	Study strengths	Study limitations
Maslin, ³⁰ UK, 1994	Attending a breast unit and were patients with a breast cancer diagnosis or asymptomatic women with a family history of breast cancer	Cancer	Gender: only female Age: median 47 (range 24–81) Education/ deprivation: not reported Ethnicity: not reported	213/300 (71%)	Postal questionnaire	Random	Simple descriptive statistics	Study purpose, voluntariness, study methods, risks, benefits and confidentiality	Participants chosen at random but from a subset of those attending a breast unit	Demographics not representative of general population as the study only included women and was limited to those with breast cancer
Sand, ³¹ Norway, 2008	Participants eligible for the parent study (all lung cancer patients)	Cancer	Gender: 57% male Age: median 69 (range 44–84) Education/ deprivation: range of backgrounds Ethnicity: not reported	21/33 (64%)	Semi-structured interviews	Convenience	Identification and categorisation of themes and alternatives analysis based on deductive and inductive categories	Voluntariness, study methods and treatment alternatives	No inclusion/exclusion criteria stated but 11 potential participants were not invited Technical problems with 3 recordings Demographics not representative of the general population as participants were more often men, had a median age of 69 years and were limited to lung cancer patients	

What potential participants want to know about research

Table 2 Empirical evidence linked to NRES participant information sheet recommended headings

NRES Heading	What does NRES say should be included?	Number of studies	Empirical evidence for inclusion in PIS from literature
What is the purpose of the study?	Purpose is an important consideration for subjects and should be included	2 ²³ 3 ²	Pooled results showed that 76% (95% CI 27% to 100%) participants wanted to know about study purpose
Why have I been invited?	Why and how participants have been chosen and how many will be in the study	0	No empirical evidence
Do I have to take part?/What will happen if I don't want to carry on with the study?	The voluntary nature of the research should be included	4 ²¹⁻²³ 3 ²	Pooled results from the 3 quantitative studies ^{20 29 30} showed that 39% (95% CI 2% to 100%) participants wanted to know about voluntariness The one qualitative study reported that it was the most important piece of information to be included in a participant information sheet ²¹
What will happen to me if I take part?/What will I have to do?	How long the participant will be involved in the research/ how long the research will last	3 ²¹ 2 ³ 3 ²	Pooled results from all three studies ^{20 29 30} showed that 61% (95% CI 16% to 97%) participants wanted to know how long the research would last
	How often they need to attend a clinic	1 ²¹	68% (27/40; 95% CI 53% to 82%) wanted to know the frequency of additional study visits ²⁹
	How long visits will be Exactly what will happen to them	0 2 ²¹ 2 ²	No empirical evidence Specific information types varied considerably between studies, so no meaningful pooled results could be calculated The proportion of people wanting to know what would happen to them ranged from 9.5% (2/21; 95% CI 0% to 22.1%) ³¹ to 20% (8/40; 95% CI 7.6% to 32.4%) ²⁹ depending on what the specific information was. For example, 20% (8/40; 95% CI 7.6% to 32.4%) wanted to know about burdens to friends or family caused by study participation, ²⁹ 12% (5/40; 95% CI 2.3% to 22.8%) wanted to know how much work they would miss because of study participation, ²⁹ 10% (4/40; 95% CI 0.7% to 19.3%) wanted to know how much time would be spent waiting in clinic during study visits ²⁹ and 9.5% (2/21; 95% CI -3% to 22.1%) wanted to know practical information about trial procedures ³¹
Expenses and payments	Expense claims available and if there is any kind of payment for participation	1 ²¹	25% (10/40; 95% CI 11.6% to 38.4%) wanted to know if free medication would be available during or after trial ²⁹
What is the drug, device or procedure that is being tested?	Short description of the drug, device or procedure and given the stage of development state the dosage of the drug and method of administration, and details of any contraindicated drugs included over the counter drugs	2 ²¹ 3 ¹	The one quantitative study ²⁹ showed that specific questions about the medication regime ranged from 25% (10/40; 95% CI 11.5% to 38.4%) that wanted to know what control they had over medication dose during the study to 70% (28/40; 95% CI 55.8% to 84.2%) that wanted to know the frequency with which study medication must be taken. ²⁹ The study also showed that 62% (25/40; 95% CI 47.5% to 77.5%) wanted results of previous studies of safety and 45% (18/40; 95% CI 29.5% to 60.4%) of efficacy, and 15% (6/40; 95% CI 3.9% to 26.1%) wanted to know if study medication had been approved for clinical use ²⁹ The one qualitative study showed that participants wanted to know how to use the intervention ²¹

Continued

Table 2 Continued

NRES Heading	What does NRES say should be included?	Number of studies	Empirical evidence for inclusion in PIS from literature
What are the alternatives for diagnosis or treatment?	What other managements/ treatments are available and a list of all important comparative risks and benefit	1 ²²	5% (1/21; 95% CI 0% to 13.9%) wanted as much information about treatment alternatives as they received about the study medication ³¹
What are the possible disadvantages and risks of taking part?/What are the side effects of any treatment received when taking part?	Any risks, discomforts or inconvenience should be outlined	4 ^{16 23 31 32}	Specific information types varied considerably between studies so no meaningful pooled results could be calculated. Results ranged from no participants that asked about study risks (0/57) ²⁰ to 97% (207/213; 95% CI 95% to 99.4%) who wanted to be informed about any possible emotional or physical discomforts and side effects ³⁰
Radiation and the Ionising Radiation Regulations	If the use of additional ionising radiation is required as part of the study, then information must be given to the participant on the radiation involved	0	No empirical evidence
Harm to the unborn child: therapeutic studies	Clear warnings must be given where there could be harm to an unborn child, if there was a risk in breast feeding or if taking the medication is likely to cause fertility problems	0	No empirical evidence
What are the possible benefits of taking part?	Benefits should be included, but where there is no intended clinical benefit it should be stated clearly	3 ^{23 31 32}	Pooled results of the two quantitative studies ^{20 30} suggest that 57% (95% CI 7% to 98%) wanted to know about study benefits Two studies provided relevant data relating to specific benefits. ^{29 31} Specific requests ranged from 14% (3/21; 95% CI -0.7% to 29.3%) that wanted to know about hopes for better treatment ³¹ to 55% (22/40; 95% CI 39.5% to 70.4%) that wanted an opportunity to learn about condition or medication under study. ²⁹ Specific information types varied considerably between studies so no meaningful pooled results could be calculated
What happens when the research study stops?	Arrangements for after the trial finishes must be given, and it must be clear if participants will have continued access to any benefits or intervention they may have obtained during the research. If treatment will not be available after the study, it should be explained what treatment will be available instead	1 ²¹	55% (22/40; 95% CI 39.6% to 70.4%) wanted to know about the availability of medication after the study was over ²⁹
What if there is a problem?	How complaints will be handled and what redress may be available	0	No empirical evidence
Will my taking part in the study be kept confidential?	How data will be collected, stored, what it will be used for, who will have access to it, how long it will be retained for and how it will be disposed of	2 ^{23 32}	Pooled results showed that 44% (95% CI 10% to 82%) participants wanted to be given information about confidentiality and the protection of their privacy

Continued

What potential participants want to know about research

Table 2 Continued

NRES Heading	What does NRES say should be included?	Number of studies	Empirical evidence for inclusion in PIS from literature
Involvement of the GP/family doctor	If the participants GP needs to be notified of involvement or asked for consent	0	No empirical evidence
What will happen to any samples I give?	Clear description of whether new samples will be taken, if excess samples will be taken, and if access to existing stored samples will be required. The same type of information as for data is required to be provided	0	No empirical evidence
Will any genetic tests be done?	A separate consent form for genetic studies should be used	0	No empirical evidence
What will happen to the results of the research study?	What will happen to the results of the research, if it is intended to be published and how results will be made available to participants and that they will not be identified in any publication	3 ²⁸ 30 33	Pooled results showed that 91% (95% CI 85% to 95%) wanted to know about study results Specific information types varied considerably between studies, so no meaningful pooled results could be calculated. Two studies provided relevant data relating to specific aspects of what they wanted to know about results. ^{23 28} 78% (31/40; 95% CI 64.6% to 90.4%) of participants wanted a description of what researchers had learnt that was important, ²³ 35% (14/40; 95% CI 20.2% to 49.8%) wanted it to include follow-up contacts for the researcher ²³ and 98% (29/40; 95% CI 58.7% to 86.3%) wanted a list of medical publications written as a results of the research. ²³ 90% (46/51; 95% CI 82% to 98.4%) wanted their family or loved ones to be informed of the results if they were unable to learn them. ²⁸

Continued

Table 2 Continued

NRES Heading	What does NRES say should be included?	Number of studies	Empirical evidence for inclusion in PIS from literature
Who is organising and funding the research?	The organisation or company sponsoring the research and funding the research if these are different and if the researcher conducting the research is being paid	6 ²⁰ 24–27 34	<p>Pooled results from the four quantitative studies showed that 48% (95% CI 27% to 69%) wanted to know about any type of Col, but there was general disagreement over whether patients wanted to be told about financial Col</p> <p>Three studies provided relevant data relating to what participants wanted to know about specific aspects of Col.^{24 27 34} When financial Col were broken down into subcategories, 82.5% (4519/5478; 95% CI 81.48% to 83.5%) wanted to be told about commercial funding,²⁷ 69% (3779/5478; 95% CI 67.8% to 70.2%) about personal income,²⁷ between 41% (105/259; 95% CI 34.6% to 46.5%) and 82% (4492/5478; 95% CI 81% to 83%) about patents and stocks and shares^{27 34} and 40% (101/253; 95% CI 34% to 46%) thought researchers should have told participants only about the oversight system²⁴</p> <p>One study reported that participants wanted to know specifically how money was spent, with proportions ranging from 25% (65/259; 95% CI 19.8% to 30.4%) that wanted to know how much of the funding was spent on administration³⁴ to 38% (98/259; 95% CI 31.9% to 43.8%) that wanted to know how spare accrued funds were used at study completion²⁴</p> <p>One qualitative study reported that participants wanted to know the name of the sponsor²⁷ and one quantitative study reported that 57% (148/259; 95% CI 51.1% to 63.2%)³⁴ wanted to know the name of the funder</p> <p>Some participants wanted help understanding the potential consequences of Col, some did not²⁵</p> <p>Specific information types varied considerably between studies so no meaningful pooled results could not be calculated</p>
Who has reviewed the study?	Explain the role of the research ethics committees and which committee reviewed the current study	1 ²³	No participants asked about institutional review board approval (0/57) ²³

GP, general practitioner; NRES, National Research Ethics Service; PIS, participant information sheet.

suggested what information research participants wanted to know (table 2). No further themes, beyond the NRES categories, were identified. We were able to calculate pooled proportions for seven themes. Participants wanted to be told about dissemination of study results (91% (95% CI 85% to 95%)), investigator conflicts of interest (48% (95% CI 27% to 69%)), the purpose of the study (76% (95% CI 27% to 100%)), voluntariness (39% (95% CI 2% to 100%)), how long the research would last (61% (95% CI 16% to 97%)), benefits (57% (95% CI 7% to 98%)) and confidentiality (44% (95% CI 10% to 82%)). Although the majority of participants appeared to want information for most of these themes, some participants did not and the level of detail that participants wanted was not explored comprehensively.

DISCUSSION

Of the 14 papers that met inclusion criteria, five looked broadly at what information research participants

wanted to know. These studies focused on the category of information required rather than how much detail participants wanted. All 14 studies had substantial limitations to generalisability when applied to the wider research population because, for example, they focused on specific subsections of the population, for example, six studies included only cancer patients^{23 24 26 28 30 31} and only one study conducted in the UK.³⁰ A number of studies included only women^{21 26 28 30} and participants that were mostly Caucasian^{23 26} and well educated.^{23–25}

In the absence of empirical evidence to suggest what information potential research participants want, the NRES have based their guidance on expert opinion. It does, however, mean that current information provision for research may not adequately address the informational needs of the general population or 'hard to reach' groups such as socially deprived or African-American and minority ethnic groups. While the NRES recognise that one size does not fit all and that low-risk studies with

Conclusions

There is limited empirical evidence as to what information potential participants want to know at the time they are deciding whether or not to participate in research. Real-time studies need to be conducted to explore what information potential participants access when given a choice. This will enable us to determine exactly what information research participants want to know and could, in addition to other sources such as expert opinion, help tailor PIS towards specific population subgroups and enable appropriate high-quality information to be provided to meet individual needs.

Contributors HMK, MC, SW and HD conceived and designed the research. HMK and TK collected, validated and extracted the data. All authors made substantial contribution to the analysis and interpretation of the data. HMK drafted the manuscript and SW, HD, MC and TK revised it.

Funding The study was funded by the Medical Research Council Midland Hub for Trials Methodology Research (Medical Research Council Grant ID G0800808). The study sponsor had no role in study design, collection, analysis or interpretation of the data, in the writing of the report or in the decision to submit the article for publication. HMK and TK are PhD students funded by Medical Research Council Midland Hub for Trials Research Methodology and MC is Education Lead for the Medical Research Council Midland Hub for Trials Research Methodology.

Competing interests All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) HMK, MC, HD, TK and SW have support from the University of Birmingham for the submitted work; (2) HMK, MC, HD, TK and SW have no relationships with any companies that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners or children have no financial relationships that may be relevant to the submitted work and (4) HMK, MC, HD, TK and SW have no non-financial interests that may be relevant to the submitted work. HD is an author of one of the papers included discussion.³⁷ SW was also acknowledged in this paper for comments on an early draft.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement All authors had full access to all the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. Technical appendix and data set available from the corresponding author at hmk592@bham.ac.uk. Referenced Manager (Version 12) was used to analyse data. Stats Direct was used to calculate pooled proportions with random effects.

REFERENCES

1. The World Medical Association. *The World Medical Association Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects*. 2008. <http://www.ncbi.nlm.nih.gov/eproc/nd/bham.ac.uk/pmc/articles/PMC1816102/pdf/bmedj02559-0071.pdf>
2. General Medical Council. *Seeking Patients' Consent: The Ethical Considerations*. 1998. <http://www.opengrey.eu/item/display/10068/387679>
3. Joffe S, Cook EF, Cleary PD, et al. Quality of informed consent: a new measure of understanding among research subjects. *J Natl Cancer Inst* 2001;93:139–47.
4. NHS East of England. *NHS Values*. https://www.eoe.nhs.uk/nhs_constitution/values.php (accessed 27 Sep 2010).
5. NHS East of England. *Principles That Guide the NHS*. http://www.eoe.nhs.uk/nhs_constitution/principles.php (accessed 27 Sep 2010).
6. Manson N. Consent and informed consent. In: Ashcroft R, Dawson A, Draper H, et al, eds. *Principles of Health Care Ethics*. 2nd edn. Chichester: John Wiley & Sons Ltd, 2007:298–303.
7. Hewlett S. Consent to clinical research—adequately voluntary or substantially influenced? *J Med Ethics* 1996;22:232–7.
8. Idanpaan-Heikkilä JE. WHO guidelines for good clinical practice (GCP) for trials on pharmaceutical products: responsibilities of the investigator. *Ann Med* 1994;26:89–94.

9. Doyal L, Tobias J. *Informed Consent in Medical Research*. 1st edn. London: BMJ Books, 2001.
10. National Research Ethics Service. *Information Sheets and Consent Forms Guidance for Researchers and Reviewers*. 2009. <http://www.nrc.nhs.uk/research/researchers/documents/hpsa-guidance.pdf>
11. Wager E, Tolley PJ, Emanuel MB, et al. How to do it. Get patients' consent to enter clinical trials. *BMJ* 1995;311:734–7.
12. World Health Organisation. *Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products*. 1995. <http://www.nus.edu.sg/irb/Articles/WHO%20GCP%201995.pdf>
13. National Cancer Institute, US National Institutes of Health. *A Guide to Understanding Informed Consent*. <http://www.cancer.gov/clinicaltrials/conducting/informed-consent-guide/allpages> (accessed 5 Jun 2009).
14. Davis TC, Holcombe RF, Berkel HJ, et al. Informed consent for clinical trials: a comparative study of standard versus simplified forms. *J Natl Cancer Inst* 1998;90:668–74.
15. Fortun P, West J, Chalkey L, et al. Recall of informed consent information by healthy volunteers in clinical trials. *QJM* 2008;101:625–9.
16. Grossman SA, Plantadosi S, Covahey C. Are informed consent forms that describe clinical oncology research protocols readable by most patients and their families? *J Clin Oncol* 1994;12:2211–15.
17. Priestley K, Campbell C, Valentine C, et al. Are patient consent forms for research protocols easy to read? *BMJ* 1992;305:1263–54.
18. Lynoe N, Hoeyer K. Quantitative aspects of informed consent: considering the dose response curve when estimating quantity of information. *J Med Ethics* 2005;31:736–8.
19. Sharpe N. Clinical trials and the real world: selection bias and generalisability of trial results. *Cardiovasc Drugs Ther* 2002;16:75–7.
20. Walkup J, Bock E. What do prospective research participants want to know? What do they assume they know already? *J Empir Res Hum Res Ethics* 2009;4:59–63.
21. Bento SF, Hardy E, Osis MJ. Process for obtaining informed consent: women's opinions. *Dev World Bioeth* 2008;8:197–206.
22. Gray SW, Hlubocky FJ, Ratain MJ, et al. Attitudes toward research participation and investigator conflicts of interest among advanced cancer patients participating in early phase clinical trials. *J Clin Oncol* 2007;25:3488–94.
23. Fernandez CV, Santor D, Weijer C, et al. The return of research results to participants: pilot questionnaire of adolescents and parents of children with cancer. *Pediatr Blood Cancer* 2007;48:441–6.
24. Hampson LA, Agrawal M, Joffe S, et al. Patients' views on financial conflicts of interest in cancer research trials. *N Engl J Med* 2006;355:2330–7.
25. Weinfurt KP, Friedman JY, Allsbrook JS, et al. Views of potential research participants on financial conflicts of interest: barriers and opportunities for effective disclosure. *J Gen Intern Med* 2006;21:901–6.
26. Partridge AH, Wong JS, Knudsen K, et al. Offering participants results of a clinical trial: sharing results of a negative study. *Lancet* 2005;365:963–4.
27. Kim SY, Millard RW, Nisbet P, et al. Potential research participants' views regarding researcher and institutional financial conflicts of interest. *J Med Ethics* 2004;30:73–9.
28. Partridge AH, Burstein HJ, Gelman RS, et al. Do patients participating in clinical trials want to know study results? *J Natl Cancer Inst* 2003;95:491–2.
29. Casarett D, Karlawish J, Sankar P, et al. Obtaining informed consent for clinical pain research: patients' concerns and information needs. *Pain* 2001;92:71–9.
30. Maslin A. A survey of the opinions on 'informed consent' of women currently involved in clinical trials within a breast unit. *Eur J Cancer Care (Engl)* 1994;3:153–62.
31. Sand K, Loge JH, Berger O, et al. Lung cancer patients' perceptions of informed consent documents. *Patient Educ Couns* 2008;73:313–17.
32. Edgman-Levitan S, Cleary P. What information do consumers want and need? *Health Aff (Millwood)* 1996;15:42–56.
33. Grady C, Horstmann E, Sussman JS, et al. The limits of disclosure: what research subjects want to know about investigator financial interests. *J Law Med Ethics* 2000;34:592–9.
34. Hutchinson A, Rubinfeld AR. Financial disclosure and clinical research: what is important to participants? *Med J Aust* 2008;189:207–9.
35. Wyke S, Entwistle V, France E, et al. Information for choice: what people need, prefer and use. 2011. Report number 08/1710/153. http://www.netsoc.ac.uk/hsdr/files/project/SDO_ES_08-1710-153_V01.pdf
36. Manson NC. Why do patients want information if not to take part in decision making? *J Med Ethics* 2010;36:834–7.
37. Antoniou E, Draper H, Reed K, et al. An empirical study on the preferred size of the participant information sheet in research. *J Med Ethics* 2011;37:557–62.

Kirkby HM, Wilson S, Calvert M, Draper H. Using e-mail recruitment and an online questionnaire to establish effect size: A worked example. *BMC Research Methodology* 2011, 11:89.

RESEARCH ARTICLE

Open Access

Using e-mail recruitment and an online questionnaire to establish effect size: A worked example

Helen M Kirkby, Sue Wilson*, Melanie Calvert and Heather Draper

Abstract

Background: Sample size calculations require effect size estimations. Sometimes, effect size estimations and standard deviation may not be readily available, particularly if efficacy is unknown because the intervention is new or developing, or the trial targets a new population. In such cases, one way to estimate the effect size is to gather expert opinion. This paper reports the use of a simple strategy to gather expert opinion to estimate a suitable effect size to use in a sample size calculation.

Methods: Researchers involved in the design and analysis of clinical trials were identified at the University of Birmingham and via the MRC Hubs for Trials Methodology Research. An email invited them to participate. An online questionnaire was developed using the free online tool 'Survey Monkey[®]'. The questionnaire described an intervention, an electronic participant information sheet (e-PIS), which may increase recruitment rates to a trial. Respondents were asked how much they would need to see recruitment rates increased by, based on 90%, 70%, 50% and 30% baseline rates, (in a hypothetical study) before they would consider using an e-PIS in their research. Analyses comprised simple descriptive statistics.

Results: The invitation to participate was sent to 122 people; 7 responded to say they were not involved in trial design and could not complete the questionnaire, 64 attempted it, 26 failed to complete it. Thirty-eight people completed the questionnaire and were included in the analysis (response rate 33%; 38/115). Of those who completed the questionnaire 44.7% (17/38) were at the academic grade of research fellow 26.3% (10/38) senior research fellow, and 28.9% (11/38) professor. Dependent upon the baseline recruitment rates presented in the questionnaire, participants wanted recruitment rate to increase from 6.9% to 28.9% before they would consider using the intervention.

Conclusions: This paper has shown that in situations where effect size estimations cannot be collected from previous research, opinions from researchers and trialists can be quickly and easily collected by conducting a simple study using email recruitment and an online questionnaire. The results collected from the survey were successfully used in sample size calculations for a PhD research study protocol.

Background

Ideally, a study should be large enough to have a high probability (power) of detecting a statistically significant and clinically important difference [1] and sample size calculations are used to determine how large a study needs to be to achieve this [2-4]. For a simple sample size calculation to be made four values need to be

known; the variance in the outcome, the effect size of interest, the level of significance and the power of the test [2,3].

In many studies, an estimate of effect size and standard deviation of the measurement may not be readily available, particularly if efficacy is unknown because it is a new or developing intervention, or if the trial is in a new target population. In situations such as these effect size can be estimated by gathering expert opinion on the likely effect size or necessary effect size to impact on clinical practice [5].

