

**A Randomised Controlled Trial of an Audiovisual Patient
Information Intervention in Cancer Clinical Trials**

Volume I of II

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ABSTRACT

Introduction and background

Recruitment to cancer clinical trials needs to be improved, as does patient understanding about clinical trials, to enable patients to make an informed choice about whether or not to take part. The main reason that clinically eligible patients do not take part in clinical trials is because they refuse; poor understanding of the research has been associated with patient refusal. Audiovisual patient information (AVPI) has been shown to improve knowledge/understanding in various areas of practice but there is limited information about its effect in the cancer clinical trial setting, particularly in relation to recruitment rates. Understanding the research is necessary for informed consent, and it was hypothesised that if patient understanding about clinical trials was increased with AVPI, then this could result in a reduction in the number of patients refusing clinical trials, and therefore provide an ethical approach to improving recruitment. This study aimed to test the impact of an audiovisual patient information intervention on recruitment to randomised cancer clinical trials (refusal rates), patient understanding of the information given, and levels of anxiety. Reasons for patients' decisions about trial participation were also assessed.

Method

An AVPI intervention was developed that aimed to address the common misconceptions associated with randomisation and clinical equipoise, as well as improve patient understanding generally of randomised cancer trials, and of other core clinical trial informational requirements, such as voluntariness. Patients were randomised to receive either AVPI in addition to the standard trial-specific written information, or the written information alone. A new questionnaire was developed to assess patient understanding (also referred to as knowledge) in the randomised trial setting and, following testing with patients and research nurses, this was shown to be reliable and valid. Patients completed self-report questionnaires to assess their understanding (new knowledge questionnaire)

and anxiety (Spielberger State-Trait Anxiety Inventory), at baseline and after they had made their decision about clinical trial entry, when their perceptions of the intervention, as well as factors contributing to their decision were also determined (this tool incorporated Jenkins and Fallowfield's (2005) questionnaire which assessed reasons for accepting and declining randomised cancer trials).

Results

A total of 173 patients with breast cancer (65%), colorectal cancer (32%) and lung cancer (3%) were entered into the main study. The median age was 60 (range 37-92 years). There was no difference in clinical trial recruitment rates between the two groups: 72.1% in the AVPI group and 75.9% in the standard information group. The estimated odds ratio for refusal (intervention/no intervention) was 1.19 (95% ci 0.55-2.58, $p=0.661$). Knowledge scores increased more in the intervention group compared to the standard group ($U=2029$, $p=0.0072$). The change in anxiety score between the arms was also statistically significant ($p=0.011$) with anxiety improving in the intervention arm more than in the no-intervention arm. The estimated difference in the median anxiety change score between the groups is -4.6 (95% ci -7.0 to -2.0).

Clinical trial entry was not influenced by tumour type, stage of cancer, age, educational qualifications or previous research experience, however, there was a modest association with deprivation status ($p=0.046$) where more affluent patients were the least likely to consent to a trial. Educational qualifications and stage of cancer were independently associated with knowledge: patients who were better educated had higher levels of knowledge about randomised trials, and patients who had limited stage of cancer had higher baseline knowledge than patients with advanced cancer. Acceptability of the intervention was high with 93% of those who watched it finding it useful, and 42% stating that it made them want to take part in the clinical trial. Personal benefit and altruism were

key motivating factors for clinical trial participation, with reasons for refusal being less clear.

Discussion and conclusions

Although the potential for AVPI to increase clinical trial recruitment rates was highlighted in the literature, in this study, AVPI was not shown to have any effect on refusal rates to randomised cancer trials. However, by improving patient understanding prior to decision making, AVPI was shown to be a useful addition to the consent process for randomised cancer trials. AVPI addresses the fundamental ethical challenges of informed consent by improving patient understanding, and supports the ethical framework integral to Faden and Beauchamp's (1986) theory of informed consent. The new knowledge questionnaire was shown to be a sensitive and effective instrument for measuring understanding of randomised clinical trials in the cancer setting, although it would benefit from further testing. The AVPI appears to reduce anxiety at the decision making time point and has been shown to be an acceptable medium for patients. This study confirms existing findings from studies assessing factors affecting decision making, with personal benefit and altruism being key motivating factors, and reasons for refusal being less clear. The need for further qualitative work in this area is highlighted to gain a deeper understanding of what is important to patients, in terms of why they refuse clinical trial participation.

Implications for practice and further research

Several implications for practice have been identified, including using AVPI as part of the standard information package for patients considering randomised cancer trials, and focussing on patient and staff education in this area. The knowledge questionnaire could be introduced to routine practice as a tool to determine patient understanding prior to decision making, allowing clinicians the opportunity to correct any misconceptions prior to consent. Further research focussing on AVPI specific to individual trials would be helpful, to determine if a more customised approach would be of benefit in terms of clinical trial

recruitment. The importance of studying other aspects of the consent process such as the interaction between the clinician and the patient, in addition to more detailed exploration of the factors affecting patients' decisions were highlighted.

PROLOGUE

For most of my nursing career, I have been involved with patients participating in clinical trials of new cancer treatments, both as an individual cancer nurse striving to make the experience as good as possible for each patient and their families/significant others, and also as a manager responsible for a team of research nurses aiming to deliver the best standard of care and support for patients participating in cancer clinical trials. As well as a strong clinical interest derived from experience, my research interests have also developed in this area and my Masters dissertation was focussed on patients' motivations for taking part in trials, with subsequent work in related areas since.

Clinical research is a challenging area of nursing practice, balancing the needs of the individual patient with the need to increase recruitment to cancer trials, in order to further research and improve treatments for future patients with cancer. Despite advances in cancer treatments and a variety of different approaches to research around the consent and information-giving processes, it was apparent that patients still appeared to be making their decision about whether or not to participate in a clinical trial without fully understanding what was being asked of them.