* Correspondence: s.Wilson@bham.ac.uk
MRC Midlands Hub for Trials Methodology Research (HTMR), School of Health and Population Science, University of Birmingham, Edgbaston, B15 2TT, UK

Two potential advantages of using email rather than traditional mail to conduct questionnaires are lower costs [6,7] and quicker data collection [8], but a disadvantage of this method is a potentially lower response rate [7,9-11].

The aim of this study was to assess the feasibility of using a simple email recruitment strategy and online questionnaire to produce an estimated effect size based upon expert opinion to inform sample size estimation for a randomised controlled trial.

Methods

Electronic Participant Information Sheet (e-PIS) study

A randomized controlled trial (RCT) is being developed at the University of Birmingham that aims to determine if an e-PIS (as compared to traditional paper based Patient Information Sheets), can improve recruitment to a study. The e-PIS differs from the more usual paper-based Patient Information Sheets in that it is available electronically (Internet-based) and gives potential research participants control/choice over the level and degree of detail of the information they access. An e-PIS has not been evaluated before, so no estimate of effect size (recruitment to the trial) exists to inform sample size estimation.

If the e-PIS, once developed, is to be used by researchers, its effect on recruitment rate needs to be sufficient to justify its additional cost. The effect size estimation from this questionnaire study will be used to calculate the sample size i.e. the number of participants needed for the e-PIS study to detect a statistically significant difference in recruitment rates.

Development of the questionnaire

An online questionnaire was developed using the free online tool 'Survey Monkey' [12] that allows development of a questionnaire with up to 10 questions and 100 responses without cost, and is ideal for conducting short, quick questionnaires of a relatively small sample. The questionnaire (appendix 1), designed specifically for this trial, aimed to estimate an effect size for the e-PIS study. The questionnaire briefly described the hypothetical e-PIS trial and then gave respondents a scenario in which an e-PIS that aimed to increase recruitment rates had been developed that cost approximately £1,000 (based on an estimated cost of development provided by the Medical Education Technology Team at the University of Birmingham). Participants were asked by how much they would need to see recruitment rates increase before they would consider using an e-PIS in their research, based upon expected baseline recruitment rates without using an e-PIS being 90%, 80%, 70%, 50% and 30% respectively. The likely recruitment rate for the e-PIS study was unknown, so the baseline recruitment

rates aimed to cover a wide range of potential recruitment rates (30-90%).

Study Participants

If the provision of an e-PIS increases recruitment rates, the findings are likely to be of relevance to any researcher undertaking human research. For this questionnaire study, therefore, any academic involved in such research was eligible to participate. This questionnaire study used a convenience study sample and included researchers involved in the design and analysis of clinical trials at the University of Birmingham and from the MRC Hubs for Trials Methodology Research (HTMR) [13]. The HTMR include trialists based in seven regional hubs throughout the UK with expertise in trials methodology research, and expertise in a range of areas such as improving patient recruitment and retention into trials, assessing new trial designs, and testing different approaches to data analysis. Researchers were invited to participate in the study by email with a URL link to the survey.

Analysis

Analyses comprised simple descriptive statistics and were performed using Microsoft Excel Version 2007.

Results

The invitation was sent to 122 people; 7 responded to say they were not involved in trial design and could not complete the questionnaire, 64 attempted it, 26 failed to complete it. Thirty-eight people completed the questionnaire and were included in the analysis giving a response rate of 33% (38/115).

Of the 26 participants who failed to complete the questionnaire, all exited before answering the scenario question (see Appendix 1 - Questionnaire).

Of those who completed the questionnaire 44.7% (17/38) were research fellows, statisticians or lecturers, 26.3% (10/38) were senior research fellows, senior statisticians or senior lecturers, and 28.9% (11/38) were professors or MRC Hubs for Trials Methodology Regional Directors.

The results demonstrate that on average, respondents wanted an e-PIS to increase baseline recruitment rates by between 6.9% and 28.9% before they would consider using it in their own studies (Table 1). The increase in recruitment rates sought was in adverse proportion to the baseline recruitment rates offered in the questionnaire. For example, for a baseline recruitment rate of 90%, participants wanted the e-PIS to improve recruitment rates by an average of 6.9% before they would consider using it, whereas for a baseline recruitment rate of 30% the average improvement required was 28.9%.

Table 1 Results from the online questionnaire

Expected consent rate without using the e-PIS	90%	80%	70%	50%	30%
Mean percentage increase experts wanted	6.9	10.7	13.5	20.2	28.9
Standard deviation	3.19	5.61	24.05	8.53	18.13
Median percentage increase wanted	9	10	11	20	25
Inter quartile range	5	5	10	17.5	30
Range of responses seen	0-10	0-20	0-30	0-50	0-70

At all baseline recruitment rates a smaller effect size was required for implementation of the e-PIS by more senior grades of staff (as compared with research fellows) (Table 2).

Discussion

This study demonstrates that email recruitment and an online survey provide a rapid method to obtain a meaningful estimate of effect size and associated variability, which can be used to inform sample size calculations. Whilst the example in this paper shows how the methodology could be used to establish an effect size based on an increase in recruitment rates, it could be easily adapted to suit other studies. For example, for a study that tests the effectiveness of an intervention to increase vaccination rates it is reasonable to expect that the intervention would only be used outside of a research environment if it increased vaccination rates sufficiently. The questionnaire (appendix 1) could be adapted to ask participants how much the intervention would need to increase the vaccination rate by before they would implement the intervention in their area. The result would still be a meaningful effect size that could be used in a sample size calculation.

The results of the questionnaire demonstrate that for this scenario (increasing recruitment rates), even though the cost of the proposed e-PIS was relatively low, participants required a larger increase in recruitment rates when the baseline recruitment rate was low. This may

reflect researchers perceptions on acceptable response rates required for validity and generalisability.

As seen in other Internet based questionnaire studies [7,9-11], response rate was low (33%). The study sample, however, included academics at various stages of their career with relevant trials experience. Notably, over half of the participants were senior academics with extensive experience in trial design and analysis.

Twenty-six participants started but failed to complete the questionnaire, and since questionnaire responses were anonymous and no follow up of participants was conducted, reasons for non-completion could not be collected. It may be that once they started they realised they did not have experience required to provide answers, they did not understand the questions, or they became distracted and because it was online rather than a paper questionnaire on their desk, they forgot to go back to complete it. Participants also may have accidentally closed their browser before submitting the completed questionnaire meaning they would have lost their answers up to that point and did not want to complete it again. This is a further potential problem not encountered with paper questionnaires. If this questionnaire study were to be adapted for use in other studies it would be useful to collect feedback from participants.

Three grades of academics completed the questionnaire: research fellows, senior research fellows, and professors. Lower grades of academics tended to want the e-PIS to have a greater impact on consent rate before they would consider using it. For example, for a common baseline consent rate of 70%, only 8.3% of research fellows wanted to see an increase of below 5%, whereas 16.7% of academics above the level of senior research fellow would have accepted an increase of below 5%. At the other end of the scale, 25% of research fellows wanted to see an increase of above 20%, whereas no academics above senior research fellow level required an increase in recruitment rates above 20% in order for them to use an e-PIS. Whilst this small questionnaire study was not powered to evaluate between group

Table 2 Between group effect sizes (in %)

Baseline consent rate	Research fellow		Senior research fellow and above	
	Mean % (SD)	Median % (IQR)	Mean % (SD)	Median % (IQR)
90%	8.13 (2.59)	10 (5)	6.83 (3.46)	7.5 (5)
80%	12.5 (5.35)	10 (6.25)	9.85 (5.55)	10 (10)
70%	17.5 (8.12)	17.5 (11.25)	11.39 (5.57)	10 (4.375)
50%	28.08 (9.02)	25 (5)	13.45 (7.82)	10 (10)
30%	37.14 (16.95)	30 (15.08)	19.63 (13.50)	20 (20)

differences, these exploratory analyses show that different levels of academics may have different criteria for deciding whether or not to use an e-PIS in their research and therefore want different effect sizes.

Limitations

We utilised a convenience sample of participants with a broad range of research expertise, and this may have introduced bias. The observed variability in responses by different grades of academic staff illustrates the need, for future applications of this method of estimating effect sizes, to carefully consider the sampling frame and to use random sampling to improve the generalisability of results.

If the methodology described in this paper were to be used in other studies, a questionnaire specific to that study would need to be developed that took into account the study's estimated recruitment rate and related costs. This paper aimed to describe the methodology of using email recruitment and an online questionnaire to estimate effect size, and did not aim to produce a validated questionnaire for use in other studies.

Conclusions

This paper has shown that in situations where effect size estimations cannot be collected from previous research, opinions from researchers and trialists could be quickly and easily collected by conducting a simple study using email recruitment and an online questionnaire. The results collected from the survey were successfully used in sample size calculations for a PhD research study protocol. Nevertheless, this worked example was restricted to one research study and further evidence is required to determine the application of the methodology to other studies.

Appendix 1 - Questionnaire

Job Description

Job title

Role in research design

Which sector do you work in?

Scenario: Imagine that an Internet based electronic patient information sheet (e-PIS) has been shown to improve patient recruitment into a trial. There is a cost of around £1000 to develop and host e-PIS for each study. Thank you for taking the time to complete this questionnaire. Answers will be used to establish an effect size and carry out sample size calculations for a PhD project.

By how much would you need to see patient recruitment increase by before you would consider using e-PIS in your study?

1. If the expected patient recruitment using the standard paper patient information sheet is 90% of patients contacted?..... %
2. If the expected patient recruitment using the standard paper patient information sheet is 80%..... %

3. If the expected patient recruitment using the standard paper patient information sheet is 70%..... %
4. If the expected patient recruitment using the standard paper patient information sheet is 50%..... %
5. If the expected patient recruitment using the standard paper patient information sheet is 30%..... %

Thank you

That is the end of the questionnaire, thank you again for your time.

Acknowledgements

The authors would like to thank all those who participated in the research. HK is a PhD student funded by the Medical Research Council Midland Hub for Trials Methodology Research (Medical Research Council Grant ID G0800808).

Authors' contributions

HK conceived and designed the research, collected data, made substantial contribution to the analysis and interpretation of the data and drafted the manuscript.

MC, SW and HD helped to design the research, made substantial contribution to the analysis and interpretation of the data and revised the manuscript for important intellectual content. All authors have read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Received: 1 October 2010 Accepted: 9 June 2011 Published: 9 June 2011

References

1. Consort. Sample size: 2010 [http://www.consort-statement.org/consort-statement/3-12—methods/item7a_sample-size/], (last accessed 9-8-2010). Ref Type: Online Source.
2. Eng J: Sample size estimation: how many individuals should be studied? *Radiology* 2003, **227**:309-313.
3. Florey CD: Sample size for beginners. [Review] [9 refs]. *BMJ* 1993, **306**:1181-1184.
4. Torgerson DJ, Miles JN: Simple sample size calculation. *Journal of Evaluation in Clinical Practice* 2007, **13**:952-953.
5. Scales DC, Rubenfeld GD: Estimating sample size in critical care clinical trials. [Review] [38 refs]. *Journal of Critical Care* 2005, **20**:6-11.
6. Kiesler S, Sproull L: Response Effects in the Electronic Survey. *The Public Opinion Quarterly* 1986, **50**:402-413.
7. Sproull L: Using Electronic Mail for Data Collection in Organizational Research. *The Academy of Management Journal* 1986, **29**:159-169.
8. Watt J: Internet Systems for Evaluation Research. *New Directions for Evaluation* 1999, **84**:23-34.
9. Kongsved S, Basnov M, Holm-Christensen K, Hjøllund N: Response Rate and Completeness of Questionnaires: A Randomized Study of Internet Versus Paper-and-Pencil Versions. *J Med Internet Res* 2007, **9**:e25.
10. Cook C, Heath F, Thompson R: A Meta-Analysis of Response Rates in Web or Internet-Based Surveys. *Educational and Psychological Measurement* 2000, **60**:821.
11. Yun G, Trumbo C: Comparative Response to a Survey Executed by Post, E-Mail, and Web Form. *Journal of Computer-Mediated Communication* 2000, **6**:0.
12. Survey Monkey. 2010 [http://www.surveymonkey.com/], (last accessed 9-8-2010). Ref Type: Online Source.
13. MRC. MRC Network of Hubs for Trials Methodology Research: 2010 [http://www.methodologyhubs.mrc.ac.uk/], (last accessed 29-9-2010). Ref Type: Online Source.

Pre-publication history

The pre-publication history for this paper can be accessed here:
http://www.biomedcentral.com/1471-2288/11/89/prepub

doi:10.1186/1471-2288-11-89

Cite this article as: Kirkby et al.: Using e-mail recruitment and an online questionnaire to establish effect size: A worked example. *BMC Medical Research Methodology* 2011, **11**:89.

9.2 INFORMATION INCLUDED IN THE IIS

Welcome to the Blood Pressure Monitoring Study information website

You are being invited to take part in a research study about the different ways of measuring blood pressure. Before you decide if you are willing to get involved, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with your friends and relatives if you wish. Ask us if there is anything that is not clear or if you would like more information.

How to use this website

This study information website is an interactive website. This is a new way of providing information about a research study to patients. To the left of this page you will see a list of frequently asked questions (FAQ's) about medical research. You should click on as many of these as you want to before deciding whether or not you want to take part.

When you click on a FAQ you will be given a short response. If you want to know more, please click on the + button under that text.

Some pieces of information are coloured blue and underlined – these are called hyperlinks. If you click on one of these hyperlinks, it will take you to an external website which will give you even more information. An example of a hyperlink might look like this –

[Blood pressure](#) is likely to be lower when measured at home.

If you click on the hyperlink '[Blood pressure](#)' it would take you to an external website which would tell you more about blood pressure.

Please click on as many of the links as you like, and spend as long reading the information as you like before you decide whether or not you would like to take part in this blood pressure monitoring study.

When you have finished

To the right of each page you will see a box which says 'Finished?'. When you have finished reading all of the information you wish to read and have decided whether or not you want to take part in the study, please click this button.

[stats – Flesch Reading Ease score= 73.2; Flesch-Kincaid Grade Level Score 7.6]

What is the purpose of the study?

Level one

Blood pressure is likely to be lower when it is measured at home. This study is to see if blood pressure measurements are lower in all ethnic groups when taken at home.

[stats – Flesch Reading Ease score= 74.2; Flesch-Kincaid Grade Level Score 6.8]

Level two

Blood pressure can be measured in a number of different ways. The most common method is to have it measured at your GP practice by your doctor or nurse. However, it is also possible to measure it yourself at home, or to wear a cuff for a day with a small machine which will measure it for you.

Research has shown that blood pressures measured at home are likely to be lower than those measured at the GP practice. However, no studies have been done to look at whether the differences between blood pressure measured at home and at the GP surgery are the same for different ethnic groups (for example White British, Asian, White Irish, African-Caribbean): this is what we will be looking at in this study.

[stats – Flesch Reading Ease score= 61.8; Flesch-Kincaid Grade Level Score 10.9]

Level three

[Blood pressure](http://www.bhf.org.uk/keeping_your_heart_healthy/preventing_heart_disease/blood_pressure.aspx) <external link to 'What is blood pressure' > is measured by a blood pressure machine. There are two main types of blood pressure machines which you could be asked to use at home:

- An electronic blood pressure machine. This is similar to the one you may have seen at your GP surgery. If you were asked to measure your blood pressure in this way at home, you would be trained to use the machine. You would then be given a machine to take away and use at home and asked to keep a record of your blood pressure readings.
- A 24-hour blood pressure monitor. If you were asked to use this, you would have to wear a cuff for a day with a small machine attached. This machine automatically measures your blood pressure at set intervals over 24 hours. The blood pressure readings are stored on the machine and would give your GP a range of blood pressure readings over an entire day.

If you would like to know more about home blood pressure monitors, [please click here.](http://www.bhf.org.uk/plugins/PublicationsSearchResults/DownloadFile.aspx?docid=dd61a3e7-e0a9-4082-9f87-b4cda0e5bad2&version=-1&title=IS42+Blood+Pressure+Monitors&resource=IS42) <http://www.bhf.org.uk/plugins/PublicationsSearchResults/DownloadFile.aspx?docid=dd61a3e7-e0a9-4082-9f87-b4cda0e5bad2&version=-1&title=IS42+Blood+Pressure+Monitors&resource=IS42>

Research has shown that blood pressure may be lower when it is taken at home. Blood pressure can increase when you are worried or stressed, and some people get worried about going to see their GP or nurse. This means that for some people blood pressure may be higher at their GP surgery because they are worried. These people may have normal blood pressure when they are not at their GP surgery. This appearance of raised blood pressure only when people go to see their doctor is known as 'white coat hypertension'.

<<http://www.bpassoc.org.uk/BloodPressureandyou/Medicaltests/Whitecoateffect> > If you would like to know more about why blood pressure may be lower at home, [please click here](#). <Link to external paper – Ambulatory Blood Pressure Monitoring and Blood Pressure Self-Management in the Diagnosis and Management of Hypertension. Appel LJ, Stason WB >

People in some ethnic groups tend to develop high blood pressure more often than people in other ethnic groups. We do not fully understand yet why this is the case. High blood pressure is more common in African-Caribbean and South Asian people living in the UK. Research has shown that blood pressure measurements are likely to be lower when taken at home. However, no research has been done to see if blood pressure is lower at home for members of different ethnic groups. (For example White British, Asian, White Irish, and African Caribbean). This study is trying to find out two things:

- Blood pressure may be lower when measured at home. We want to see if blood pressure is lower at home than at the GP surgery for all of the ethnic groups being tested.
- Blood pressure measurements may be lower when measured at home. We want to see if home blood pressure measurements even are lower when taken at home for some ethnic groups than for others.

[stats – Flesch Reading Ease score= 70.8; Flesch-Kincaid Grade Level Score 7.5]

Why Have I been Chosen?

Level one

You expressed an interest in taking part when you returned our questionnaire.

[stats – Flesch Reading Ease score= 60.7; Flesch-Kincaid Grade Level Score 7.7]

Level two

The study will involve 800 people from four different ethnic groups (White British, Asian, White Irish, African-Caribbean). You kindly expressed your interest in taking

part when you returned our initial questionnaire, and we have chosen you on the basis of this.

[stats – Flesch Reading Ease score= 43.6; Flesch-Kincaid Grade Level Score 12.2]

Level three

We recently sent a survey to about 8000 people who go to a GP practice in the area. Your GP practice was asked to take part because it has patients from one or more of the ethnic groups we are studying. The ethnic groups we are studying are White British, Asian, White Irish and African-Caribbean. You were invited to take part because you fall into one of these groups.

All patients from the GP practices taking part in this study were randomly selected (like tossing a coin) to be sent a survey through the post. You were one of the 8000 patients chosen to receive a survey. The survey invited all patients to take part in this blood pressure study. You filled in the survey and kindly said you were interested in taking part in this study. Of those patients who were interested in taking part, the first 800 patients to respond were invited to take part. We invited a mixture of people to take part. We invited:

- 100 White patients with high blood pressure.
- 100 Black patients with high blood pressure.
- 100 Asian patients with high blood pressure .
- 100 Irish patients with high blood pressure.
- 100 White patients who do not have high blood pressure.
- 100 Black patients who do not have high blood pressure.
- 100 Asian patients who do not have high blood pressure .
- 100 Irish patients who do not have high blood pressure.

[stats – Flesch Reading Ease score= 67.7; Flesch-Kincaid Grade Level Score 7.9]

Do I have to take part?

Level 1

It is up to you to decide whether or not to take part and your decision will not affect your healthcare.

[stats – Flesch Reading Ease score= 76.6; Flesch-Kincaid Grade Level Score 7.7]

Level 2

It is up to you to decide whether or not to take part. If you decide that you would like to get involved then we will ask you to sign a consent form. We will need to let your GP know that you are involved, and will also ask for your permission to access your medical records at your GP's practice. Once the study has started you are still free to withdraw at any time without giving a reason: this will not affect the care that you receive from your GP.

[stats – Flesch Reading Ease score= 77.7; Flesch-Kincaid Grade Level Score 8.0]

Level 3

You may have been asked to sign a [consent form](#) <Link to PDF of consent form used in study> before for other medical things such as surgery or treatment. The process is similar to this. Before you sign the consent form we need to make sure you understand the study. We do this by giving you an information sheet about the study (this is what you are reading now). We then give you time to talk to a research nurse to make sure you understand the study. Once you and the research nurse are happy that you understand the study, you will be asked to sign a consent form. This gives your official consent to say that you want to take part in the study. Signing the consent form does not mean that you cannot pull out of the study later on. You can decide you no longer want to take part in the study at any point after you have signed it.

If you do decide to take part in this study, we would like to let your GP know that you are involved. If you are found to have high blood pressure we will tell your GP so that they can treat you appropriately. The research team cannot treat patients found to have high blood pressure and we would feel uncomfortable thinking you needed treatment that we could not provide. Therefore, if you do not want us to tell your GP that you are involved then you will not be able to take part in this study. For more information about the risks of high blood pressure and why treating high blood pressure is important, [please click here](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Introduction.aspx) < [http://www.nhs.uk/Conditions/Blood-pressure-\(high\)/Pages/Introduction.aspx](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Introduction.aspx) >

We need to look at your medical records to look for important things in your past medical history. We may look to see if you already have high blood pressure or to see if you are taking any medication. Only those giving medical care can look at your medical records without asking you. Not all of the researchers that need to look at your medical records for this study give you medical care. This is why we need to ask your permission for us to look at your medical records.

If you agree to take part in this blood pressure monitoring study and then decide it is not for you then you do not have to continue. We would appreciate you letting us know straight away if you decide to pull out. We will ask you to return the equipment to us. You will be asked at this time whether your data can be kept or not. You do not have to agree to this. We will also ask you why you no longer want to take part in the study. This is so we can see if you were unhappy with the study and then try to improve the study for other patients. You do not have to tell us why you no longer want

to take part. If you do pull out of the study once it has started this will not affect the care that you receive from your GP or any other health care provider.

[stats – Flesch Reading Ease score= 77.9; Flesch-Kincaid Grade Level Score 7.2]

What will happen to me if I take part?

Level one

You will make three visits to your GP surgery over 8 days. During that time you will be asked to have a 24 hour blood pressure monitor and take your own blood pressure for a week.

[stats – Flesch Reading Ease score= 85.1; Flesch-Kincaid Grade Level Score 5.7]

Level two

You will be involved in the study for a period of eight days. This will involve three visits to our research nurse / facilitator, as follows:

Visit 1 (day 1) – You will initially come in to have your blood pressure measured by the nurse and to answer a questionnaire. You will then be taught to measure your own blood pressure at home: you will need to do this both in the morning and the evening for the next seven days and we will lend you equipment to do this. The equipment will store the readings that are taken, but you will also need to write them down.

Visit 2 (day 7) – You will return the home monitoring equipment and have your blood pressure taken by the nurse again. You will then be fitted with a cuff which will measure your blood pressure automatically over the next 24 hours: this should not interfere with your daily activities.

Visit 3 (day 8) - You will come back to return the cuff, have your blood pressure taken by the nurse for the last time and complete a final questionnaire.

Each visit to the nurse should not take more than 30 minutes.

[stats – Flesch Reading Ease score= 69.9; Flesch-Kincaid Grade Level Score 9.2]

Level 3

This study will take place at your normal GP surgery within normal surgery hours. We will try to make these visits as convenient for you as possible.

Visit 1 (day1).

On the first visit you will have your blood pressure measured by the nurse. You will also be taught to take your blood pressure at home. We want to see if the blood pressure readings you take at home are different to those taken by the nurse. This is why we need to take a blood pressure reading at your GP practice as well as ask you to take them yourself at home.

During this visit we will also ask you to complete a [questionnaire](#) <Link to PDF copy of the questionnaire used in this study>. This questionnaire will ask about your health, things about you, and then about your feelings to having your blood pressure measured at the GP practice.

The nurse will then teach you how to measure your own blood pressure at home. You will be lent an electronic blood pressure machine that you can use to measure your blood pressure at home. You will also be given a written set of instructions in case you need reminding how to use the machine. You will also be given a telephone number that you can call the research team on if you have any problems. You will be asked to take two blood pressure readings each day for 7 days. Once in the morning between 6am-12pm and once in the evening between 6pm and 12am. The blood pressure machine will record the readings that are taken. We also need you to write down the readings in case they are lost or deleted from the blood pressure monitor. You will also be asked to write down all of the readings on a [home monitoring blood pressure record sheet](#). <Link to PDF copy of the sheet used in the questionnaire> You will be asked to return the blood pressure monitor at your next visit.

A picture of the type of blood pressure monitor you are likely to be given can be seen below.

<picture of electronic blood pressure monitor>

Visit 2 (day 7)

We will compare the blood pressure readings that are taken by the nurse with the blood pressure readings that you take at home. When doctors take blood pressure readings they measure it at three different visits. Only if your blood pressure is found to be high at all three visits will they diagnose you with high blood pressure. We want to make the readings taken at the surgery as close to 'normal' as possible. You would normally have your blood pressure taken three times by your doctor. Therefore we want to measure your blood pressure at the surgery three times. The nurse will measure your blood pressure again during this visit.

You will also complete a [second questionnaire](#) <Link to PDF copy of the second questionnaire> that will ask you about your feelings towards measuring your blood pressure at home using an electronic blood pressure machine.

You will then be fitted with a [24-hour blood pressure monitoring machine](#) <<http://www.bpassoc.org.uk/BloodPressureandyou/Medicaltests/24-hourtest>>. You will be given an [information sheet about this 24-hour monitor](#). <link to PDF copy of 24-hour BP monitor

information sheet used in the study>. This 24-hour monitor will collect blood pressure measurements over a 24-hour period. The recordings will provide a detailed picture of your blood pressure. It will record your blood pressure every half hour between 7am and 11pm. It will then record your blood pressure every hour between 11pm and 7am. Wearing the 24-hour monitor should not stop you from doing most of your normal activities. A cuff will be fitted to your arm like the cuff on the electronic blood pressure machine. This will blow up tight on your arm to make a reading. You should be able to sleep during the night as normal. Depending on how deep a sleeper you are you may be woken up each time a blood pressure reading is taken. After 24 hours you may remove the cuff and switch the monitor off. We ask you to return the monitor at the next visit.

Visit 3 (day 8)

This will be the last visit to the GP practice for this blood pressure study. You will be asked to return the 24-hour blood pressure monitor and cuff at this visit. You will then have your blood pressure taken by the nurse for the third and last time.

You will also complete a [final questionnaire](#) <Link to PDF copy of the final questionnaire used in the study> which will ask you about your feelings towards measuring your blood pressure at home using a 24-hour blood pressure machine.

If you have any problems with taking recordings, using any of the equipment of any other questions you can contact the research team. They can be contacted on 0800 234 6 432.

If you would like to know more about how blood pressure is measured and how high blood pressure (hypertension) is diagnosed, [please click here.](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Diagnosis.aspx) <
[http://www.nhs.uk/Conditions/Blood-pressure-\(high\)/Pages/Diagnosis.aspx](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Diagnosis.aspx)>

[stats – Flesch Reading Ease score= 72.6; Flesch-Kincaid Grade Level Score 7.3]

Expenses and payments

Level one

Travel expenses will be refunded.

[stats – Flesch Reading Ease score= 33.5; Flesch-Kincaid Grade Level Score 9.5]

Level 2

Any traveling expenses you incur will be refunded for this study.

[stats – Flesch Reading Ease score= 41.8; Flesch-Kincaid Grade Level Score 10.1]

Level 3

We will refund travel expenses for traveling to and from the GP practice if you provide a receipt for your journey.

We ask you to travel to the surgery in the way that you normally would. For example, if you would normally get a taxi or bus to the surgery then you can claim the cost of the taxi or bus journey back from us. However, if you would normally travel by car then we ask you do this. Please do not get a taxi to the surgery if you would not normally do so.

We refund traveling expenses because they are costs involved for patients to take part in research. We do not provide expenses to cover missed days of work or any other expenses. We also do not pay you for your time to take part in this study. We do not pay participants because they might then only take part because they want the money and not because they actually want to take part. This wouldn't be ethical because it would be bribing people to take part. Therefore we do not pay participants to take part in this study.

[stats – Flesch Reading Ease score= 71.9; Flesch-Kincaid Grade Level Score 7.5]

What are the possible benefits of taking part?

Level one

Your GP will be given the blood pressure measurements and offer you treatment if you need it.

[stats – Flesch Reading Ease score= 70.1; Flesch-Kincaid Grade Level Score 7.6]

Level two

The information that we get from this study will hopefully help to treat future patients with high blood pressure more effectively. In addition, your taking part will give us some really accurate information about your blood pressure: this will be passed on to your GP. Should the results suggest that you need treatment for high blood pressure (or a change in treatment if you are already taking it) then your GP will let you know.

[stats – Flesch Reading Ease score= 60.7; Flesch-Kincaid Grade Level Score 10.9]

Level three

The results of this study may help us to treat other patient's blood pressure better. We hope to get a better understanding of how much lower blood pressure is when measured at home. We also hope to find out if blood pressure is lower when

measured at home for different ethnic groups. We hope that the results of this study will help us to treat the right patients for high blood pressure. For example, we hope that fewer patients who only have high blood pressure when they visit their doctor will be treated.

This study may help you personally, as it will tell us if your blood pressure really is high or not. These readings will be passed onto your GP straight away. This will provide them with a detailed picture of your blood pressure. Your GP can then recommend the best management for your blood pressure. This may mean that your doctor:

- Gives you treatment for high blood pressure.
- Increases your treatment if you are already taking it.
- Takes you off treatment if you are already taking it.
- Lowers your treatment if you are already taking it.

If you want to know more about high blood pressure (hypertension) [please click here](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Introduction.aspx).
<[http://www.nhs.uk/Conditions/Blood-pressure-\(high\)/Pages/Introduction.aspx](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Introduction.aspx)>

[stats – Flesch Reading Ease score= 76; Flesch-Kincaid Grade Level Score 6.1]

What are the risks of taking part?

Level one

Some people find it uncomfortable to have their blood pressure measured.

[stats – Flesch Reading Ease score= 57.2; Flesch-Kincaid Grade Level Score 8.0]

Level two

The study does not involve any long term risks to you. Some people may find having their blood pressure measured uncomfortable.

[stats – Flesch Reading Ease score= 67.2; Flesch-Kincaid Grade Level Score 6.4]

Level three

To [measure your blood pressure](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Diagnosis.aspx) <[http://www.nhs.uk/Conditions/Blood-pressure-\(high\)/Pages/Diagnosis.aspx](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Diagnosis.aspx)> a cuff is put around your arm. This cuff inflates to allow the machine to take a measurement. The cuff will feel slightly uncomfortable as blood can't get through to your lower arm, but this is normal. There is a small chance that the blood pressure cuff can cause slight bruising to your arm although this is very

unlikely. If you find it too uncomfortable you can remove the cuff quickly by pulling open the Velcro fastening.

On the day that you are wearing the [24-hour monitor](http://www.bpassoc.org.uk/BloodPressureandyou/Medicaltests/24-hourtest) <
<http://www.bpassoc.org.uk/BloodPressureandyou/Medicaltests/24-hourtest>> you may be distracted when measurements are being taken. You also need to keep your arm still when measurements are being taken. We advise you not to drive or operate electrical tools when you are wearing the cuff. This is because you may become distracted or move your arm around. The blood pressure monitor will take readings every half an hour during the day and every hour during the night. You may drive/operate electrical tools between measurements. You can return to normal activities as soon as you have removed the cuff. Do not worry about this. If this is inconvenient to you we can try our best to work around your needs.

[stats – Flesch Reading Ease score= 69.9; Flesch-Kincaid Grade Level Score 7.1]

What if there is a problem?

Level one

Any problem you have will be addressed.

[stats – Flesch Reading Ease score= 78.8; Flesch-Kincaid Grade Level Score 3.9]

Level two

If you have a concern about any aspect of this study, you can contact the researchers on [REDACTED]

[stats – Flesch Reading Ease score= 36.4; Flesch-Kincaid Grade Level Score 14.4]

Level three

If you are worried about any part of this study you should speak to the researchers. They will do their best to answer your questions. Any complaint you have about the study will be dealt with as quickly as possible. If you are still unhappy after talking to the researchers, you can complain formally. You can do this by speaking to Ms Sarah Bathers. She can be contacted at:

Primary Care Clinical Trials Unit Manager,

Ms Bathers is responsible for the safety of patients involved in research at the University of Birmingham. She will also address the problem personally if possible, otherwise she will advise you on what you can do.

If something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against The University of Birmingham. You may have to pay your legal costs.

[stats – Flesch Reading Ease score= 66.4; Flesch-Kincaid Grade Level Score 7.6]

Will my taking part in this study be kept confidential?

Level one

Yes.

[stats – Flesch Reading Ease score= 100.0; Flesch-Kincaid Grade Level Score 0]

Level two

We will follow ethical and legal practice and all information about you will be handled in confidence. If you agree to take part then you will be given a copy of this information sheet, and a signed consent form for you to keep.

The study data will be collected by questionnaire, measurement (eg blood pressure, weight) and from your medical records (eg past medical history, current medications). Under the Data Protection Act of 1988, all personal data (names and addresses for example) will be stored securely at the University of Birmingham overseen by Dr Richard McManus. Personal data (names and addresses) will be kept separately from study results. Anonymised data from the study will be used in the main analysis and may be used in future work, for example comparing blood pressure levels in different parts of the country.

Personal data (names and addresses) will be only accessible by authorised persons such as researchers, sponsors, regulatory authorities and for R&D audit (for monitoring of the quality of the research) and will be retained for approximately three years (as long as needed to inform participants of the results of the study). It will then be disposed of securely.

[stats – Flesch Reading Ease score= 39.0; Flesch-Kincaid Grade Level Score 13.9]

Level three

345

We will follow legal practice and keep data in line with the [Data Protection Act of 1988](http://www.opsi.gov.uk/acts/acts1998/ukpga_19980029_en_1). <http://www.opsi.gov.uk/acts/acts1998/ukpga_19980029_en_1>

Anonymised data is data that does not include any personal details such as name and address. You cannot be identified from anonymised data.

Personal data is details such as your name, address and anything else that can be used to identify you.

To anonymise the data in this study we will give you a unique ID number that can be used to identify you. This means that personal data can be kept separate to your results. Only your ID number needs to be given out to people who do not need your personal details. For example when the data is being analysed, your personal data will not be given to people such as statisticians. They will be able to identify you by ID number only.

This anonymised data may also be used in future work, for example to compare blood pressures in different parts of the country. Passing on anonymised data from the study might mean passing on details such as:

- Age.
- Sex.
- Ethnicity.
- If you have high blood pressure or not.
- Results of blood pressure measurements from the study.

This allows relevant data to be used for future studies without the need to collect that data again. Collecting the same data again would be time consuming, costly, and a burden to patients.

If you would like to know more about how anonymised data is used in research, [please click here](http://www.ncrm.ac.uk/research/outputs/publications/WorkingPapers/2006/0706_anonymising_research_data.pdf) <

http://www.ncrm.ac.uk/research/outputs/publications/WorkingPapers/2006/0706_anonymising_research_data.pdf>

Your personal data will be password protected to stop people accessing it who are not authorized to do so. Before you agree to take part in the study only the healthcare team such as your nurse and doctor at your GP surgery will have access to your personal data. If you agree to take part in this study then members of the research team will also have access to it. This information is required by the research team so that they can

- Arrange follow up visits.

- Send reminder letters.
- Send you information about the results of the study.

All staff at the University of Birmingham have confidentiality clauses in their contracts. This means they have agreed to keep all information about you and any other patients confidential.

Personal data will be kept for three years after the study has finished so that we can write to patients to let them know the results of the study. After this time the data will be destroyed. This means that anything stored on a computer will be deleted in such a way that it cannot be restored. Any paper documents will be cross-shredded.

We need to keep anonymised data for many years after the study has finished in case the study is called for a [Research and Development \(R&D\) audit](#).

<<http://www.nres.npsa.nhs.uk/rec-community/quality-assurance/accreditation/?locale=en>> All research in the UK has to meet approvals and follow strict guidelines which protect patients and staff. R&D audits are done on around 10% of all studies taking place in the UK. They make sure that these guidelines and approvals are being stuck to. If a study is called for R&D audit then all of the data and documents for the study must be available. This is why we need to keep your anonymised data for many years after the end of the study. No identifiable data will be passed onto any other bodies or third parties.

[stats – Flesch Reading Ease score= 64.2; Flesch-Kincaid Grade Level Score 7.9]

What will happen if I don't want to carry on with the study?

Level one

You do not have to carry on and it will not affect your care.

[stats – Flesch Reading Ease score= 84.9; Flesch-Kincaid Grade Level Score 3.6]

Level two

You are free to withdraw from the study at any time without affecting your treatment by your GP. If you withdraw from the study, we will need to use the data collected up to your withdrawal.

[stats – Flesch Reading Ease score= 71.0; Flesch-Kincaid Grade Level Score 7.8]

Level three

You are free to withdraw from the study. If you pull out of the study this will not affect any treatment from your GP or anyone else involved in your care. We will ask you why you would like to withdraw from the study, but you do not have to tell us. We will

ask you so that we can see if you were unhappy with the study and then try to improve the study for other patients. We will let your GP know about your decision so that they are not waiting for blood pressure results.

We would like to use the data collected up until the time you pulled out. The researchers involved in this study have a professional duty to care for you. With your permission we would like to give your GP any blood pressure information we have in case this affects your care. We will also ask whether you are willing to let us continue to use the data and information from your records that may help our research. You do not have to agree to this.

[stats – Flesch Reading Ease score= 78.1; Flesch-Kincaid Grade Level Score 6.8]

Involvement of your General Practitioner/Family doctor (GP)

Level one

We would like to let your GP know that you are taking part.

[stats – Flesch Reading Ease score= 92.2; Flesch-Kincaid Grade Level Score 2.2]

Level two

We will ask your permission to inform your GP regarding the results from the study.

[stats – Flesch Reading Ease score= 67.5; Flesch-Kincaid Grade Level Score 6.5]

Level three

If you do decide to take part in this study we would like to let your GP know that you are involved. This is because we would like to give your GP your blood pressure results. If you are found to have high blood pressure, your GP may like to start treatment or change your current treatment. The research team cannot treat patients found to have high blood pressure. If you do not agree for us to tell your GP then you will not be able to take part in the study because we would not be able to provide the appropriate follow up for you.

For more information about the risks of high blood pressure and why treating high blood pressure is important, [please click here](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Introduction.aspx). <[http://www.nhs.uk/Conditions/Blood-pressure-\(high\)/Pages/Introduction.aspx](http://www.nhs.uk/Conditions/Blood-pressure-(high)/Pages/Introduction.aspx)>

[stats – Flesch Reading Ease score= 79.4; Flesch-Kincaid Grade Level Score 7.3]

What will happen to any samples I give?

This study does **not** involve the taking of blood or other samples.

[stats – Flesch Reading Ease score= 74.8; Flesch-Kincaid Grade Level Score 5.8]

Will any genetic tests be done?

No.

[stats – Flesch Reading Ease score= 100.0; Flesch-Kincaid Grade Level Score 0]

Who is organising and funding the research?

Level one

The research is being done at the University of Birmingham and funded by the Department of Health.

[stats – Flesch Reading Ease score= 55.2; Flesch-Kincaid Grade Level Score 9.7]

Level two

The research is organised by the University of Birmingham. It is funded by the Research for Patient Benefit Programme which is part of the National Institute for Health Research and is funded by the Department of Health.

[stats – Flesch Reading Ease score= 50.8; Flesch-Kincaid Grade Level Score 10.7]

Level three

The study is run from the University Of Birmingham. The study has been designed by staff at the University, who are part of a larger research community there.

The research is funded by the [Research for Patient Benefit Programme \(RfPB\)](http://www.nihr-ccf.org.uk/site/programmes/rfpb/default.cfm). <http://www.nihr-ccf.org.uk/site/programmes/rfpb/default.cfm> The RfPB aims to improve how health care is delivered for patients, the public and the NHS. It does this by funding research to improve health services and social care.

The RfPB is part of the [National Institute for Health Research \(NIHR\)](http://www.nihr.ac.uk/Pages/default.aspx). <http://www.nihr.ac.uk/Pages/default.aspx> which is funded by the [Department of Health](http://www.dh.gov.uk/en/index.htm). <http://www.dh.gov.uk/en/index.htm> They fund NHS and social care research that helps to improve public health and social services. The main aim of the NIHR is to improve

the quality, relevance and focus of research in the NHS and social care. It does this by giving out funds after open competition and peer review. The NIHR funds a range of programmes, which cover a wide range of health priorities.

The funding we have pays for the following:

- Wages for staff in the research team.
- Admin costs such as sending letters and making telephone calls.
- Equipment needed for the study such as blood pressure monitors.
- Costs to publish results.

[stats – Flesch Reading Ease score= 68.4; Flesch-Kincaid Grade Level Score 7.0]

What will happen to the results of the research study?

Level one

We hope to publish the results in professional magazines and present them at meetings.

[stats – Flesch Reading Ease score= 53.6; Flesch-Kincaid Grade Level Score 9.2]

Level two

We are hoping to publish the results of this study in one or more medical journals and to present them at one or more conferences. We will also write to you with the main findings of the study after it has finished unless you do not want us to. We will not identify you in any report/publication unless you have specifically given your consent for this.

[stats – Flesch Reading Ease score= 60.4; Flesch-Kincaid Grade Level Score 10.3]

Level three

It is important for us to publish our results so that other researchers can see them. The results can then hopefully be used to improve health care. Publishing helps to stop the same piece of research being repeated, which wastes patient's time and funder's money. It also allows other researchers to see what has already been done so that they can build on the work. It would be unethical not to publish our results for these reasons. We will publish the results of this study in one or more medical journals and present them at one or more conferences.

The results will also be produced as an internal report. This means that other staff at the University can see what research is currently being done. The results of this study will also be put on a website so that everyone who is interested can see them. They will be distributed through patient groups for example the [Blood Pressure Association](#). <<http://www.bpassoc.org.uk/Home>>. This will allow patients to see what research is being done. None of your personal details will be included in any reports.

If you agree to take part in this study will ask you if you would like to be told the results. If you tell us that you would like to see the results you will be sent a summary of the results. You will also be given the opportunity to receive full details such as published papers if you wish.

[stats – Flesch Reading Ease score= 68.3; Flesch-Kincaid Grade Level Score 7.6]

Who has reviewed this study?

Level one

This study has been reviewed by an ethics committee.

[stats – Flesch Reading Ease score= 66.1; Flesch-Kincaid Grade Level Score 6.2]

Level two

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the Black Country Research Ethics Committee.

[stats – Flesch Reading Ease score= 45.0; Flesch-Kincaid Grade Level Score 11.6]

Level three

The [National Research Ethics Service \(NRES\)](#) <<http://www.nres.npsa.nhs.uk/>> helps to protect the rights and safety of people involved in research. They also help to make sure that only research that might help patients or improve science is done. NRES is made up of RECs. They look at applications and decide whether they think the research is ethical. They balance the need for the piece of research to go ahead against the safety and care of the people involved. RECs are separate from investigators and those funding and hosting the research.

[stats – Flesch Reading Ease score= 62.3; Flesch-Kincaid Grade Level Score 8.3]

9.3 PRE DEFINED DATA EXTRACTION SHEET FOR THE SR

Reference ID
Study title
Authors
Year of Publication
Country of Study
Journal
Background
Study Design and Sampling Strategy
Aims
Method
Inclusion criteria
Exclusion criteria
Analysis
Number of Participants and Response Rate
Demographics of participants
What they wanted to know
Limitations
Authors conclusions

9.4 BLOOD PRESSURE MONITORING IN DIFFERENT ETHNIC GROUPS STUDY PROTOCOL

Is my blood pressure high? An investigation of the optimum method of diagnosing and monitoring hypertension in different ethnic groups

Date: v1 17 08 2009

Acronym
BPM-ETH

Name and address of the sponsor
University of Birmingham
Edgbaston
Birmingham B15 2TT

Principal Investigator
Dr Richard McManus

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

The need for a Study

What is the problem to be addressed?

Cardiovascular outcomes for people from some minority ethnic groups are worse than those of the White British group. This increase in cardiovascular risk is due to an interplay of complex factors that includes genotype, phenotype, environment and inequalities in access to health care. Measurement of risk factors including blood pressure (BP) is assumed to be equivalent between populations but no evidence exists to underpin this assumption which is vital in both the diagnosis and management of hypertension. Should these assumptions be erroneous, subsequent inadequate care maybe partly to blame for the observed outcomes. This has importance locally where significant proportions of patients are drawn from diverse and disadvantaged minority populations. This research will investigate blood pressure monitoring activity, preferences and results from different methods in four different ethnic groups.

Research Questions

This study has four main research questions:

1. How often and in what ways does monitoring of blood pressure occur (including professional monitoring, community monitoring and self monitoring) and how does it differ between White and *minority ethnic populations?
2. Are the thresholds for diagnosis and management of hypertension comparable for White and minority ethnic populations using different measurement modalities: office blood pressure, ambulatory blood pressure monitoring (ABPM) and self monitoring?
3. What preferences for blood pressure measurement do people from White and minority ethnic populations have?

* This includes South Asian (i.e. of Indian, Pakistani or Bangladeshi origin), Black African-Caribbean, and Irish.

4. What information are research participants interested in knowing when they are deciding whether or not to participate in research and does an interactive information sheet influence participation rates?

Why is a study needed now?

Cardiovascular Outcomes in Ethnic Minority Populations

Cardiovascular outcomes for people of South Asian, Caribbean and Irish origin are worse than those of the White British group.(2,8) For example, South Asians have a 40-50% higher mortality from coronary heart disease (CHD) than the population average (9,10) with evidence that the poorest groups of Pakistani and Bangladeshi origin have the highest rates.(2,11,12) The mortality of migrant Caribbeans from CHD is lower than the national average but stroke deaths are higher (in women by 57%, men 24%) with hypertension (HT) being the major associated risk.(2) What data there are suggest little improvement in mortality of UK-born Caribbeans.(13) Similarly, the Irish living in Britain experience higher mortality from both CHD (in women by 20%, men 24%) and strokes (in women by 23%, men by 38%). Little is known about CHD and stroke mortality among UK-born Irish but reported cardiovascular mortality for men with Irish names living in Scotland was found to be increased by 51%.(14)

This increase in cardiovascular risk in ethnic minority groups is due to an interplay of complex factors including genetic, cultural (smoking habits, diet, barriers to health care) and deprivation.(13,15) HT remains a significant and treatable risk factor in all groups. For example, in a Bangladeshi population with type 2 diabetes the authors identified a prevalence rate 23.2% for systolic HT.(16) There is also evidence HT may go undetected and under treated in ethnic minority groups. Cappuccio et al found a 2-3 fold increase in HT in South Asians and Caribbeans; only 49% of hypertensives had adequate control; 18% were undiagnosed before the survey and 17% were not receiving medication.(17)

Cardiovascular Process Measures in UK Primary Care

Data from the Quality and Outcomes Framework suggests that practices providing care to minority ethnic populations achieve lower quality scores.(3) Few studies of BP monitoring undertaken over the last 20 years have included people from South Asian, Caribbean or Irish populations with the result that very little is known about comparative measurements including self monitoring. For instance, it is not clear whether the white coat effect seen in white populations is similar, greater or less amongst these ethnic minorities. Nor is it known whether observed differences between office and home measurements in Whites are similar or different in Asian, Caribbean or Irish populations.

Diagnosis and management of blood pressure

The diagnosis and management of blood pressure are informed by guidelines largely based on research from White populations.(18,19) These guidelines recommend diagnostic and treatment thresholds for hypertension on the basis of office BP readings with the option of 24 hour ambulatory monitoring (ABPM) but make no distinction between ethnic groups.

Blood Pressure Monitoring

Increased availability of various automated devices has encouraged individuals to monitor their BP at home. The use of ABPM has also led to a realisation that multiple readings may improve accuracy of diagnosis. In general, both ABPM and home monitoring may help to improve treatment,(20,21) identify resistant HT,(22) diagnose white coat HT (1,23,24) and predict cardiovascular outcomes.(25,26,27) ABPM is the only method that can identify poor night time dipping which is a poor prognostic indicator.(28) The definitive diagnosis of white-coat HT by means of ABPM may ultimately reduce health care costs.(27)

Conclusions

The proposed study will look at accuracy and acceptability of home, ABPM and clinic readings in minority ethnic populations in relation to the White British group. The local setting is ideal for the proposed study as 70% of the population in the Heart of Birmingham PCT are from black minority ethnic groups and the Birmingham and Black Country locality has a high prevalence of people describing themselves as Irish. This work has the potential for significant impact on local policy-making and improvement in service delivery both in terms of increased access to services in a deprived local population and also of improvements in service stemming from new knowledge.

References

- 1 Guidelines Committee. 2003 European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens* 2003; 21:1011-1053.
- 2 Gill PS et al. Health Care Needs Assessment: Black and Minority Ethnic Groups. In: Raftery J, Stevens A, Mant J (ed). *Health Care Needs Assessment. The epidemiologically based needs assessment reviews. Third Series.* Abingdon: Radcliffe Publishing Ltd, 2007.
- 3 QOF Clinical Domain Results 2006-7. NHS Information Centre: <http://www.ic.nhs.uk/our-services/improving-patient-care/the-quality-and-outcomes-framework-qof-2006/07/qof-2006-07-data-tables>
- 4 Appel LJ, Stason WB. Ambulatory blood pressure monitoring and blood pressure self-measurement in the diagnosis and management of hypertension. *Ann Intern Med* 1993; 118:867-882.
- 5 QOF Prevalence Results 2006-7. NHS Information Centre: <http://www.ic.nhs.uk/our-services/improving-patient-care/the-quality-and-outcomes-framework-qof-2006/07/qof-2006-07-data-tables>
- 6 Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. *Lancet.* 2003;362:1527-35.
- 7 Cappuccio FP et al. Blood pressure control by home monitoring: meta-analysis of randomised trials. *BMJ* 2004; 329:145.
- 8 Wild S, McKeigue P. Cross sectional analysis of mortality by country of birth in England and Wales, 1970-92. *BMJ* 1997; 314:705-710.
- 9 Balarajan R. Ethnicity and variations in mortality from coronary heart disease. *Health Trends* 1996 28:45-51
- 10 Bhopal R et al. Cardiovascular risks and outcomes: ethnic variations in hypertensive patients. *Heart* 2000; 83:495-496.
- 11 Bhopal R et al. Heterogeneity of coronary heart disease risk factors in Indian, Pakistani, Bangladeshi, and European origin populations: cross sectional study. *BMJ* 1999; 319:215-220.
- 12 Nazroo J. *The health of Britains ethnic minorities.* London: Policy Studies Institute. London: Policy Studies Institute 1997.
- 13 Abbotts J et al. Cardiovascular risk profiles in UK-born Caribbeans and Irish living in England and Wales. *Atherosclerosis* 2004; 175:295-303.
- 14 Abbotts J et al. Association of medical, physiological, behavioural and socio-economic factors with elevated mortality in men of Irish heritage in West Scotland. *J Public Health Med* 1999; 21:46-54.
- 15 Lip GY et al. Ethnicity and cardiovascular disease prevention in the United Kingdom: a practical approach to management. *J Hum Hypertens* 2007; 21:183-211.
- 16 Sayeed MA et al. Blood pressure and coronary heart disease in NIDDM subjects at diagnosis: prevalence and risks in a Bangladeshi population. *Diabetes Res Clin Pract* 1998; 39:147-155.
- 17 Cappuccio FP et al. Prevalence, detection, and management of cardiovascular risk factors in different ethnic groups in south London. *Heart* 1997; 78:555-563.
- 18 CG18 Hypertension (persistently high blood pressure) in adults - NICE guideline. National Institute for Clinical Excellence. <http://www.nice.org.uk/page.aspx?o=218469>. NICE London 2004 updated by CG 34 2006.
- 19 Williams B et al. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. *BMJ.* 2004 Mar 13;328(7440):634-40.
- 20 Cappuccio FP et al. Blood pressure control by home monitoring: meta-analysis of randomised trials. *BMJ* 2004; 329:145.
- 21 Pickering T et al. Second international consensus meeting on 24-hour ambulatory BP measurement: consensus and conclusions. *J Hypertens* 1991; 9:S63-S65.

- 22 O'Brien E et al. Use and interpretation of ambulatory blood pressure monitoring: recommendations of the British hypertension society. *BMJ* 2000; 320:1128-1134.
- 23 Appel LJ, Stason WB. Ambulatory blood pressure monitoring and blood pressure self-measurement in the diagnosis and management of hypertension. *Ann Intern Med* 1993; 118:867-882.
- 24 Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension* 2008; 42:1206-1252.
- 25 Imai Y et al. Predictive power of screening blood pressure, ambulatory blood pressure and blood pressure measured at home for overall and cardiovascular mortality: a prospective observation in a cohort from Ohasama, northern Japan. *Blood Press Monit* 1996; 1:251-254.
- 26 Ohkubo T et al. Prediction of stroke by ambulatory blood pressure monitoring versus screening blood pressure measurements in a general population: the Ohasama study. *J Hypertens* 2000; 18:847-854.
- 27 O'Brien E, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens* 2003; 21:821-848.
- 28 Ohkubo T et al. Prognostic significance of the nocturnal decline in blood pressure in individuals with and without high 24-h blood pressure: the Ohasama study. *J Hypertens* 2002; 20:2183-2189.
- 29 Brueren MM et al. A series of self-measurements by the patient is a reliable alternative to ambulatory blood pressure measurement. *Br J Gen Pract* 1998; 48:1585-1589.
- 30 Jula A, Puukka P, Karanko H. Multiple clinic and home blood pressure measurements versus ambulatory blood pressure monitoring. *Hypertension* 1999; 34:261-266.
- 31 Pickering TG et al. Ambulatory blood-pressure monitoring. *N Engl J Med* 2006; 354:2368-2374.

Has a systematic review been carried out and what were the findings?

No systematic review of blood pressure monitoring in different ethnic groups has been carried out. Few studies have directly compared both methods of home monitoring with clinic readings (29,30) and ethnic minorities have not been included as a separate group. It is recommended that thresholds for treatment be adjusted down by 10/5 mmHg when home readings are used but these standards have not been specifically set in ethnic minority groups. Some patients may find it difficult to comply with ABPM which requires them to keep the arm still while the cuff is inflating and to avoid physical exertion during monitoring.(31) In addition, measurement of night time readings may interrupt sleep. The impact of these practicalities on use of home monitoring has not been addressed in different ethnic groups where language barriers and cultural differences may be relevant.

How will the results of this trial be used?

Over 12% of the adult population are currently receiving treatment for hypertension however despite this many people still have inadequate blood pressure control. One reason for this may be that current monitoring regimes are inappropriate for sections of the population both in the diagnosis and further management of hypertension. In Birmingham, ethnic minority populations form the majority of constituents in many wards and yet monitoring regimes are tailored to the White population with little research evidence that this is appropriate. This is important because each 5mmHg reduction in usual systolic blood pressure is associated with reductions in stroke and coronary heart disease risk of around 20% and 10% respectively.

Information about norms for ambulatory and self monitoring in minority ethnic groups is vital to allow optimum care to be provided both in the diagnosis of hypertension and in further management by intensifying care for those with high risk and removing unnecessary treatment (and therefore side effects) where appropriate. The White Irish population are in particular often ignored in research despite high levels of cardiovascular disease. Self monitoring has the potential to achieve reductions of blood pressure whilst encouraging increased use of non pharmacological interventions and the work will identify which method of monitoring is most acceptable to patients, which may vary among ethnic groups.

Risks to the safety of participants involved in the trial

Potential Risks

We anticipate that the potential risks of this study are low and similar to those attributable to usual care. Particular issues are where a patient finds an excessively high or low reading in the home monitoring arm and the possibility of increased anxiety due to the study. The patient guideline will advise contact with the supervising physician or nurse in the case of excessively high or low readings. Training of participants will cover repeated measurements in the case of unusually high or low readings and a help line will be available should subjects require advice over and above that available in the guideline.

Potential Benefits

Potential benefits for an individual taking part include better information about their usual blood pressure and the possibility that either new hypertension or poor blood pressure control will be recognised during the study. Furthermore, from a societal view point, information about norms for ambulatory and self monitoring in minority ethnic groups is vital to allow optimum care to be provided both in the diagnosis of hypertension and in further management by intensifying care for those with high risk and removing unnecessary treatment (and therefore side effects) where appropriate.

The Study

Study design

Part 1

A cross sectional survey of 8000 people including representative samples of four ethnic groups (as given in part 2 below) chosen to cover both normotensive and hypertensive blood pressure ranges will elucidate current blood pressure monitoring patterns (self, third party (pharmacy etc), health professional), confirm ethnic group and identify participants for the validation study.

Part 2

This is a validation study comparing the ability of the different modes of BP measurement to diagnose hypertension and to detect thresholds for up or down titration of medication. Typically three office measurements are required to make a diagnosis of hypertension and a threshold of 140/90 mmHg (standard office measurement) is used by NICE guidelines in both diagnosis and treatment targets for people with uncomplicated hypertension. Similar standard thresholds are available for ambulatory and self measurements and the thresholds for treatment targets vary depending on co-morbidity, most notably for diabetes. We will use the office standard measurement as the reference from which to ascertain differences to ambulatory blood pressure, self monitored BP and research (see below) office measurements in order to ascertain whether such differences are similar in White, Black, South Asian and Irish populations and therefore whether or not the same diagnostic and treatment target thresholds are appropriate.

Embedded study: Interactive Information Sheet (IIS)

Those participants who have access to the internet, and are willing to do so, will be offered information electronically. Half will receive a .pdf file of the paper information sheet and the other half an interactive Internet information sheet (IIS), with three increasingly detailed levels of information, the second of which is identical to the .pdf file.

Part 3

Focus groups including patients from each ethnic group will consider patient preferences for and experiences of blood pressure measurement in each of the three ways considered by the study.

Study Methods

1 Survey of blood pressure monitoring in representative White and minority ethnic Populations.

Population and Rationale for sampling strategy,

A postal questionnaire with telephone follow up where required by bi-lingual researcher(s) will be sent to a random sample of people who appear on the hypertension and general population registers of approximately twenty practices, from the Birmingham and Black Country Area (8000 individuals in total). Within each practice we will approach a random stratified sample of approximately 250 people with hypertension and an equivalent sized random population not known to be hypertensive to ensure that people with a range of blood pressures are included as well as diagnosed and undiagnosed hypertension. People whom the general practitioner feels that it would be inappropriate to approach, for example those with a terminal illness, acutely unwell with a severe mental illness or recent bereavement will be excluded.

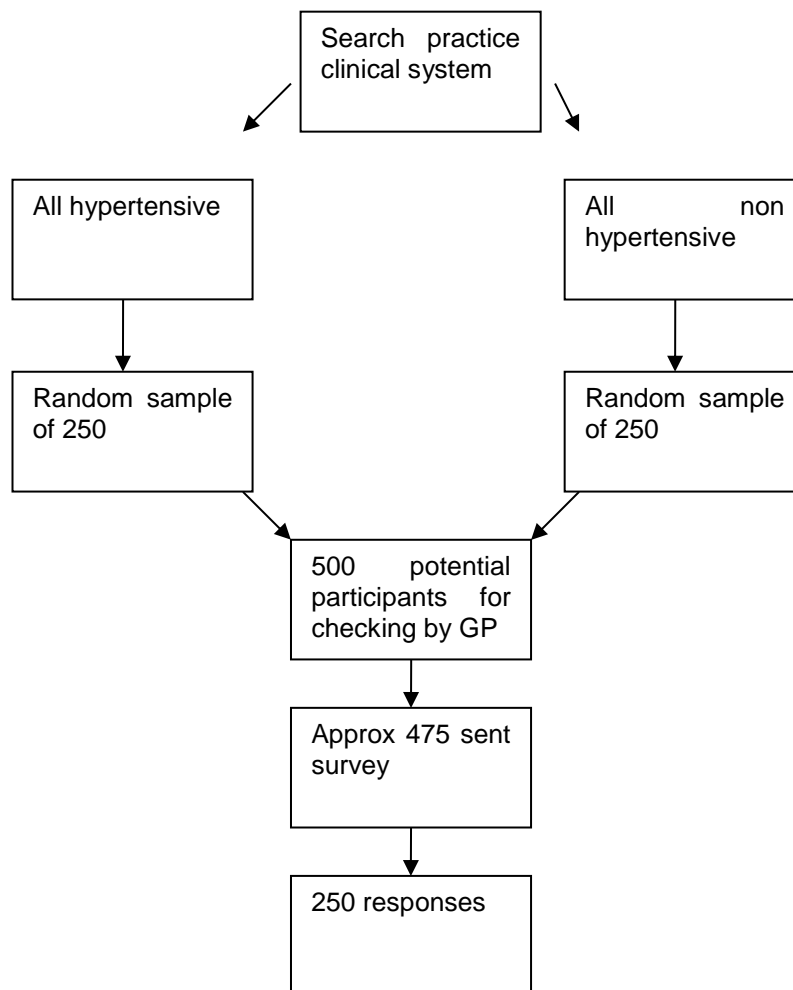


Figure 1 Recruitment strategy for phase 1

The survey will be kept short (2 sides of A4 max). Practices will be chosen on the basis of census data for their practice area, and using specialist knowledge from previous research which include a majority of people from one or more of the four ethnic groups of interest. Patients will be targeted using practice ethnicity records (both to include and exclude potential participants) along with local knowledge with the aim of recruiting a sample including similar proportions of people of South Asian (ie Indian, Pakistani and Bangladeshi), Black African-Caribbean, Irish and White origin. The success of this sampling strategy will be reviewed as the study goes on and recruitment targeted with additional questionnaires towards under represented groups as necessary.

Pilot/Previous Work

Previous work in a general (largely white) population sample (2931 respondents) has shown that around 9% of adults have self monitored blood pressure and that a response rate to a simple questionnaire of around 60% is feasible. Pilot work (RCGP Scientific Board Small Grant, Baral S, McManus RJ 2007-8) surveyed self monitoring in people with hypertension, diabetes or both, again in a general population, and found a prevalence of between 15-30% varying with diagnosis. Work in ethnic minority populations has shown that additional measures are required in order to get reasonable response rates and hence generalisable populations: it is often stated that the responses to surveys by minority ethnic groups are low but this is not borne out by the extensive study by Bhopal et al who achieved a 68% response rate by engaging with the local communities, providing information in appropriate languages and using bilingual staff to answer any questions. These measures are currently being utilised in a large heart failure screening study that the BHF has recently funded (E-Echoes – screening 3000 people from minority ethnic populations) and will be implemented in the proposed study.

Method of data collection

A survey, with covering letter translated into appropriate languages, will ascertain the blood pressure monitoring experience of respondents in the last year including prevalence of self monitoring as well as use of community pharmacies for monitoring and uptake of clinical professional monitoring at surgeries or outpatients. The questionnaire, developed from the previous and pilot work above, will in addition elicit basic socio-demographic characteristics (e.g. age, sex, ethnic group and employment status) as well as type of monitoring used in the case of self monitoring (wrist/upper arm, model if known). We will explicitly request permission to review practice records to corroborate professional monitoring responses and to allow inclusion of co-morbidities and medication history with the results of the survey. The investigators have a track record of linking survey results with multiple professional datasources. Lists will be verified by General Practitioners (GPs) from participating practices prior to being sent out to patients. The survey will include an invitation for stage 2 (validation) of the study as a means to recruit participants. An email address will be requested so that participants can be invited to receive information about part 2 electronically as an alternative to the standard paper participant information sheet (PIS).

Embedded Interactive Information Sheet (IIS) study methods

Participants who choose to access information electronically can do so via the Bp-Eth website (see appendix one for the email invitation). Those participants who choose to take part in the embedded study will be randomised to either the .pdf file or the interactive information sheet (appendix two). Those participants who do not wish to take part will be sent the standard paper version. The understanding, and satisfaction (appendices three & four) with the information provided, of all participants will be assessed and compared.

Figure 2 shows where the embedded study of electronic information fits into the Blood Pressure Monitoring Study.

2 Comparison of acceptability and agreement of different measures of blood pressure in representative White and minority ethnic Populations.

200 each of White, Black, Asian and Irish participants recruited from respondents to study 1 (half with diagnosed hypertension and half without known hypertension) will be invited to undergo blood pressure measurement by three methods: office measurement in both arms using a BP-Tru (BHS A/A rated) automated sphygmomanometer (BP measured three times: at the beginning, middle and the end of study period of eight days; this will be used to generate two sets of readings: standard office (mean of second and third readings on three occasions) and research office (mean of second to sixth readings on three occasions)), 24 hour ambulatory blood pressure x 1 (BHS validated monitor rated to record mean 24, mean day time and mean night time), and self monitoring consisting of paired readings taken twice daily for one week (28 readings in all stored in monitor memory) using a validated monitor (BHS validated). Office readings will be taken in both arms simultaneously at baseline and postural hypotension will be checked for by measurement after 1 minute standing. All patients will have measurements taken in the following order:

Day 1	Days 1-7	Day 7	Day 8
Office Measurement	Home Measurement	Office Measurement	Office Measurement
Trained to do home readings		ABPM applied	ABPM removed

Table 1 Overview of measurements

For both ambulatory and self monitoring, bespoke training developed by our team for previous projects and clinical work will be used and will be delivered to participants by the research nurses. Training will include timing, positioning, and setting of measurement with careful instruction on safe use of ambulatory monitoring including for instance care if the monitor starts when driving. Close cooperation between the research team and colleagues in the Wellcome Clinical Research Facility and MidReC will ensure that appropriate standard operating procedures and clinical supervision is available. Drs McManus and Martin will take responsibility for any clinical issues arising through the study and will liaise with individual's GPs as required.

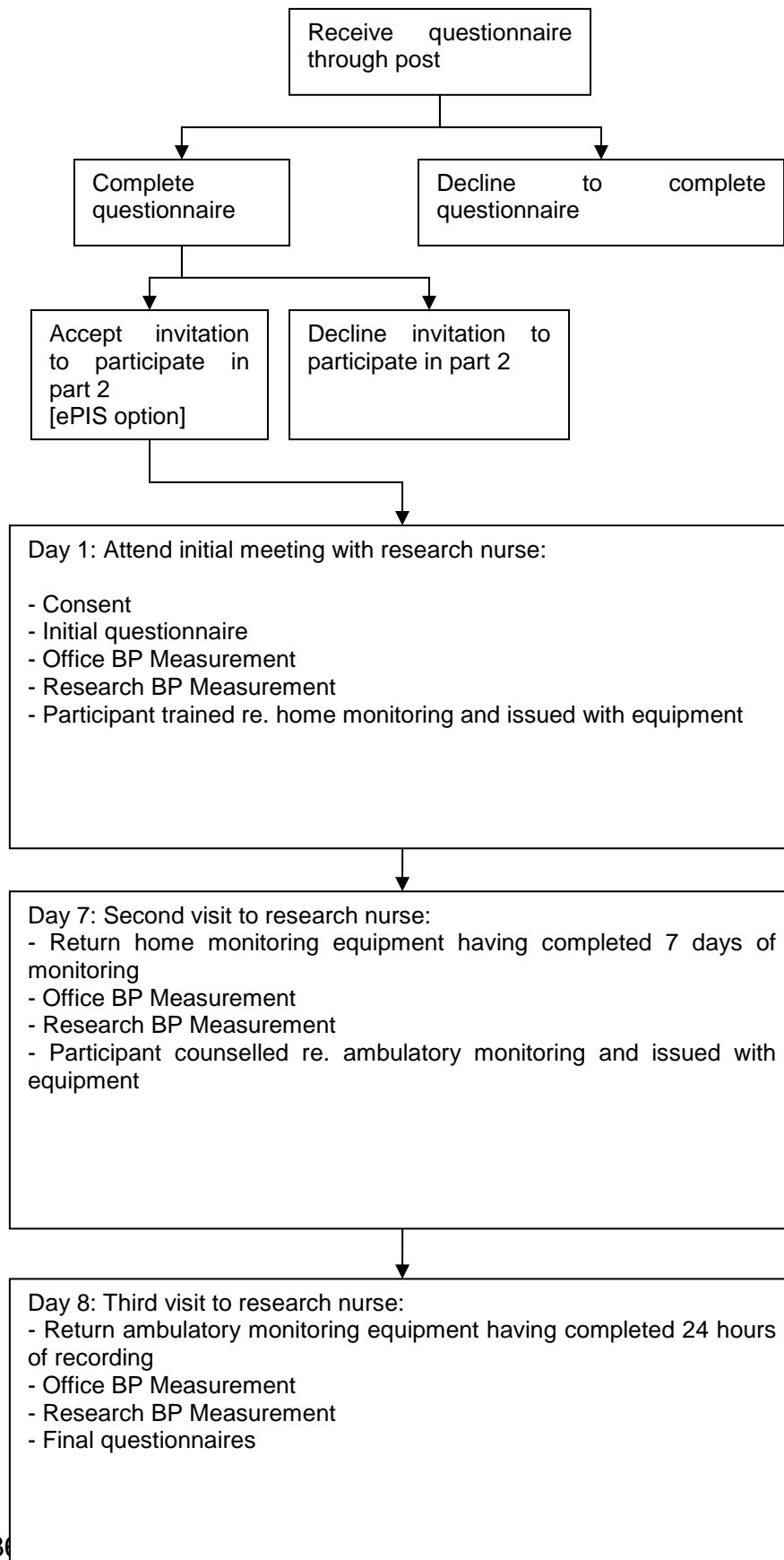


Figure 2 Overview of Phase 2

In each case the differences between office and the other modes of measurement will be compared between the White British Group and the other minority ethnic groups. The order of home and ambulatory measurement undertaken within each group will be randomly varied. A further comparison will be between the study readings and routinely collected measurements from the practice clinical systems made by both GPs and nursing staff. Once all three modalities of measurement are complete, participants will be asked to complete a questionnaire assessing the acceptability of the various methods of blood pressure measurement.

During the study it is likely that new cases of hypertension, poor control of treated hypertensives and the presence of other features including white coat hypertension and lack of nocturnal dipping will be detected. In view of this we will specifically report back the results of all modalities of monitoring with appropriate interpretation and/or recommendations to the GPs of participating patients in terms of the meaning of results and suggested further management and/or referral where indicated. Patients will also receive individualised reports. These are issues identified as important in our feasibility discussions with patients and local practices.

Patients will be offered the opportunity to be seen in their own practices and/or the Wellcome Clinical Research Facility at the UHB hospital. Study nurses will liaise with practice staff and where appropriate service support costs for practices' out of pocket expenses will be applied for from the relevant Comprehensive Research Network (CLRN). Participants travelling expenses will be reimbursed. An 0800 helpline number will be available for queries during office hours. All study data will be kept secure in accordance with university procedures and the Data Protection Act.

3 Qualitative Component

Participants will be asked to indicate in the questionnaires from phase 2 if they are willing to be contacted again to take part in a focus group. Focus groups will take place following the monitoring phase to provide richer outcome data regarding the acceptability of the various monitoring modalities. The emphasis will be on participants' experiences of taking part in and satisfaction with monitoring, perceptions of the relative advantages and disadvantages of office, home and ambulatory monitoring (e.g. level of stress experienced, discomfort and inconvenience, length of time procedure takes, understanding and interpretation of differences in readings from different monitoring methods, preferences for and value of BP reading taken by Doctor, nurse, patient themselves). Focus groups will comprise 6-8 individuals and will include members of a single ethnicity and gender in any given group (i.e. 10 focus groups in total) as our previous experience has shown that participants are often more forthcoming in the presence of those with similar characteristics. To ensure inclusion of participants with limited English, two language specific focus groups will be held for South Asian participants. As the potential participants are from 'hard to reach' groups in order to ensure we capture the views of the range of study subjects if some subjects of interest remain under represented, we will provide the option of individual interviews for people who want to contribute (e.g. working men) but who cannot make the times stated. A range of venues will be offered for the focus groups e.g. healthcare location, community location, university. They will be facilitated by two members of the study team, one will facilitate the group and the other will observe and take detailed field notes to note non-verbal interactions and proceedings will be taped with the permission of participants.

	White British	White Irish	African-Caribbean	Asian (language 1)*	Asian (language 2)*
Male					
Female					

Table 1 Grid showing make up of ten focus groups. (* language specific groups to be chosen depending on requirements of participants eg Urdu & Hindi)

Analysis will be carried out by reading the transcripts and identifying emerging themes and categories with attention to the interaction between participants. Each transcript will be independently analysed using the principles of thematic content analysis, by two of the researchers. Additionally the co-applicants from different disciplines will read and analyse some of the transcripts to allow the data to be considered from the range of perspectives within the study team. An overall summary of themes and categories emerging from the focus groups will be compiled as well as a summary for individual focus group which will allow for between focus group comparison and the identification of any similarities and differences.

Duration of study period / follow up

The initial survey will take approximately 10 minutes to complete. The validation study will require each patient to participate for three visits to the research nurse over eight days. On each occasion it should take no more than 30 minutes to complete the follow up activities. Focus groups are expected to last approximately 1 hour.

Inclusion / exclusion criteria

The study population will comprise people with both diagnosed hypertension and those not known to have hypertension recruited from primary care.

Subject inclusion criteria.

Eligibility criteria will be age between 40-74 and belonging to one of the four ethnic groups under investigation (White, Irish, Asian, African-Caribbean) .

Subject exclusion criteria.

Exclusion criteria will include inability to self monitor or use an ambulatory blood pressure monitor, pregnancy, inability to consent, terminal disease, or those felt by their GP not to be suitable.

Subject withdrawal criteria:

Subjects will be withdrawn from the study if they choose not to continue.

Outcome Measures

Part 1

The primary outcome measure will be prevalence of self, professional (practice, pharmacy, outpatient) and ambulatory monitoring over the last 12 months in each ethnic group. Secondary outcomes will include preferences for types of monitoring.

Part 2

The primary outcome will be the mean between difference in standard office (mean of second and third readings on three occasions) , ambulatory mean day time blood pressure, self monitored BP, office research (mean of second to sixth readings) and routine practice blood pressures (GP and practice nurses) in White, South Asian, Black African –Caribbean and Irish populations in people being treated for hypertension and in people not being treated for hypertension. Ambulatory monitoring will be treated as the reference standard with other measurements compared to it. The effect of these differences on diagnostic and treatment target thresholds will be evaluated.

Interactive Information Sheet

The primary outcome measure will be the proportion of eligible participants agreeing to participate in the blood pressure monitoring study. Secondary outcomes include participant satisfaction, understanding and information needed to make a decision to participate

Frequency / Duration of Follow up

Each patient will be in the study for eight days (3 visits). Each follow up visit will be timetabled for no more than ½ hour.

Measurement of Outcome measures

The primary outcome measures of blood pressure will be measured using a validated electronic sphygmomanometer so as to reduce bias potentially introduced by the unblinded nature of the investigation. Secondary outcomes will be measured using validated questionnaires where appropriate or by collection of original data (weight and height) or extracted data from notes (past medical history).

Methods for protecting against other forms of bias

Because of the nature of the investigation, blinding will not be possible for patients taking part in the study. In order to minimise the effects of this, researchers measuring blood pressure for the end points will use validated automated electronic sphygmomanometers where measurement will not be affected by knowledge of allocation.

Sample size and power calculation

Part 1:

Twenty practices with mean list size of 5000 adult patients (lower than normal to take into account the typical practices in majority ethnic population areas such as the inner city) with a conservative prevalence of hypertension of 10% will result in a potential sample of at least 10000 patients with hypertension and many times this without. We will send questionnaires to a random sample of 4000 stratified by practice and ethnic group (where known) with a Read code for hypertension and 4000 with no such Read code but who have at least one blood pressure recorded on the practice computer in the last 5 years- stratification will be based on ethnicity. A 50% response rate (realistic in this population from previous work) will mean 4000 responses. We anticipate that a proportion of responses will fall outside of the four ethnic groups we are studying hence may need to send further questionnaires (up to 10000) in order to receive responses from 1000 individuals in each main ethnic group being studied, half of which will have hypertension and half not (see appendix 1). This will allow us to estimate the overall prevalence of the different types of monitoring with and without hypertension to within 2.7% assuming a 10% prevalence of monitoring in each case (the approximate community prevalence of self monitoring in a white population).

Part 2

100 patients with and without hypertension will be recruited from each ethnic group.(see appendix 1) Based on previous work in a white population, 200 patients per ethnic group, ie 800 people in total, will be sufficient to detect a difference of 5mmHg in mean differences between any two populations (this is sufficient across the plausible range of standard deviations between 12-18 mmHg, power 80%). Differences of less than 5 mmHg are unlikely to be clinically significant given the day to day variation of blood pressure within individuals. A further approximately 5% will be recruited as required to take into account drop outs or equipment malfunction.

Recruitment and Rationale for sampling strategy,

Because we will have already identified potentially willing participants in study 1, any problems in recruitment for study 2 will be identified at an early stage. Patients will be identified from practices who are members of the Midlands Research Practice Consortium (MidReC) and/or the Central England Primary Care Research Network (PCRN-CE). MidReC includes around 300 practices in the West Midlands which have been shown to be generalisable to wider primary care. In the event of the responses from study 1 suggesting that recruitment may be difficult, then further practices will be recruited for study 2 and participants identified through invitation letter following further practice searches. The sampling strategy, is designed to recruit populations representative of the target ethnic groups with a range of blood pressure including both those receiving treatment and those not.

Planned recruitment rate

The study has a two year timetable (see Gant chart):

The initial survey will be distributed in a stepped fashion covering 6 or 7 practices at a time allowing sufficient gaps between each tranche to undertake the measurement comparisons and avoiding long gaps between inviting a person to take part and undertaking the monitoring. 15 months of monitoring with a maximum of 20 patients per week and taking into account holidays will be sufficient for 1100 patients to be monitored. Monitoring will occur within practices and/or the Welcome CRF facility as determined by patient preference. The study requires 800 (840 including 5% drop put) patients which allows leeway for clinics where not all places are filled. Six months for analysis including 3 months for writing up provides a small contingency should slippage in time occur.

20 patients per week: 5 x 24 hr monitors: Mon Tues Weds Thursday & Friday clinics with five –ten slots each for fitting and removal of 24 hour monitors and/or training for home monitoring. The latter will need 20 x home monitors to be available, each for a week. We know from experience that practices have variable room availability which is taken into account in this schema.

Gant Chart Showing Study Plan

Month	1-3	4-6	7-9	10-12	13-15	16-18	19-21	22-24
Recruit Practices,								
Survey								
Validation study								
Analyses								
Write up								
Steering groups								

Potential problems with compliance

Compliance in this study will comprise compliance to the protocol with respect to ambulatory and self monitoring. This will be monitored by self report and by review of self monitored blood pressures.
Likely rate of loss to follow up

The TASMINH1 and 2 studies with a similar group of patients achieved a 91% follow up rate of patients after 1 year. Once patients are recruited they will have three visits in short succession and so drop outs should be minimal. We have conservatively estimated a 5% drop out rate in our recruitment calculations but will aim to maintain less than this.

Centres involved

20 General Practices drawn from the Midlands Research Practice Consortium from within the Birmingham and Solihull area. For each site the relevant primary care physicians will retain direct medical responsibility for trial patients.

Assessment of Safety

Specification of safety parameters.

Where office, ABPM or HBPM readings suggest a diagnosis of previously undetected hypertension or that increased or new medication may be required for blood pressure, a letter will be sent to the patients GP suggesting this and patients will be advised to make an appointment for review. All patients' results will be communicated to their GP in any case with Dr Una Martin providing specialist input where required.

Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.

We do not anticipate a high level of adverse events as this is an observational study. Patients experiencing adverse events (eg discomfort from blood pressure monitoring) will be asked to contact the study helpline or their own primary care physician as appropriate.

Analysis

Part 1

The prevalence of blood pressure monitoring will be estimated and the variation in prevalence between different age groups, sex, employment status and deprivation as measured by the Index of Multiple Deprivation as well as the association with ethnic group will be explored using logistic and multi level logistic regression

Part 2

Between groups, t tests will be used to compare mean differences in ambulatory vs office, home monitored and routine blood pressure between White, South Asian, African-Caribbean, Irish populations separately for people with a diagnosis of hypertension, and for people without a prior diagnosis of hypertension (ambulatory used as reference standard). Because we are interested in the differences between each ethnic minority groups and White British, each comparison is of interest and will be dealt with individually. Thus no adjustment for multiple comparisons is required. Within groups, repeated measures General Linear Modelling (GLM) and multi level models will be used to evaluate differences between the different methods of measurement and routinely collected BP data with post hoc tests where significant differences are found. Baseline covariates will be examined for similar age/gender/ blood pressure distribution and adjustment will be incorporated in the analysis where necessary. We will investigate whether differences or errors are related to level of blood pressure.

Level of significance to be used.

367

P<0.05

Procedure for accounting for missing, unused, and spurious data.

A sensitivity analysis will examine the potential effect of missing data.

Procedures for reporting any deviation(s) from the original analysis plan

Any deviation from the original analysis plan will be described in the final report and publications.

Frequency of analysis

Analyses will be performed at the end of the study after all data has been collected. No interim analysis will be performed as this is an observational study.

Planned sub group analysis

Planned sub group analyses will be of diabetic vs non diabetic patients, older vs younger (65 as threshold), males vs females, higher vs lower blood pressure (threshold 150 systolic).

Analysis for IIS part of study

Analysis will be carried out based on intention to treat.

Primary Outcome

The primary outcome of this study is the proportion of eligible participants agreeing to participate in Bp-Eth. The primary analysis will assess the impact of IIS on consent using a mixed model with a logit link and binomial error accounting for baseline age and gender and with practice as random effects. Odds ratio 95% CI and p value will be presented.

Secondary Outcomes:

Exploratory analysis will be undertaken to assess patient satisfaction, understanding and the level of information needed to make a decision. The relationship between patient characteristics and these outcomes will be considered (age, gender, deprivation etc).

Ethical Issues

Ethical and R&D approval for the full study will be gained. Consideration will be given to the potential sensitivities of individuals from minority ethnic groups. Telephone contacts will be used to ensure that people from hard to reach groups are given appropriate opportunity to take part. Written consent will be sought from the patients for access to their medical records. Any data stored about the patients The main ethical issues relating to the study are regarding confidentiality and data protection. Initial invitations will be sent by the practices. All of the research team with access to patient identifiable data will have honorary contracts with the relevant primary care organisations. All participating patients will be asked for permission to gain access to their medical records. The research project is registered with the Data Protection Commissioner via the University of Birmingham Data Protection Officer. It is possible that blood pressure monitoring may increase anxiety in participants but previous work by our team has not found this to be common. Should an individual feel excessively anxious due to study procedures then they will be free to withdraw.

For the interactive information sheet part of the study

As this is an observational study (albeit electronic observation), we will not be able to inform participants that we will record the type and amount of information they access as this would bias results. Participants will be informed of all aims that are not likely to invite bias into the study. They will know that the information provided online is to evaluate and pilot a new way of providing study information to participants. Our results will inform how future research participants receive information.

Study Management

Day to day management

The study will be managed on a day to day basis by the research team led by Dr RJ McManus.

Responsibilities of Team Members

Dr RJ McManus: overall responsibility for the study

Dr Una Martin: specialist hypertension input

Steering group: strategic direction for the study

Research Nurses: Research Clinics

Study statistician

Mr Roger Holder

Study Steering Group

Dr Richard McManus

Dr Una Martin

Dr Paramjit Gill

Prof Jonathan Mant

Mr Roger Holder

Dr Jamie Coleman

Dr Mohammed Mohammed

Dr Sheila Greenfield

Dr Sally Wood

Dr Tehreem Butt

Lay representatives

Data Handling and Record Keeping

Data will be recorded onto a combination of electronic and paper case record forms. In the case of electronic forms, underlying data will be stored in password protected files with strong patient identifiers kept separately from the rest of the data.

Direct Access to Source Data/Documents

The investigators will permit study-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/documents as necessary.

Quality Control and Quality Assurance

Data for this study will be entered onto an electronic database which will have built in safeguards regarding data quality. All research staff and practice staff involved in the study will be subject to quality control checks by the Primary Care Clinical Trials Unit.

The identification of any data to be recorded directly on the CRFs (i.e. no prior written or electronic record of data), and to be considered to be source data.

Source data will consist of:

Initial Survey Questionnaires

Demographics and past medical history

Current Medication

Blood pressure readings

Questionnaires from phase 2

Qualitative transcripts from phase 3

Financing and Insurance

The trial is funded by the NIHR Research from Patient Benefit Programme. Study insurance to cover negligent harm will be provided by the sponsors, the University of Birmingham. Individual medical indemnity insurance (typically by the MDU or MPS) will cover negligent harm arising from clinical care provided by participating primary care physicians. No funding is available for non negligent harm.

Publication Policy

The results from this study will be published in a peer reviewed journal. This publication and the data on which it will be based will remain independent of the funders.

9.5 ELECTRONIC INVITATION LETTER

Dear participant,

You have kindly filled in a questionnaire for this study and indicated that you would be happy for us to contact you again.

We would like to invite you to attend a study clinic held by the research team here at the surgery on xyz days between *a and b*. This will initially involve further information about the study and a discussion as to whether you would like to take part in the research. If you do decide to take part your blood pressure will be measured in three different ways (by a nurse, at home and with an automatic machine) and we will ask you to attend clinics on two further occasions.

Please read the patient information sheet which can be found at www.studyurl.bham.ac.uk that will tell you about the study and help you decide whether you may be interested in taking part.

Your username for the website is X

Because we value your potential participation and because we know that using electronic information sheets is a new way of giving out information, if we do not hear from you within 7 days of sending this email, we will send you a standard paper information sheet in the post. This is to ensure that you have got the information you have requested.

If you decide you would like to attend a study clinic at the surgery, could you please telephone the research study helpline on 0800 234 6 432 (not the surgery) to make an appointment. If you are not available at the times outlined above but would still like to take part then the researchers will do their best to make other arrangements. If you have any questions about the research and would like to talk to someone before deciding to attend a study clinic then please also telephone the study helpline (0800 234 6 432).

We would like to emphasise that you do not have to take part, and if you decide not to, your medical care will not be affected. It is also important for you to understand that even if you agree to attend the study clinic to find out more about the research, this does not commit you to taking part.

Yours sincerely,

Professor Richard McManus
Chief Investigator

9.6 PIS FOR INTERVIEWS WITH PARENT STUDY PILOT PARTICIPANTS AND RESEARCH NURSES

UNIVERSITY OF
BIRMINGHAM

Hub for Trial Methodology Research
University of Birmingham
Edgbaston
Birmingham
B15 2TT
25th March 2010

Dear participant,

I am a PhD student at the University of Birmingham, conducting research into the type and amount of information that participants want to know before they are able to make a decision about whether or not to take part in a research study. You have been invited by the research nurse from the hypertension study you are taking part in / Dr Paramjit Gill to take part in an interview.

This research is designed to look at the amount and type of information that potential research participants want to know before they agree or refuse to take part in a study. The information collected during these interviews will be used to design a new type of participant information sheet and to improve the way in which research participants are informed about research studies.

If you agree to take part, the interviews will last approximately an hour and a half. More detailed information about this study can be found in the participant information sheet, which is included with this letter.

You have been asked by your research nurse/Dr Paramjit Gill and agreed that your contact details can be provided to me. I will contact you in the next few days to ask if you are interested in taking part in an interview. If you are willing to take part I will also arrange a suitable time and place for the interview.

If you have any questions or prefer to contact me yourself, please ring Helen Kirkby on [REDACTED]

Thank you for your time,

Yours sincerely,

Miss Helen M Kirkby

PhD Student,
Hub for Trials Methodology Research,
The University of Birmingham

9.7 PROPORTIONS OF PARTICIPANTS ACCESSING EACH LEVEL OF INFORMATION FOR EACH FAQ BY AGE, GENDER AND ETHNICITY

Proportions of participants accessing each level of information for each FAQ by age

Age group	Level one			Level two			Level three		
	45-55	55-65	65+	45-55	55-65	65+	45-55	55-65	65+
Purpose of the study	10/24 (41.7%)	6/14 (42.9%)	2/6 (33.3%)	3/24 (12.5%)	1/14 (7.1%)	0/6 (0%)	1/24 (4.2%)	1/14 (7.1%)	0/6 (0%)
Have to take part	4/24 (16.7%)	2/14 (14.3)	2/6 (33.3%)	0/24 (0%)	0/14 (0%)	0/6 (0%)	0/24 (0%)	0/14 (0%)	0/6 (0%)
Why been chosen	9/24 (37.5)	5/14 (35.7%)	4/6 (66.7%)	1/24 (4.2%)	2/14 (14.3%)	1/6 (16.7%)	0/24 (0%)	1/14 (7.1%)	0/6 (0%)
Expenses	10/24 (41.7%)	8/14 (57.1%)	4/6 (66.7%)	1/24 (4.2%)	3/14 (21.4%)	1/6 (16.7%)	1/24 (4.2%)	1/14 (7.1%)	0/6 (0%)
What will happen	10/24 (41.7%)	8/14 (57.1%)	4/6 (66.7%)	2/24 (8.3%)	1/14 (7.1%)	1/6 (16.7%)	1/24 (4.2%)	0/14 (0%)	0/6 (0%)
Risks	10/24 (41.7%)	8/14 (57.1%)	4/6 (66.7%)	3/24 (12.5%)	3/14 (21.4%)	1/6 (16.7%)	1/24 (4.2%)	1/14 (7.1%)	0/6 (0%)
Benefits	9/24 (37.5%)	8/14 (57.1%)	4/6 (66.7%)	2/24 (8.3%)	2/14 (14.3%)	1/6 (16.7%)	1/24 (4.2%)	0/14 (0%)	0/6 (0%)
Problems	7/24 (29.2%)	6/14 (42.9%)	3/6 (50%)	1/24 (4.2%)	0/14 (0%)	0/6 (0%)	0/24 (0%)	0/14 (0%)	0/6 (0%)
Confidentiality	4/24 (16.7%)	4/14 (28.6%)	2/6 (33.3%)	1/24 (4.2%)	0/14 (0%)	0/6 (0%)	0/24 (0%)	0/14 (0%)	0/6 (0%)

Don't want to carry on	4/24 (16.7%)	2/14 (14.3)	1/6 (16.7%)	0/24 (0%)	0/14 (0%)	0/6 (0%)	0/24 (0%)	0/14 (0%)	0/6 (0%)
GP	5/24 (20.8%)	6/14 (42.9%)	3/6 (50%)	1/24 (4.2%)	1/14 (7.1%)	1/6 (16.7%)	1/24 (4.2%)	0/14 (0%)	0/6 (0%)
Samples	7/24 (29.2%)	4/14 (28.6%)	4/6 (66.7%)						
Genetic tests	5/24 (20.8%)	3/14 (21.4%)	2/6 (33.3%)						
Results	5/24 (20.8%)	4/14 (28.6%)	2/6 (33.3%)	2/24 (8.3%)	0/14 (0%)	1/6 (16.7%)	2/24 (8.3%)	0/14 (0%)	0/6 (0%)
Organising and funding	7/24 (29.2%)	2/14 (14.3)	2/6 (33.3%)	2/24 (8.3%)	1/14 (7.1%)	1/6 (16.7%)	2/24 (8.3%)	0/14 (0%)	0/6 (0%)
Reviewed study	4/24 (16.7%)	4/14 (28.6%)	3/6 (50%)	2/24 (8.3%)	1/14 (7.1%)	1/6 (16.7%)	2/24 (8.3%)	0/14 (0%)	0/6 (0%)
Further info and contact	4/24 (16.7%)	4/14 (28.6%)	1/6 (16.7%)						

Proportions of participants accessing each level of information for each FAQ by gender

	Level one		Level two		Level three	
	Male	Female	Male	Female	Male	Female
Purpose of the study	10/24 (41.7%)	8/20 (40.0%)	3/24 (12.5%)	1/20 (5.0%)	1/24 (4.2%)	1/20 (5.0%)
Have to take part	3/24 (12.5%)	5/20 (25.0%)	0/24 (0%)	0/20 (0%)	0/24 (0%)	0/20 (0%)
Why been chosen	9/24 (37.5%)	9/20 (45.0%)	1/24 (95.8%)	3/20 (15.0%)	0/24 (0%)	1/20 (5.0%)
Expenses	13/24 (54.2%)	9/20 (45.0%)	3/24 (12.5%)	2/20 (10.0%)	1/24 (4.2%)	1/20 (5.0%)
What will happen	13/24 (54.2%)	9/20 (45.0%)	3/24 (12.5%)	1/20 (5.0%)	0/24 (0%)	1/20 (5.0%)
Risks	12/24 (50.0%)	10/20 (50.0%)	4/24 (16.7%)	3/20 (15.0%)	0/24 (0%)	2/20 (10.0%)
Benefits	12/24 (50.0%)	9/20 (45.0%)	3/24 (12.5%)	2/20 (10.0%)	1/24 (4.2%)	0/20 (0%)
Problems	7/24 (29.2%)	9/20 (45.0%)	0/24 (0%)	1/20 (5.0%)	0/24 (0%)	0/20 (0%)
Confidentiality	4/24 (16.7%)	6/20 (30.0%)	0/24 (0%)	1/20 (5.0%)	0/24 (0%)	0/20 (0%)
Don't want to carry on	3/24 (12.5%)	4/20 (20.0%)	0/24 (0%)	0/20 (0%)	0/24 (0%)	0/20 (0%)
GP	8/24 (33.3%)	6/20 (30.0%)	2/24 (8.3%)	1/20 (5.0%)	1/24 (4.2%)	0/20 (0%)
Samples	8/24 (33.3%)	7/20 (35%)				
Genetic tests	6/24 (25.0%)	4/20 (20.0%)				
Results	7/24 (29.2%)	4/20 (20.0%)	2/24 (8.3%)	1/20 (5.0%)	1/24 (4.2%)	1/20 (5.0%)
Organising and funding	6/24 (25.0%)	5/20 (25.0%)	2/24 (8.3%)	2/20 (10.0%)	1/24 (4.2%)	1/20 (5.0%)
Reviewed study	8/24 (33.3%)	3/20 (15.0%)	2/24 (8.3%)	2/20 (10.0%)	1/24 (4.2%)	1/20 (5.0%)
Further info and contact	6/24 (25.0%)	3/20 (15.0%)				

Proportions of participants accessing each level of information for each FAQ by ethnicity

Ethnic group	Level one			Level two			Level three		
	WB	SA	BC	WB	SA	BC	WB	SA	BC
Purpose of the study	12/31 (38.7%)	1/2 (50.0%)	5/9 (55.6%)	2/31 (6.5%)	0/2 (0%)	2/9 (22.2%)	1/31 (3.2%)	0/2 (0%)	1/9 (11.1%)
Have to take part	6/31 (19.4%)	1/2 (50.0%)	1/9 (11.1%)	0/31 (0%)	0/2 (0%)	0/9 (0%)	0/31 (0%)	0/2 (0%)	0/9 (0%)
Why been chosen	14/31 (45.2%)	1/2 (50.0%)	3/9 (33.3%)	4/31 (12.9%)	0/2 (0%)	0/9 (0%)	1/31 (3.2%)	0/2 (0%)	0/9 (0%)
Expenses	15/31 (48.4%)	2/2 (100%)	5/9 (55.6%)	4/31 (12.9%)	0/2 (0%)	1/9 (11.1%)	1/31 (3.2%)	0/2 (0%)	1/9 (11.1%)
What will happen	15/31 (48.4%)	1/2 (50.0%)	6/9 (66.7%)	3/31 (9.7%)	0/2 (0%)	1/9 (11.1%)	1/31 (3.2%)	0/2 (0%)	0/9 (0%)
Risks	16/31 (51.6%)	1/2 (50.0%)	5/9 (55.6%)	5/31 (16.1%)	0/2 (0%)	2/9 (22.2%)	2/31 (6.5%)	0/2 (0%)	0/9 (0%)
Benefits	16/31 (51.6%)	1/2 (50.0%)	4/9 (44.4%)	3/31 (9.7%)	0/2 (0%)	2/9 (22.2%)	0/31 (0%)	0/2 (0%)	1/9 (11.1%)
Problems	12/31 (38.7%)	1/2 (50.0%)	3/9 (33.3%)	1/31 (3.2%)	0/2 (0%)	0/9 (0%)	0/31 (0%)	0/2 (0%)	0/9 (0%)
Confidentiality	8/31 (25.8%)	0/2 (0%)	2/9 (22.2%)	1/31 (3.2%)	0/2 (0%)	0/9 (0%)	0/31 (0%)	0/2 (0%)	0/9 (0%)
Don't want to carry on	7/31 (22.6%)	0/2 (0%)	0/9 (0%)	0/31 (0%)	0/2 (0%)	0/9 (0%)	0/31 (0%)	0/2 (0%)	0/9 (0%)
GP	11/31 (35.5%)	0/2 (0%)	3/9 (33.3%)	2/31 (6.5%)	0/2 (0%)	1/9 (11.1%)	0/31 (0%)	0/2 (0%)	1/9 (11.1%)
Samples	11/31 (35.5%)	0/2 (0%)	4/9 (44.4%)						
Genetic tests	6/31 (19.4%)	0/2 (0%)	4/9 (44.4%)						
Results	8/31 (25.8%)	0/2 (0%)	3/9 (33.3%)	2/31 (6.5%)	0/2 (0%)	1/9 (11.1%)	1/31 (3.2%)	0/2 (0%)	1/9 (11.1%)

Organising and funding	8/31 (25.8%)	1/2 (50.0%)	2/9 (22.2%)	3/31 (9.7%)	0/2 (0%)	1/9 (11.1%)	1/31 (3.2%)	0/2 (0%)	1/9 (11.1%)
Reviewed study	9/31 (29.0%)	0/2 (0%)	2/9 (22.2%)	3/31 (9.7%)	0/2 (0%)	1/9 (11.1%)	1/31 (3.2%)	0/2 (0%)	1/9 (11.1%)
Further info and contact	8/31 (25.8%)	0/2 (0%)	1/9 (11.1%)						

9.8 INFORMATION INCLUDED IN THE STREAMLINED PIS

Bp-Eth Participant Invitation Sheet

You are being invited to take part in a research study about the different ways of measuring blood pressure. Please take time to read the following information carefully and discuss it with your friends and relatives if you wish. Ask us if there is anything that is not clear or if you would like more information.

If you decide to take part you will make three visits to your GP surgery over 10 days. During that time you will be asked to have a 24 hour blood pressure monitor and take your own blood pressure for a week. The possible benefits of taking part are that your GP will be given the blood pressure measurements and offer you treatment if you need it. The possible risks of taking part are that some people find it uncomfortable to have their blood pressure measured. Any travel expenses you incur during this study will be refunded. We would like to let your GP know that you are taking part. Any problems you have during the study will be addressed.

The study will involve 800 participants. It is up to you to decide whether or not to take part and your decision will not affect your healthcare. If you decide to take part you are able to withdraw your consent to participate at any time and this will not affect your healthcare. You will be informed in a timely manner if information becomes available that may be relevant to your willingness to continue in the study.

Your taking part in this study will be kept confidential and will not be made publically available. If the results of the trial are published, your identity will remain confidential. Personal data (names and addresses) will be only accessible by authorised persons such as researchers and regulatory authorities.

You can get more information about this study by:

- Accessing the study website at **www.studywebsite.co.uk**
- Contacting Professor Richard McManus's study team on [REDACTED] to request a more detailed information sheet or to ask any specific questions that you have

9.9 APPENDIX 7 – MINUTES FROM MEETING WITH NRES EXPERT PANEL

1. What do Potential Research Participants Want To Know?

Received for information/discussion: A presentation by Ms Helen Kirkby (HK), Dr Melanie Calvert (MC), Professor Heather Draper (HDr)

- Summary: “What do potential Research participants want to know?”
- What potential research participants want to know about research: a systematic review - BMJ Open 2012;2:e000509. doi:10.1136/bmjopen-2011-000509

The panel were invited to discuss the applications of the results of this study with the researchers

Professor Draper explained that they would like to seek the panel's views on two issues:

1. The format and use of the ‘reduced’ information sheet
2. How to take this work forward

SiWo explained that as a REC vice-chair his REC frequently advised researchers to produce information sheet similar to the "reduced" information sheet presented to the panel. However, he wondered how such a patient information sheet (PIS) would fit in to the overall informed consent process. Where did the PIS sit within this process. He noted that the GMC state that in taking consent researchers “must ensure that any individuals whom you invite to take part in research are given the information which they want or ought to know, and that is presented in terms and a form that they can

understand.”⁶ The question of what the participant ought to know is an area that RECs will have an opinion on.

HDr asked, if we accept that the role of the consent interview is more important and takes precedence over the information provided in the PIS, what things must be patients know before deciding whether to take part in a piece of research. She also asked whether the "24-hour rule" might be reduced in appropriate circumstances. The panel informed HDr that allowing potential participants at least 24 hours to consider their participation had never been a "rule" nor stipulated in any guidance.

SiWo stated that patients rely on many sources of knowledge some of which they have prior to being approached to take part in research e.g. knowledge gained from being a patient etc. AG agreed stating that RECs may not always take into account the prior knowledge of the intended audience.

JS commented that the study population in the team's research was probably younger than the average clinical research participant. HK acknowledged that one of their concerns was that the use of technology might not be appropriate for many older people.

JS stated that the PIS was not as important as what is said verbally to potential participants and their relationship with the researcher/HCP. RT commented that whilst this was probably correct it highlighted the need for impartial written information to be provided.

JS felt that the issue of gaining consent had parallels with the 'paradox of enquiry' presented in Plato's Meno: "...*man cannot enquire either about that which he knows,*

⁶ GMC, Research: The Role and Responsibilities of Doctors (2002) para 19. http://www.gmc-uk.org/Research_the_role_and_responsibilities_of_doctors_2002.pdf_31588009.pdf

(NB guidance withdrawn April 2010 and replaced by 'Good practice in research and Consent to research – supplementary guidance' (04 May 2010) which now states: "You must give people the information they want or need in order to decide whether to take part in research. How much information you share with them will depend on their individual circumstances. You must not make assumptions about the information a person might want or need, or their knowledge and understanding of the proposed research project."

http://www.gmc-uk.org/static/documents/content/Research_guidance_FINAL.pdf

*or about that which he does not know; for if he knows, he has no need to enquire; and if not, he cannot; for he does not know the, very subject about which he is to enquire.*⁷ i.e. potential research participants do not know what it is they need to know. HDr agreed saying that there were circles of information: patient judgement was overlaid with what is required to be given to the patient. However, we do have a consent process whereby patients are verbally given information that it is considered necessary for them to know.

AG commented that if a REC thinks there are a core number of items that potential participants should know then that REC has to decide what they are. It might be possible that the researcher or other person taking consent might then test the participant on those core items to ensure that they have taken in the essential information. HDr agreed but felt that there would then need to be guidance on what the core items should be. If a participant did not wish to know one of those pieces of information then they might be barred from the research.

SiWo explained that he had been working recently on the concept of therapeutic misconception and noted that if patients do fail to perceive that research aims are different to the aims of treatment that at least the current governance framework means that we are dealing with well-defined and relatively "safe" research studies. Participants who took part in such studies even though they had an incomplete understanding of the true aims would at least be taking part in a relatively safe activity.

RT noted that all medicines come with an information leaflet included in the box. If something untoward happens to the patient then they immediately go to the leaflet. He felt this was similar to research information sheets in that there needed to be a document that participants could refer to when needed. SiWo noted that there are occasions where clinical trials will have very serious side effects and asked whether we can really afford for patients not to be made aware about such things. RT agreed and felt that this is where the interview process comes in.

RT felt one of the main issues was one of "trust". He felt that patients in this country particularly are still very trusting of their healthcare professionals, not as much as they once were still more than in other countries. This culture of trust was still very important factor in a patient's decision to take part or not in research as they will tend to trust an invitation coming from their doctor or other healthcare professional.

NT was concerned that the research presented to the panel involved a lower risk study and that there was a real danger in extrapolating from this to other higher risk studies. In addition, he felt that not everybody would be able to access the extra layers of information provided through the Internet. He stated that he felt the purpose of a PIS was for future referral and also as a "legal" document to prove that the researchers have provided the necessary information to the participant.

⁷ <http://classics.mit.edu/Plato/meno.html>

HDr asked whether the panel thought that RECs would be happy if the use of streamlined information was applied to higher risk studies. She added that the more complex the study the more likely patients are to return to the study information and that by using an Interactive Information Sheet (IIS) it would be possible to track exactly what information they are accessing and how often.

NT stated that he understood where Prof Draper's team were coming from but felt it was important to note that RECs do constantly ask for information sheets to be simplified. FW agreed but felt that information sheets still required a number of essential items. NT agreed but felt that these could be much shorter for low-risk information sheets.

AT stated that in his opinion information sheets are primarily intended to provide protection for the pharmaceutical industry. The reason that 20 page information sheets are produced by pharma companies was so that they can avoid being sued for not providing sufficient information.

AG noted that RECs would often use the information sheet as a test of whether the researcher was able to communicate effectively. An incomprehensible information sheet would invite the REC to question whether the researcher would be able to communicate the necessary information to the patient verbally.

HD congratulated the team on the work and stated that he would be very happy to work with them to take this work forward. He suggested that at this stage it might be sensible to collect more data in high risk studies regarding what information patients are actually using before going on to conduct a randomised trial of different PIS formats. He also thought that they might usefully talk to Pfizer as they were currently in the process of setting up studies using Internet-based information. HD also noted that Jane Kaye was looking at similar areas and referred Prof Draper's team to her recent article in 'Nature Reviews Genetics 13, 371-376 (May 2012), doi:10.1038/nrg3218 "From patients to partners: participant-centric initiatives in biomedical research"⁸ he also felt it might be useful to discuss this with the EFGCP in order to investigate proceeding with this work as there were a large number of people in Europe who would be interested. He suggested they contact Jan Geissler at EFGCP (<http://www.efgcp.be/Bio.asp?membid=753>).

RT also suggested that they might like to talk to INVOLVE about this work and how to take it forward.

HDr asked whether the panel thought they would be able to get REC approval for such studies. AG felt that the use of IISs might be extended to higher risk studies provided that appropriate safeguards were put in place such to ensure that all participants have real access to the full information if they required it. An easy way to

⁸ <http://www.nature.com/nrg/journal/v13/n5/abs/nrg3218.html>

initially simplify and stratify information provided would be to separate the information along the lines of the current part one and part two sections of the NRES standard information sheet format. Information regarding insurance, confidentiality etc might be separated out into a separate layer of information that could be accessed if required. AG felt that whilst there was clearly a risk in trialling the use of reduced information he also noted that it was in line with NRES' wish to produce more evidence-based guidance.

HD suggested that it might be useful if they attend the EFGCP Annual Conference in Brussels on 29 & 30 January 2013 entitled "Virtual Future: what are the ethical dimensions of using emerging technologies in clinical trials and research?".

10 REFERENCE LIST

- (1) Joffe S, Cook EF, Cleary PD, Clark JW, Weeks JC. Quality of informed consent: a new measure of understanding among research subjects. *Journal of the National Cancer Institute* 2001; 93(2):139-147.
- (2) General Medical Council. Seeking patients' consent: The ethical considerations. GB_1999:10488;GB. 1998.
- (3) Hewlett S. Consent to clinical research--adequately voluntary or substantially influenced? *Journal of Medical Ethics* 1996; 22(4):232-237.
- (4) Royal College of Nursing. Informed consent in Health and Social Care Research. www.rcn.org.uk.ezproxye.bham.ac.uk/data/assets/pdf_file/0010/78607/002267.pdf Last accessed 10-9-2012
- (5) Legislation.gov.uk. Mental Capacity Act 2005. <http://www.legislation.gov.uk/ukpga/2005/9/contents> [2005 [cited 2011 Mar. 15]; Available from: URL:<http://www.legislation.gov.uk/ukpga/2005/9/contents>
- (6) Antoniou E, Draper H, Reed K, Burls A, Southwood T, Zeegers M. An empirical study on the preferred size of the participant information sheet in research. *Journal of Medical Ethics* 2011; 37:559-562.
- (7) ICH Expert Working Group. ICH Harmonised Tripartite Guideline; Guideline for Good Clinical Practice E6(R1). 10-6-1996. 28-6-0012.
- (8) World Health Organisation. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products. 850. 1995.
- (9) European Medicines Agency. ICH Topic E6 (R1) Guideline for Good Clinical Practice. CPMP/ICH/135/95. 2002.
- (10) The European Parliament and the Council of the European Union. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. L 121/34. 2001.
- (11) The Council for International Organisations of Medical Sciences (CIOMS) in collaboration with the World Health Organisation (WHO). International Ethical Guidelines for Biomedical Research Involving Human Subjects. 2002.

- (12) Faden R, Beauchamp TL. A History and theory of informed consent. 1 ed. New York: Oxford University Press Inc; 1986.
- (13) Stoljar N. Theories of Autonomy. In: Ashcroft R, Dawson A, Draper H, McMillan JR, editors. Principles of health Care Ethics. Second ed. Chichester: John Wiley & Sons Ltd; 2007. 11-17.
- (14) McLean S. Autonomy, Consent and the Law. 1 ed. Oxon: Routledge-Cavendish; 2010.
- (15) Manson N. Consent and Informed Consent. In: Ashcroft R, Dawson A, Draper.H, McMillan JR, editors. Principles of Health Care Ethics. Second ed. Chichester: John Wiley & Sons Ltd; 2007. 298-303.
- (16) Idanpaan-Heikkila JE. WHO guidelines for good clinical practice (GCP) for trials on pharmaceutical products: responsibilities of the investigator. *Annals of Medicine* 1994; 26(2):89-94.
- (17) The Dudley Group of Hospitals NHS Trust. Policy for taking and documenting informed consent for research studies. 2009.
- (18) The Hillingdon Hospitals NHS Foundation Trust. SOP: Taking Informed Consent. 2.0. 1-8-2011.
- (19) Wirral University Teaching Hospital NHS Foundation Trust. SOP: Informed Consent. SOP007. 5-11-2009.
- (20) National Research Ethics Service. After applying/gaining ethical approval: Do I need to re-consent participants if I have amended the Participant Information Sheet or Consent Form? <http://www.nres.nhs.uk/applications/faq/after-applying/#FAQsAfterReconsent> . 2012. Last accessed 29-8-2012.
- (21) Doyal L, Tobias J. Informed Consent in Medical Research. 1st ed. London: BMJ Books; 2001.
- (22) National Patient Safety Agency, National Research Ethics Service. Information Sheets and Consent Forms Guidance For Researchers and Reviewers. 2009.
- (23) Wager E, Tooley PJ, Emanuel MB, Wood SF. How to do it. Get patients' consent to enter clinical trials. *BMJ* 1995; 311(7007):734-737.
- (24) Freedman B. A Moral Theory of Informed Consent. *The Hastings Center Report* 2011; 5(4):32-39.

- (25) Meisel A, Kuczewski M. Legal and ethical myths about informed consent. *Archives of Internal Medicine* 1996; 156(22):2521-2526.
- (26) Lantos J. Informed consent. The whole truth for patients? *Cancer* 1993; 72(9:Suppl):Suppl-5.
- (27) Birnbaum M, Mellers B. Mediated Models for the Analysis of Confounded Variables and Self-Selected Samples. *Journal of Educational Statistics* 1989; 14(2):146-158.
- (28) ICH. ICH Harmonised Tripartite Guideline: General Considerations for Clinical Trials E8. 17-7-1997.
- (29) Jonas M. Competence to Consent. In: Ashcroft R, Dawson A, Draper H, McMillan J, editors. *Principles of Health Care Ethics*. Second ed. Chichester: John Wiley & Sons Ltd; 2007. 254-261.
- (30) Mental Capacity Act Working Party. Conducting research with people not having the capacity to consent to their participation. A practical guide for researchers. 2008. The British Psychological Society 2008.
- (31) Welie J, Wlie S. Patient decision making competence: Outlines of a conceptual analysis. *Medicine, Health Care and Philosophy* 2001; 4:127-138.
- (32) Doyal L. Informed consent: moral necessity of illusion? *Quality in Health Care* 2001; 10(Suppl I):i29-i33.
- (33) Legislation.gov.uk. Mental Capacity Act 2005 Explanatory Notes. 2005. Crown.
- (34) Hockton A. The law of consent to medical treatment. 1 ed. London: Sweet and Maxwell Limited; 2002.
- (35) World Medical Association. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. 2008.
- (36) Edwards SJ. Research participation and the right to withdraw. *Bioethics* 2005; 19(2):112-130.
- (37) Department of Health. Good practice in consent implementation guide: consent to examination or treatment. 2001.
- (38) Quill TE, Brody H. Physician recommendations and patient autonomy: finding a balance between physician power and patient choice. *Annals of Internal Medicine* 1996; 125(9):763-769.
- (39) Tattersall M. Examining informed consent to cancer clinical trials. *The Lancet* 2001; 358(9295):1742-1743.

- (40) Jenson A, Madsen B, Anderson P, Rose C. Information for cancer patients entering a clinical trial - an evaluation of an information strategy. *European Journal of Cancer* 1993; 29(16):2235-2238.
- (41) Brown R, Butow P, Ellis P, Boyle F, Tattersall M. Seeking informed consent to cancer clinical trials: describing current practice. *Social Science and Medicine* 2004; 58(12):2445-2457.
- (42) Medicines for Human Use (Clinical Trials) Regulations 2004. 1031. 1-5-2004.
- (43) Medicines for Human Use (Clinical Trials) Amendment Regulations 2006. 1928. 2006.
- (44) Medicines for Human use (Clinical Trials) Amendment No. 2 regulations 2006. 2984. 2006.
- (45) Medicines for Human use (Clinical Trials) and Blood Safety and Quality (Amendment) Regulations 2008. 941. 2008.
- (46) Carome M, Grodin M, King N, Churchill L, Tenery R. Letters to the Editor: Is Informed Consent Always Necessary for Randomized, Controlled Trials. *The New England Journal of Medicine* 1999;(340):804-807.
- (47) Chwang E. A puzzle about consent in research and in practice. *Journal of Applied Philosophy* 2010; 27(3):258-272.
- (48) Freedman B. Equipoise and the Ethics of Clinical Research. *The New England Journal of Medicine* 1987;(317):141-145.
- (49) Truog R, Robinson W, Randolph A. Is informed consent always necessary for randomized, controlled trials? *The New England Journal of Medicine* 1999; 340(10):804-807.
- (50) ICH. ICH: harmonisation for better health. www.ich.org . 2012. Last accessed 29-8-2012.
- (51) ICH. FAQs: ICH Objectives. www.ich.org/about/faqs.html . 2012. Last accessed 29-8-2012.
- (52) Sugarman J, McCrory DC, Powell D, Krasny A, Adams B, Ball E et al. Empirical research on informed consent. An annotated bibliography. *Hastings Center Report* 1999; 29(1):S1-42.
- (53) Hawkins M. Early Cancer Clinical Trials: Safety, Numbers, and Consent. *Journal of the National Cancer Institute* 1993; 85(20):1618-1619.

- (54) Kenny T, Wilson RG, Purves IN, Clark J, Sr., Newton LD, Newton DP et al. A PIL for every ill? Patient information leaflets (PILs): a review of past, present and future use. *Family Practice* 1998; 15(5):471-479.
- (55) Paasche-Orlow MK, Taylor HA, Brancati FL. Readability standards for informed-consent forms as compared with actual readability. *The New England Journal of Medicine* 2003; 3(348):721-726.
- (56) Terblanche M, Burgess L. Examining the readability of patient-informed consent forms. *Open Access Journal of Clinical Trials* 2010; 2:157-162.
- (57) Stead M, Eadie D, Gordon D, Angus K. "Hello, hello--it's English I speak!": a qualitative exploration of patients' understanding of the science of clinical trials. *Journal of Medical Ethics* 2005; 31(11):664-669.
- (58) Kang EY, Fields HW, Kiyak A, Beck FM, Firestone AR. Informed consent recall and comprehension in orthodontics: Traditional vs improved readability and processability methods. *American Journal of Orthodontics and Dentofacial Orthopedics* 2009; 136(4).
- (59) Dawson A. What should we do about it? Implications of the Empirical Evidence in Relation to Comprehension and Acceptability of Randomisation. In: Holm S, Jonas M, editors. *Engaging the World: The use of Empirical Research in Bioethics and the Regulation of Biotechnology*. 1 ed. Amsterdam: IOS Press; 2004. 41-53.
- (60) Behrendt C, Golz T, Roesler C, Bertz H, Wunsch A. What do our patients understand about their trial participation? Assessing patients' understanding of their informed consent consultation about randomised clinical trials. *Journal of Medical Ethics* 2011; 37:74-80.
- (61) Marshall PA, Adebamowo CA, Adeyemo AA, Ogundiran TO, Vekich M, Strenski T et al. Voluntary participation and informed consent to international genetic research. *American Journal of Public Health* 2006; 96(11):1989-1995.
- (62) Joseph P, Schackman BR, Horwitz R, Nerette S, Verdier RI, Dorsainvil D et al. The use of an educational video during informed consent in an HIV clinical trial in Haiti. *Journal of Acquired Immune Deficiency Syndromes: JAIDS* 2006; 42(5):588-591.
- (63) Davis TC, Holcombe RF, Berkel HJ, Pramanik S, Divers SG. Informed consent for clinical trials: a comparative study of standard versus simplified forms. *Journal of the National Cancer Institute* 1998; 90(9):668-674.
- (64) Flory J, Emanuel E. Interventions to improve research participants' understanding in informed consent for research: a systematic review. *JAMA* 2004; 292(13):1593-1601.

- (65) Cohn E, Larson E. Improving participant comprehension in the informed consent process. *Journal of Nursing Scholarship* 2007; 39(3):273-280.
- (66) Freer Y, McIntosh N, Teunisse S, Anand KJ, Boyle EM. More information, less understanding: a randomized study on consent issues in neonatal research. *Pediatrics* 2009; 123(5):1301-1305.
- (67) Yuval R, Halon DA, Merdler A, Khader N, Karkabi B, Uziel K et al. Patient comprehension and reaction to participating in a double-blind randomized clinical trial (ISIS-4) in acute myocardial infarction. *Archives of Internal Medicine* 2000; 160(8):1142-1146.
- (68) Joffe S, Cook F, Cleary PD, Clark JW, Weeks JC. Quality of informed consent in cancer clinical trials: a cross sectional survey. *The Lancet* 2001; 358:1772-1777.
- (69) Daugherty C, Ratain MJ, Grochowski E, Stocking C, Kodish E, Mick R et al. Perceptions of cancer patients and their physicians involved in phase I trials. *Journal of Clinical Oncology* 1995; 13(5):1062-1072.
- (70) Tait AR, Voepel-Lewis T, Robinson A, Malviya S. Priorities for disclosure of the elements of informed consent for research: a comparison between parents and investigators. *Paediatric Anaesthesia* 2002; 12(4):332-336.
- (71) Lynoe N, Sandlund M, Dahlqvist G, Jacobsson L. Informed consent: study of quality of information given to participants in a clinical trial. *BMJ* 1991; 303(6):610-613.
- (72) Agre P, Campbell FA, Goldman BD, Boccia ML, Kass N, McCullough LB et al. Improving informed consent: the medium is not the message. *Irb: a Review of Human Subjects Research Suppl* 25(5):S11-S19, 2003 Sep-Oct 2003;(5):S11-S19.
- (73) Benson PR, Roth LH, Appelbaum PS, Lidz CW, Winslade WJ. Information disclosure, subject understanding, and informed consent in psychiatric research. *Law & Human Behavior* 1988; 12(4):455-475.
- (74) Fureman I, Meyers K, McLellan AT, Metzger D, Woody G. Evaluation of a video-supplement to informed consent: injection drug users and preventive HIV vaccine efficacy trials. *AIDS Education & Prevention* 1997; 9(4):330-341.
- (75) Weston J, Hannah M, Downes J. Evaluating the benefits of a patient information video during the informed consent process. *Patient Education & Counseling* 1997; 30(3):239-245.
- (76) Agre P, Rapkin B. Improving informed consent: a comparison of four consent tools. *Irb: a Review of Human Subjects Research* 2003; 25(6):1-7.

- (77) Dunn LB, Lindamer LA, Palmer BW, Golshan S, Schneiderman LJ, Jeste DV. Improving understanding of research consent in middle-aged and elderly patients with psychotic disorders. *American Journal of Geriatric Psychiatry* 2002; 10(2):142-150.
- (78) Llewellyn-Thomas HA, Thiel EC, Sem FW, Woermke DE. Presenting clinical trial information: a comparison of methods. *Patient Education & Counseling* 1995; 25(2):97-107.
- (79) Bjorn E, Rossel P, Holm S. Can the written information to research subjects be improved?--an empirical study. *Journal of Medical Ethics* 1999; 25(3):263-267.
- (80) Stiles PG, Poythress NG, Hall A, Falkenbach D, Williams R. Improving understanding of research consent disclosures among persons with mental illness. *Psychiatric Services* 2001; 52(6):780-785.
- (81) Young DR, Hooker DT, Freeberg FE. Informed consent documents: increasing comprehension by reducing reading level. *Irb: a Review of Human Subjects Research* 1990; 12(3):1-5.
- (82) Taub HA. Informed consent, memory and age. *Gerontologist* 1980; 20(6):686-690.
- (83) Taub HA, Baker MT, Kline GE, Sturr JF. Comprehension of informed consent information by young-old through old-old volunteers. *Experimental Aging Research* 1987; 13(4):173-178.
- (84) Taub HA, Baker MT, Sturr JF. Informed consent for research. Effects of readability, patient age, and education. *Journal of the American Geriatrics Society* 1986; 34(8):601-606.
- (85) Coyne CA, Xu R, Raich P, Plomer K, Dignan M, Wenzel LB et al. Randomized, controlled trial of an easy-to-read informed consent statement for clinical trial participation: a study of the Eastern Cooperative Oncology Group. *Journal of Clinical Oncology* 2003; 21(5):836-842.
- (86) Murphy DA, O'Keefe ZH, Kaufman AH. Improving comprehension and recall of information for an HIV vaccine trial among women at risk for HIV: reading level simplification and inclusion of pictures to illustrate key concepts. *AIDS Education and Prevention* 1999; 11(5):389-399.
- (87) Dresden GM, Levitt MA. Modifying a standard industry clinical trial consent form improves patient information retention as part of the informed consent process. *Academic Emergency Medicine* 2001; 8(3):246-252.
- (88) Epstein LC, Lasagna L. Obtaining informed consent. Form or substance. *Archives of Internal Medicine* 1969; 123(6):682-688.

- (89) Rogers CG, Tyson JE, Kennedy KA, Broyles RS, Hickman JF. Conventional consent with opting in versus simplified consent with opting out: an exploratory trial for studies that do not increase patient risk. *Journal of Pediatrics* 1998; 132(4):606-611.
- (90) Guarino P, Elbourne D, Carpenter J, Peduzzi P. Consumer involvement in consent document development: a multicenter cluster randomized trial to assess study participants' understanding. *Clinical Trials* 2006; 3(1):19-30.
- (91) Aaronson NK, Visser-Pol E, Leenhouts GH, Muller MJ, van der Schot AC, van Dam FS et al. Telephone-based nursing intervention improves the effectiveness of the informed consent process in cancer clinical trials. *Journal of Clinical Oncology* 1996; 14(3):984-996.
- (92) Kucia AM, Horowitz JD. Is informed consent to clinical trials an "upside selective" process in acute coronary syndromes? *American Heart Journal* 2000; 140(1):94-97.
- (93) Fitzgerald DW, Marotte C, Verdier RI, Johnson WD, Pape JW. Comprehension during informed consent in a less-developed country. *Lancet* 2002; 360(9342):1301-1302.
- (94) Tindall B, Forde S, Ross MW, Goldstein D, Barker S, Cooper DA. Effects of two formats of informed consent on knowledge amongst persons with advanced HIV disease in a clinical trial of didanosine. *Patient Education & Counseling* 1994; 24(3):261-266.
- (95) Taub HA, Kline GE, Baker MT. The elderly and informed consent: effects of vocabulary level and corrected feedback. *Experimental Aging Research* 1981; 7(2):137-146.
- (96) Taub HA, Baker MT. The effect of repeated testing upon comprehension of informed consent materials by elderly volunteers. *Experimental Aging Research* 1983; 9(3):135-138.
- (97) Wirshing DA, Wirshing WC, Marder SR, Liberman RP, Mintz J. Informed consent: assessment of comprehension. *American Journal of Psychiatry* 1998; 155(11):1508-1511.
- (98) Coletti AS, Heagerty P, Sheon AR, Gross M, Koblin BA, Metzger DS et al. Randomized, controlled evaluation of a prototype informed consent process for HIV vaccine efficacy trials. *Journal of Acquired Immune Deficiency Syndromes: JAIDS* 2003; 32(2):161-169.
- (99) Rikkert MG, van den Bercken JH, ten Have HA, Hoefnagels WH. Experienced consent in geriatrics research: a new method to optimize the capacity to consent in frail elderly subjects. *Journal of Medical Ethics* 1997; 23(5):271-276.

- (100) Carpenter WT, Jr., Gold JM, Lahti AC, Queern CA, Conley RR, Bartko JJ et al. Decisional capacity for informed consent in schizophrenia research. *Archives of General Psychiatry* 2000; 57(6):533-538.
- (101) Office for National Statistics. Statistical bulletin: Internet Access Quarterly Update, 2012 Q2. 2012.
- (102) Office for National Statistics. Statistical bulletin: Internet Access - Households and Individuals 2012. 24-9-2012.
- (103) Office for National Statistics. EFS/FES Percentage of Households with home access to the Internet (UK): Household Internet Access. 2005.
- (104) Singer G, Pruulmann-Vengerfeldt P, Norbistrath U, Lewandowski D. The relationship between Internet user type and user performance when carrying out simple vs. complex search tasks. *First Monday* 2012; 17(6).
- (105) Powell J, Inglis N, Ronnie J, Large S. The Characteristics and Motivations of Online Health Information Seekers: Cross Sectional Survey and Qualitative Interview Study. *Journal of Medical Internet Research* 2011; 13(1):1.
- (106) Atkinson N, Saperstein S, Pleis J. Using the Internet for Health-Related Activities: Findings From a National Probability Sample. *Journal of Medical Internet Research* 2009; 11(1):1.
- (107) U.S.National Library of Medicine National Institutes of Health. PubMed. <http://www.ncbi.nlm.nih.gov/pubmed/> . 2011. Last accessed 23-5-2011.
- (108) John Wiley & Sons L. The Cochrane Library. <http://www.thecochranelibrary.com/view/0/index.html> . 2011. Last accessed 23-5-2011.
- (109) ProQuest. ASSIA: Applied Social Sciences Index and Abstracts on the Web. <http://www.csa.com/factsheets/assia-set-c.php> . 2011. Last accessed 23-5-2011.
- (110) GretNet International. Grey Literature Network Service. <http://www.greynet.org/> . 2011. Last accessed 23-5-2011.
- (111) NHS National Patient Safety Agency. National Research Ethics Service. <http://www.nres.npsa.nhs.uk/> . 2011. Last accessed 23-5-2011.
- (112) Paul J, Seib R, Prescott T. The Internet and Clinical Trials: Background, Online Resources, Examples and Issues. *Journal of Medical Internet Research* 2005; 7(1):1-10.

- (113) National Institutes of Health. ClinicalTrials.gov. <http://www.clinicaltrials.gov/> . 2011. Last accessed 11-5-2011.
- (114) CenterWatch. Resources for Patients and Families: Find Clinical Trials. <http://www.centerwatch.com/> . 2011. Last accessed 11-5-2011.
- (115) Cancer Research UK. Trials and Research. www.cancerhelp.org.uk/trials/ . 2011. Last accessed 11-5-2011.
- (116) NHS. Clinical trials and medical research - Clinical trials. <http://www.nhs.uk/Conditions/Clinical-trials/Pages/clinical-trial.aspx> . 2011. Last accessed 11-5-2011.
- (117) Bramstedt K. Recruiting Healthy Volunteers for Research Participation via Internet Advertising. *Clinical Medicine & Research* 2007; 5(2):91-97.
- (118) McAlindon T, Formica M, Kabbara K, LaValley M, Lehmer M. Conducting clinical trials over the internet: feasibility study. *British Medical Journal* 2003; 327:484-487.
- (119) Townsend A, Amarsi Z, Backman C, Cox S, Li C. Communications Between Volunteers and Health Researchers during Recruitment and Informed Consent: Qualitative Content Analysis of Email Interactions. *Journal of Medical Internet Research* 2011; 13(4):e84.
- (120) Soetikno RM, Mrad R, Pao V, Lenert LA. Quality-of-life research on the Internet: feasibility and potential biases in patients with ulcerative colitis. *Journal of the American Medical Informatics Association* 1997; 4(6):426-435.
- (121) McAlidon T, Formica M, LaValley M, Lehmer M, Kabbara K. Effectiveness of glucosamine for symptoms of knee osteoarthritis: Results from an internet-based randomized double-blind controlled trial. *The American Journal of Medicine* 2004; 117(9):643-649.
- (122) Jacobs BP, Bent S, Tice JA, Blackwell T, Cummings SR. An internet-based randomized, placebo-controlled trial of kava and valerian for anxiety and insomnia. *Medicine* 2005; 84(4):197-207.
- (123) Formica M, Kabbara K, Clark R, McAlidon T. Can Clinical Trials Requiring Frequent Participant Contact Be Conducted Over the Internet? Results From an Online Randomized Controllet Trial Evaluating a Topical Ointment for Herpes Labialis. *Journal of Medical Internet Research* 2004; 6(1):e6.
- (124) Jamsa K, Klander L. Verifying Information Sources Using Digital Signatures. Hacker proof: the ultimate guide to network security. New York: OnWord Press; 2011. 151-158.

- (125) Legislation.gov.uk. Electronic Communications Act 2000. 2000.
- (126) Kaye J, Curren L, Anderson N, Edwards K, Fullerton SM, Kanellopoulou N et al. From patients to partners: participant-centric initiatives in biomedical research. *Nature Reviews Genetics* 2012; 13:371-376.
- (127) Kelly M, Oldham J. The Internet and randomised controlled trials. *International Journal of Medical Informatics* 1997;(47):91-99.
- (128) Kiesler S, Sproull L. Response Effects in the Electronic Survey. *The Public Opinion Quarterly* 1986; 50(3):402-413.
- (129) Sproull L. Using Electronic Mail for Data Collection in Organizational Research. *The Academy of Management Journal* 1986; 29(1):159-169.
- (130) Schleyer TK, Forrest JL. Methods for the design and administration of web-based surveys. *Journal of the American Medical Informatics Association* 2000; 7(4):416-425.
- (131) Eysenbach G, Wyatt J. Using the Internet for surveys and health research. *Journal of Medical Internet Research* 4(2):E13-Nov.
- (132) McFarland S. Effects of Question Order on Survey Responses. *Public Opinion Quarterly* 1981; 45:208-215.
- (133) Pealer LN, Weiler RM, Pigg RM, Jr., Miller D, Dorman SM. The feasibility of a web-based surveillance system to collect health risk behavior data from college students. *Health Education & Behavior* 2001; 28(5):547-559.
- (134) Tourangeau R, Smith T. Asking Sensitive Questions: The Impact of Data Collection Mode, Question Format, and Question Context. *The Public Opinion Quarterly* 1996; 60(2):275-304.
- (135) Watt J. Internet Systems for Evaluation Research. *New Directions for Evaluation* 1999; 84:23-34.
- (136) Brogger J, Nystad W, Cappelen I, Bakke P. No Increase in Response Rate by Adding a Web Response Option to a Postal Population Survey: A Randomized Trial. *Journal of Medical Internet Research* 2011; 9(5):1-7.
- (137) Eysenbach G. Improving the Quality of Web Surveys: The Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *Journal of Medical Internet Research* 2004; 6(3):e34.
- (138) Kongsved S, Basnov M, Holm-Christensen K, Hjollund N. Response Rate and Completeness of Questionnaires: A Randomized Study of Internet Versus Paper-and-Pencil Versions. *J Med Internet Res* 2007; 9(3):e25.

- (139) Yun G, Trumbo C. Comparative Response to a Survey Executed by Post, E-Mail, and Web Form. *Journal of Computer-Mediated Communication* 2000; 6(1):0.
- (140) Buchanan T, Smith J. Using the Internet for psychological reserach: Personality testing on the World Wide Web. *British Journal of Psychology* 1999; 90:125-144.
- (141) Gosling S, Vazire S, Sricastava S, John O. Should We Trust Web-Based Studies? A Comparative Analysis of Six Preconceptions About Internet Questionnaires. *American Psychologist* 2004; 59(2):93-104.
- (142) Ritter P, Lorig K, Laurent D, Matthews K. Internet Versus Mail Questionnaires: A Randomized Comparison. *J Med Internet Res* 2004; 6(3):e29.
- (143) Wolters Kluwer. Ovid Medline. <http://ovidsp.tx.ovid.com.ezproxye.bham.ac.uk/sp-3.6.0b/ovidweb.cgi?&S=LFOJFPIKENDDBMNENCPKOCDCOAONAAA00&New+Database=Single%7c22> . 2012. Last accessed 29-8-2012.
- (144) Thomson Reuters. Web of Science. http://apps.webofknowledge.com.ezproxye.bham.ac.uk/WOS_GeneralSearch_input.do?product=WOS&search_mode=GeneralSearch&SID=N1il2kk4BKlfk2l1@Oj&preferencesSaved . 2012. Last accessed 29-8-2012.
- (145) ProQuest. Applied Social Sciences Index and Abstracts (ASSIA). <http://search.proquest.com.ezproxye.bham.ac.uk/assia/index?accountid=8630> . 2012. Last accessed 29-8-2012.
- (146) ProQuest. Sociological Abstracts. <http://search.proquest.com.ezproxye.bham.ac.uk/socabs?accountid=8630> . 2012. Last accessed 29-8-2012.
- (147) Wolters Kluwer. Health Management Information Consortium (HMIC). <http://ovidsp.tx.ovid.com.ezproxye.bham.ac.uk/sp-3.6.0b/ovidweb.cgi> . 2012. Last accessed 29-8-2012.
- (148) The Cochrane Collaboration. The Cochrane Library. www.thecochranelibrary.com.ezproxye.bham.ac.uk/view/0/index.html . 2012. Last accessed 29-8-2012.
- (149) Expert Information Ltd. Index to Theses. <http://www.theses.com.ezproxye.bham.ac.uk/> . 2012. Last accessed 29-8-2012.

- (150) Open Grey. System for Information in Grey Literature in Europe. www.opengrey.eu/ . 2012. Last accessed 29-8-2012.
- (151) Slovak Centre of Scientific and Technical Information (CVTISR), EBSCO Publishing (USA), FEDLINK, Library of Congress (USA), INIST-CNRS (France), The New York Academy of Medicine (USA) et al. GreyNet: Gret Literature Network Service. www.greynet.org . 2012. Last accessed 29-8-2012.
- (152) NHS. NHS Evidence Health Information Resources. www.library.nhs.uk/mylibrary/ . 2012. Last accessed 29-8-2012.
- (153) University of Birmingham. University of Birmingham Research Archive (UBIRA). <http://ubira.bham.ac.uk/> . 2012. Last accessed 29-8-2012.
- (154) iProspect. iProspect Search Engine User Behavior Study. 2006. iProspect.com, Inc.
- (155) Viera A, Garrett J. Understanding Interobserver Agreement: The Kappa Statistic. *Family Medicine* 2005; 37(5):360-363.
- (156) Kacmarek RM. Should noninvasive ventilation be used with the do-not-intubate patient? *Respiratory Care* 229; 54(2):223-229.
- (157) La Fond JQ, Winick BJ. Sex offender reentry courts: a cost effective proposal for managing sex offender risk in the community. *Annals of the New York Academy of Sciences* 352; 989:300-323.
- (158) Willison DJ, Steeves V, Charles C, Schwartz L, Ranford J, Agarwal G et al. Consent for use of personal information for health research: do people with potentially stigmatizing health conditions and the general public differ in their opinions? *BMC Medical Ethics* 2009; 10:10.
- (159) Maslin A. A survey of the opinions on 'informed consent' of women currently involved in clinical trials within a breast unit. *European Journal of Cancer Care* 1994; 3(4):153-162.
- (160) Walkup J, Bock E. What do prospective research participants want to know? What do they assume they know already? *Journal of Empirical Research on Human Research Ethics* 2009; 4(2):59-63.
- (161) Bento SF, Hardy E, Osis MJ. Process for obtaining informed consent: women's opinions. *Developing World Bioethics* 2008; 8(3):197-206.
- (162) Casarett D, Karlawish J, Sankar P, Hirschman KB, Asch DA. Obtaining informed consent for clinical pain research: patients' concerns and information needs. *Pain* 2001; 92(1-2):71-79.

- (163) Sand K, Loge JH, Berger O, Gronberg BH, Kaasa S. Lung cancer patients' perceptions of informed consent documents. *Patient Education and Counseling* 2008; 73(2):313-317.
- (164) Hutchinson A, Rubinfeld AR. Financial disclosure and clinical research: what is important to participants? *Medical Journal of Australia* 2008; 189(4):207-209.
- (165) Gray SW, Hlubocky FJ, Ratain MJ, Daugherty CK. Attitudes toward research participation and investigator conflicts of interest among advanced cancer patients participating in early phase clinical trials. *Journal of Clinical Oncology* 2007; 25(23):3488-3494.
- (166) Grady C, Horstmann E, Sussman JS, Hull SC. The limits of disclosure: what research subjects want to know about investigator financial interests. *Journal of Law, Medicine & Ethics* 2000; 34(3):592-599.
- (167) Hampson LA, Agrawal M, Joffe S, Gross CP, Verter J, Emanuel EJ. Patients' views on financial conflicts of interest in cancer research trials. *New England Journal of Medicine* 2006; 355(22):2330-2337.
- (168) Weinfurt KP, Friedman JY, Allsbrook JS, Dinan MA, Hall MA, Sugarman J. Views of potential research participants on financial conflicts of interest: barriers and opportunities for effective disclosure. *Journal of General Internal Medicine* 2006; 21(9):901-906.
- (169) Kim SY, Millard RW, Nisbet P, Cox C, Caine ED. Potential research participants' views regarding researcher and institutional financial conflicts of interest. *Journal of Medical Ethics* 2004; 30(1):73-79.
- (170) Harrison G, Rutstrom E. Experimental Evidence on the Existence of Hypothetical Bias in Value Elicitation Methods. In: Plott C, Smith V, editors. *Handbook of Experimental Economics Results*. 1 ed. Elsevier B.V.; 2008. 752-767.
- (171) Onwujekwe O, Khukwuogo O, Ezeoke U, Uzochukwu B, Eze S. Asking people directly about preferred health-seeking behaviour yields invalid response: an experiment in south-east Nigeria. *Journal of Public Health* 2010; 33(1):93-100.
- (172) Cummings R, Harrison G, Rutstrom E. Homegrown Values and Hypothetical Surveys: Is the Dichotomous Choice Approach Incentive-Compatible? *The American Economic Review* 1995; 85(1):260-266.
- (173) Dixon-Woods M, Ashcroft RE, Jackson CJ, Tobin MD, Kivits J, Burton PR et al. Beyond 'misunderstanding': Written information and decisions about taking part in a genetic epidemiology study. *Social Science & Medicine* 2007; 65(11):2212-2222.

- (174) Kirkby H, Calvert M, Darper H, Keeley T, Wilson S. What research participants want to know about research: a systematic review. *BMJ Open* 2012.
- (175) Eng J. Sample size estimation: how many individuals should be studied? *Radiology* 2003; 227(2):309-313.
- (176) Florey CD. Sample size for beginners. *BMJ* 1993; 306(6886):1181-1184.
- (177) Torgerson DJ, Miles JN. Simple sample size calculation. *Journal of Evaluation in Clinical Practice* 2007; 13(6):952-953.
- (178) Scales DC, Rubenfeld GD. Estimating sample size in critical care clinical trials. *Journal of Critical Care* 2005; 20(1):6-11.
- (179) Kirkby H, Wilson S, Calvert M, Draper H. Using e-mail recruitment and an online questionnaire to establish effect size: A worked example. *BMC Medical Research Methodology* 2011; 11(89).
- (180) Dunn KM, Jordan K, Lacey RJ, Shapley M, Jinks C. Patterns of consent in epidemiologic research: evidence from over 25,000 responders. *American Journal of Epidemiology* 2004; 159(11):1087-1094.
- (181) Office for National Statistics. Internet Access Households and Individuals 2009. 1-16.
- (182) Roberts C, Togerson D. Understanding controlled trials: Randomisation methods in controlled trials. *BMJ* 1998; 317(7168):1301.
- (183) Dunn LB, Nowrangi MA, Palmer BW, Jeste DV, Saks ER. Assessing decisional capacity for clinical research or treatment: a review of instruments. *American Journal of Psychiatry* 2006; 163(8):1323-1334.
- (184) Communities and Local Government, Mukund L. English Indices of deprivation 2010. 978-1-4098-2924-9. 24-3-2011.
- (185) Economic & Social Research Council. Census.ac.uk. 6-8-2012. Last accessed 8-8-2012.
- (186) Hedeker D, Gibbons R. A Random-Effects Ordinal Regression Model for Multilevel Analysis. *Biometrics* 1994;(50):933-944.
- (187) Montori VM, Guyatt GH. Intention-to-treat principle. *Canadian Medical Association* 2001; 165(10):1339-1341.
- (188) Burls A. What is critical appraisal? NPR09/1113, 5. 2009.

- (189) Stewart A. Frequencies, percentages, proportions and rates. *Basic Statistics and Epidemiology: A practical guide*. Third Edition ed. Oxon: Radcliffe Publishing Ltd; 2010. 15-19.
- (190) Ziefle M. Effects of display resolution on visual performance. *Hum Factors* 1998; 40:554-68.
- (191) Carver R. Reading rate: a review of research and theory. *Academic Press* 1990.
- (192) McCarney R, Warner J, Iliffe S, van HR, Griffin M, Fisher P. The Hawthorne Effect: a randomised, controlled trial. *BMC Medical Research Methodology* 2007; 7:30.
- (193) Al-Shahi R, Vousden C, Warlow C. Bias from requiring explicit consent from all participants in observational research: prospective, population based study. *BMJ* 2005; 331:942.
- (194) Harrell F, Lee K, Matchar D, Reichert T. Regression models for prognostic prediction: advantages, problems, and suggested solutions. *Cancer Treatment Reports* 1985; 69(10):1071-1077.
- (195) European Medicines Agency. ICH Topic E9 Statistical Principles for Clinical Trials. CPMP/ICH/363/96. 1998.
- (196) Love C. Developing the Site Design. *ASP.Net 3.5 Website Programming: Problem-Design-Solution*. First ed. Indianapolis: Wiley Publishing, Inc.; 2010.
- (197) Musciano C, Kennedy B. *HTML and XHTML: the definitive guide*. Fifth ed. Beijing: Farnham: O'Reilly; 2002.
- (198) Love C. *ASP.Net 3.5 Website Programming: Problem-Design-Solution*. First ed. Indianapolis: Wiley Publishing, Inc; 2010.
- (199) Hartman P. *Teach yourself Visual Basic 6*. Foster City, Calif: IDG Books Worldwide; 2000.
- (200) Flesch R. A New Readability Yardstick. *Journal of Applied Psychology* 1948; 32(3):221-233.
- (201) McLaughlin GH. SMOG Grading - A New Readability Formula. *Journal of Reading* 1969.
- (202) Klare GR. Assessing Readability. *International Reading Association* 1974; 10(1):62-102.

- (203) National Research Ethics Service. National Research Ethics Advisors' Panel. <http://www.nres.nhs.uk/about-the-national-research-ethics-service/nrea/> . 2012. Last accessed 8-8-2012.
- (204) National Research Ethics Service. National Research Ethics Advisors' Panel. <http://www.nres.nhs.uk/about-the-national-research-ethics-service/nrea/panel/> . 2012. Last accessed 21-8-2012.
- (205) Directgov. Key facts about the United Kingdom. 2012. Last accessed 21-8-2012.
- (206) Hoffman DL NTVA. Has the Internet become Indispensable? *Communications of the ACM* 2004; 47(7):37-42.
- (207) Hargittai E, Hinnant A. Digital Inequality: Differences in Young Adults' Use of the Internet. *Communication Research* 2008;602-621.
- (208) Howard P, Rainie L, Jones S. Days and Nights on the Internet: The Impact of a Diffusing Technology. *American Behavioral Scientist* 2001; 45(3):382-404.
- (209) Tully C. Growing Up in Technological Worlds: How Modern Technologies Shape the Everyday Lives of Young People. *Bulletin of Science Technology and Society* 2003; 23(444):456.
- (210) Buente W, Robbin A. Trends in Internet Information Behavior, 2000-2004. *Journal of the American Society for Information Science* 2008;1-34.
- (211) van Deursen A, van Dijk J, Peters O. Rethinking Internet skills: The contribution of gender, age, education, Internet experience, and hours online to medium- and content-related Internet skills. *Poetics* 2011; 39(2):125-144.
- (212) Office for National Statistics. Indices of Deprivation 2007: Local Authority Summaries: Area selected: United Kingdom (England, Scotland, Wales, Northern Ireland). Last accessed 20-8-2012.
- (213) Cohn AM, Hunter-Reel D, Hagman BT, Mitchell J. Promoting Behavior Change from Alcohol Use Through Mobile Technology: The Future of Ecological Momentary Assessment. *Alcoholism, Clinical & Experimental Research* 2011; 35(12):2209-2215.
- (214) Boulos MNK, Wheeler S, Tavares C, Jones R. How smartphones are changing the face of mobile and participatory healthcare: an overview, with example from eCAALYX. *BioMedical Engineering OnLine* 2011; 10(24):1-14.
- (215) "It's Simply Integral to What I do": Enquiries into how the Web is Weaved into Everyday Life. 12 Aug 20; 2012.

- (216) Purcell K. Search and email still top the list of most popular online activities. 9-8-2011. Pew Research Center's Internet & American Life Project.
- (217) Hewitson P, Ward AM, Heneghan C, Halloran SP, Mant D. Primary care endorsement letter and a patient leaflet to improve participation in colorectal cancer screening: results of a factorial randomised trial. *British Journal of Cancer* 2011; 105(4):475-480.
- (218) Sin JP, Leger AS. Interventions to increase breast screening uptake: do they make any difference? *J Med Screen* 1999; 6:170-181.
- (219) Redsell SA, Cheater FM. The Data Protection Act (1998): implications for health researchers. 2000.
Ref Type: Report
- (220) Dodek DY, Dodek A. From Hippocrates to facsimile: Protecting patient confidentiality is more difficult and more important than ever before. *Canadian Medical Association* 1997; 156(6):210-212.
- (221) Internet as a means of Developing Health Status: A Research on Internet Usage of Users and Their Expectations. 2010.
- (222) Kowalczyk N, Draper LJ. Trends in Patient Information Preferences and Acquisition. *Radiologic Technology* 2012; 83(4):316-314.
- (223) McClung HJ, Murray RD, Heitlinger LA. The Internet as a Source for Current Patient Information. *Pediatrics* 1998; 101(6):e2.
- (224) McNally SL, Donohue MC, Newton KP, Ogletree SP, Conner KK, Ingegneri SE et al. Can consumers trust web-based information about Celiac Disease? Accuracy, comprehensiveness, transparency, and readability of information on the Internet. *Interact J Med Res* 2012; 1(1):e1.
- (225) Ormond KE, Banuvar S, Daly A, Iris M, Minogue J, Elias S. Information preferences of high literacy pregnant women regarding informed consent models for genetic carrier screening. *Patient Education & Counseling* 2009; 75(2):244-250.
- (226) Madsen SM, Holm S, Riis P. The extent of written trial information: preferences among potential and actual trial subjects. *Bulletin of Medical Ethics* 2000;(159):13-18.
- (227) Kruse A, Kjaergard L, Krogsgaard K, Gluud C, Mortensen E, Gottschau A et al. A Randomized Trial Assessing the Impact of Written Information on Outpatients' Knowledge About and Attitude Toward Randomized Clinical Trials. *Controlled Clinical Trials* 2000;(21):223-240.

- (228) White DR, Muss HB, Michielutte R, Cooper MR, Jackson DV, Richards F et al. Informed consent: patient information forms in chemotherapy trials. *American Journal of Clinical Oncology* 1984; 7(2):183-190.
- (229) Madsen SM, Holm S, Riis P. The extent of written trial information: preferences among potential and actual trial subjects. *Bull Med Ethics* 2000; 159:13-18.
- (230) Manson NC. Why do patients want information if not to take part in decision making? *Journal of Medical Ethics* 2010; 36:834-837.
- (231) Kreiger N, Ashbury F, Cotterchio M, Macey J. A qualitative study of subject recruitment for familial cancer research. *Annals of Epidemiology* 2001; 11(4):219-224.
- (232) Eames S, Hoffmann T, Worrall L, Read S. Delivery styles and formats for different stroke information topics: Patient and carer preferences. *Patient Education and Counseling* 2011;(e18):e23.
- (233) Smith HK, Manjaly JG, Yousri T, Upadhyay N, Taylor H, Nicol SG et al. Informed consent in trauma: Does written information improve patient recall of risks? A prospective randomised study. *Injury* 2012; In press.
- (234) Carr K. The Impact of Verbal Explanation and Modified Consent Materials on Orthodontic Informed Consent. The Ohio State University; 2001.
- (235) Truong TH, Weeks JC, Cook EF, Joffe S. Altruism among participants in cancer clinical trials. *Clinical Trials* 2011; Online.
- (236) Grant J, Mackinnon A, Christensen H, Walker J. Participants' perceptions of motivation, randomisation and withdrawal in a randomised controlled trial of interventions for prevention of depression. *Journal of Medical Ethics* 2009; 35(768):773.
- (237) Taylor P, Awenat Y, Gooding P, Johnson J, Pratt D, Wood A et al. The Subjective Experience of Participation in Schizophrenia Research. A Practical and Ethical Issue. *The Journal of Nervous and Mental Disease* 2010; 198(5):343-348.
- (238) Fisher H, McKeivitt C, Boaz A. Why do parents enrol their children in research: a narrative synthesis. *Journal of Medical Ethics* 2011; 37:544-551.
- (239) Jones R, Murphy E, Crosland A. Primary care research ethics. *British Journal of General Practice* 1995; 45(400):623-626.
- (240) Kraetschmer N, Sharpe N, Urowitz S, Deber R. How does trust affect patient preferences for participation in decision-making? *Health Expectations* 2004; 7:317-326.

- (241) Entwistle V. Trust and shared decision-making: an emerging research agenda. *Health Expectations* 2004; 7:271-273.
- (242) Deber R, Kraetschmer N, Urowitz S, Sharpe N. Do people want to be autonomous patients? Preferred roles in treatment decision-making in several patient populations. *Health Expectations* 2007; 10:248-258.
- (243) Salkeld G, Solomon M, Short L, Butow P. A matter of trust - patient's views on decision-making in colorectal cancer. *Health Expectations* 2004; 7(104):114.
- (244) Trachtenberg F, Dugan E, Hall M. How patients' trust relates to their involvement in medical care. *The Journal of Family Practice* 2005; 54(4):344-352.
- (245) Cohen S. The Gettier Problem in informed consent. *Journal of Medical Ethics* 2011;(37):642-645.
- (246) Dixon-Woods M, Ashcroft RE, Jackson CJ, Tobin MD, Kivits J, Burton PR et al. Beyond "misunderstanding": written information and decisions about taking part in a genetic epidemiology study. *Social Science & Medicine* 2007; 65(11):2212-2222.
- (247) Rehbock T. Limits of Autonomy in Biomedical Ethics? Conceptual Clarifications. *Cambridge Quarterly of Healthcare Ethics* 2011; 20(4):524-532.
- (248) Buchanan A. Medical Paternalism. *Philosophy & Public Affairs* 1978; 7(4):370-390.
- (249) Miller S. Monitoring versus blunting styles of coping with cancer influence the information patients want and need about their disease: Implications for Cancer Screening and Management. *Cancer* 2011; 76(2):1-11.
- (250) Helgesson G, Ludvigsson J, Gustafsson SU. How to handle informed consent in longitudinal studies when participants have a limited understanding of the study. [Review] [17 refs]. *Journal of Medical Ethics* 2005; 31(11):670-673.
- (251) Butler I. A code of ethics for social work and social care research. *British Journal of Social Work* 2012; 32:239-248.
- (252) Majumdar S, Roe M, Peterson E, Chen A, Gilber B, Armstrong P. Better Outcomes for Patients Treated at Hospitals That Participate in Clinical Trials. *Arch Intern Med* 2008; 168(6):657-662.
- (253) Braunholtz D, Edwards S, Lilford R. Are randomized clinical trials good for us (in the short term)? Evidence for a "trial effect". *Journal of Clinical Epidemiology* 2001; 54:217-224.

- (254) Karjalainen S, Palva I. Do treatment protocols improve end results? A study of survival of patients with multiple myeloma in Finland. *British Medical Journal* 1989; 299:1069-72.
- (255) Vist G, Somerville L, Birmingham T, Oxman A. Outcomes of patients who participate in randomized controlled trials compared to similar patients receiving similar interventions who do not participate (Review). *The Cochrane Library* 2009;(2).
- (256) Tosounidis TI, Kontakis GM. Clinical research: The patients' perspectives. *Injury-International Journal of the Care of the Injured* 2008; 39(6):631-635.
- (257) Hope T, Savulescu J, Hendrick J. Three core concepts in medical ethics: best interests, autonomy and rights. *Medical Ethics and Law Core Curriculum*. Elsevier Limited; 2003. 29-39.
- (258) Mill J. *On Liberty*. New York: Bail-Ballou Press; 2003.
- (259) Reid J, Klachko D, Kardash C, Robinson R, Scholes R, Howard D. Why people don't learn from diabetes literature: influence of text and reader characteristics. *Patient Education and Counseling* 1995; 25(1):31-38.
- (260) Turner S, Maher E, Young T, Young J, Hudson G. What are the information priorities for cancer patients involved in treatment decisions? An experienced surrogate study in Hodgkin's disease. *British Journal of Cancer* 1996;(73):222-227.
- (261) General Medical Council. Consent guidance: Legal Annex - Common Law. http://www.gmc-uk.org/guidance/ethical_guidance/consent_guidance_common_law.asp . 2012. Last accessed 10-9-2012.
- (262) Pickersgill M. Research, engagement and public bioethics: promoting socially robust science. *Journal of Medical Ethics* 2011;(37):698-701.
- (263) Yoon KH, Kim HS. A short message service by cellular phone in type 2 diabetic patients for 12 months. *Diabetes Research and Clinical Practice* 2012; 79(2):256-261.
- (264) Lim MSC, Hocking JS, Hellard ME, Aitken CK. SMS STI: a review of the uses of mobile phone text messaging in sexual health. *Int J STD AIDS* 2008; 19(5):287-290.
- (265) Branson CE, Clemmey P, Mukherjee P. Text message reminders to improve outpatient therapy attendance among adolescents: A pilot study. *American Psychological Association* 2011.

- (266) Zolfaghari M, Mousavifar SA, Haghani H. Mobile phone text messaging and Telephone follow-up in type 2 diabetic patients for 3 months: a comparative study. *Journal of Diabetes & Metabolic Disorders* 2012; 11(7):1-10.
- (267) Lindquist AM, Johnansson PE, Petersson GI, Saveman B-I, Nilsson GC. The Use of the Personal Digital Assistant (PDA) Among Personnel and Students in health Care: A Review. *Journal of Medical Internet Research* 2008; 10(4):e31.
- (268) Kaplan WA. Can the ubiquitous power of mobile phones be used to improve health outcomes in developing countries? *Global Health* 2006; 2(9).
- (269) Burton C, Weller D, Sharpe M. Are electronic diaries useful for symptoms research? A systematic review. *Journal of Psychosomatic Research* 2007; 62(5):553-561.
- (270) Fjeldsoe B, Marshall AL, Miller YD. Behavior Change Interventions Delivered by Mobile Telephone Short-Message Service. *American Journal of Preventive Medicine* 2009; 36(2):165-173.
- (271) Pop-Elches C, Thirumurthy H, Habyarimana J, Zivin J, Goldstein M, deWalque D et al. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. *AIDS* 2011; 25(6):825-834.
- (272) Lane SJ, Heddle NM, Arnold E, Walker I. A review of randomized controlled trials comparing the effectiveness of hand held computers with paper methods for data collection. *Medical Informatics & Decision Making* 2006; 6(23).
- (273) Heron KE, Smyth JM. Ecological momentary interventions: Incorporating mobile technology into psychosocial and health behaviour treatments. *British Journal of Health Psychology* 2010; 15:1-39.
- (274) Woods CA, Kathryn D, Lyndon J, Desmond F. Patient use of Smartphones to communicate subjective data in clinical trials. *Optometry & Vision Science* 2011; 88(2):290-294.
- (275) Cauberghe V, Pelsmacker PD. Opportunities and thresholds for advertising on interactive digital TV: A view from advertising professionals. *Journal of Interactive Advertising* 2006; 7(1):12-23.
- (276) Fallahkhair S. Dual device user interface design for ubiquitous language learning: mobile phone and interactive television (iTV). *Wireless and Mobile Technologies in Education* 2005;85-92.
- (277) Bennett J. 'Your Window-on-the-World' The emergence of red-button interactive television in the UK. *Convergence* 2008; 14(2):161-182.

- (278) Hurling R, Catt M, De Boni M, Fairley BW, Hurst T, Murray P et al. Using Internet and Mobile phone technology to deliver an automated physical activity program: Randomized controlled trial. *J Med Internet Res* 2007; 9(2):e7.
- (279) Systematic literature reviews in software engineering: Preliminary results from interviews with researchers. 2009.
- (280) Ryobe IM. The effects of Skype-based video chats with volunteer Filipino English teachers (II): Discovering the superiority of video chat. <http://www.j-let.org/~wcf/proceedings/d-088.pdf> . 2006. Lat accessed 10-9-2012.
- (281) Kass N, Taylor H, Fogarty L, Sugarman J, Goodman SN, Goodwin-Landher A et al. Purpose and benefits of early phase cancer trials: what do oncologists say? What do patients hear? *J Empir Res Hum Res Ethics* 2008; 3(3):57-68.
- (282) Fallowfield L, Jenkins V. Communicating about Phase 1 & Phase 2 Trials. Cancer Research UK, editor. 2010. Psychosocial Oncology Group.
- (283) Macklin R. The ethical problems with sham surgery in clinical research. *The New England Journal of Medicine* 1999; 341:992-996.