In the current political climate with increasing pressure to recruit more patients to cancer clinical trials and the additional resources and infrastructure now in place for this purpose, it is important to look at ethical ways of increasing recruitment as well as improving the consent process itself. I had read a lot about different ways of improving the consent process and about the effectiveness of audiovisual information in increasing knowledge and understanding in a variety of health care settings. However, there was limited reported work testing the effect of audiovisual approaches on actual consent rates. After discussion within the clinical and research teams in the cancer centre, it was agreed that this would be worthy of further investigation, and led to the development of this study.

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CONTENTS	PAGE
CHAPTER ONE: INTRODUCTION AND BACKGROUND TO THE STUDY.....	1
1.1 Introduction	1
1.1.1 Introduction to the thesis.....	1
1.1.2 Background to the study.....	5
1.2 Clinical setting.....	6
1.2.1 Overview of The Beatson West of Scotland Cancer Centre	6
1.2.2 Clinical trials at The Beatson West of Scotland Cancer Centre.....	6
1.2.3 West of Scotland context.....	7
1.3 Political context	8
1.3.1 Cancer care.....	8
1.3.2 Recruitment to clinical trials.....	9
1.3.3 Ethical issues and informed consent	11
1.3.3.1 European Union Directives	11
1.3.3.2 Consent.....	12
1.4 Summary.....	13
CHAPTER TWO: INTRODUCTION TO LITERATURE REVIEW AND PART I	15
2.1 Introduction to the literature review.....	15
2.2 Introduction to recruitment to clinical trials.....	16
2.3 Literature search	17
2.4 Clinical trials in cancer.....	19
2.4.1 Randomised clinical trials	19
2.5 Recruitment to clinical trials.....	20
2.5.1 Challenges with the literature reporting recruitment rates	20
2.5.2 Recruitment rates to cancer trials	21
2.6 Factors affecting clinical trial recruitment.....	23
2.6.1 Patient factors	26
2.6.1.1 Health behaviour theory	26
2.6.1.2 Patient refusal.....	31
2.6.1.3 Reasons for patient refusal.....	34
2.6.1.4 Randomisation.....	36
2.6.1.5 Relationship with physician.....	37
2.6.2 Clinician factors	38
2.6.3 Trial	41
2.6.4 Organisational/system factors.....	41
2.6.5 Summary of the patient, clinician, trial and organisational factors	42
2.7 Socio-demographic and socioeconomic factors.....	43
2.7.1 General literature.....	43
2.7.1.1 Age and education status	43
2.7.2 Cancer.....	44
2.7.2.1 Age.....	44
2.7.2.2 Gender, education, and stage of disease.....	45
2.7.2.3 Socioeconomic status.....	45
2.7.2.4 Minority groups	46
2.8 Strategies to increase clinical trial recruitment.....	47
2.8.1 General literature.....	47
2.8.2 Cancer clinical trials.....	48
2.9 Summary of Part I – Recruitment	49

CHAPTER THREE: LITERATURE REVIEW PART II.....54

3.1 Introduction to informed consent54
3.2 Literature search56
3.3 Definitions of informed consent58
 3.3.1 Informed consent and informed choice59
3.4 Ethical and legal background to informed consent.....60
 3.4.1 Ethical background60
 3.4.2 Legal position for informed consent61

Theoretical Perspective

3.5 Introduction62
3.6 Autonomy63
3.7 Autonomous actions63
 3.7.1 Understanding65
 3.7.2 Noncontrol67
 3.7.3 Competence68
3.8 Other relevant ethical principles69
 3.8.1 Beneficence.....69
 3.8.2 Justice69
 3.8.3 Balancing the principles in informed consent70
3.9 Informed consent as part of a wider ethics of communication70
3.10 Implications of the theory72

Empirical Literature

3.11 Introduction73
3.12 Information75
 3.12.1 Overview75
 3.12.2 Randomisation77
 3.12.3 Equipoise.....80
 3.12.3.1 Clinical equipoise v personal equipoise81
 3.12.3.2 Patient-centred equipoise82
 3.12.3.3 Therapeutic misconception83
3.13 Disclosure83
 3.13.1 Overview83
 3.13.2 Medium85
 3.13.3 Interaction.....85
3.14 Understanding90
 3.14.1 Overview90
 3.14.2 Knowledge and understanding92
 3.14.3 Knowledge and anxiety.....93
3.15 Decision making94
 3.15.1 Decision making in the context of informed consent94
 3.15.1.1 Decision aids95
 3.15.1.2 Shared decision making96
 3.15.2 Voluntariness.....97
 3.15.3 Consent capacity/competence to consent.....98
3.16 Measures of informed consent99
 3.16.1 Overview99
 3.16.2 Measures of informed consent.....100
3.17 Summary of Part II - Informed Consent100

CHAPTER FOUR: LITERATURE REVIEW PART III	108
4.1 Introduction to audiovisual patient information (AVPI).....	108
4.2 Literature search	109
4.3 Types of AVPI	111
4.3.1 Format.....	111
4.3.2 Comparison of approaches.....	112
4.4 AVPI use in health care	114
4.4.1 Overview	114
4.4.2 Health promotion	117
4.4.3 Screening	120
4.4.4 Surgery and rehabilitation.....	122
4.4.5 Cancer care.....	124
4.5 Content of AVPI.....	126
4.5.1 Tailoring information	126
4.5.2 Framing information.....	128
4.5.3 Tailoring and framing AVPI.....	129
4.6 Clinical trials	129
4.6.1 Clinical trials in health care generally.....	129
4.6.2 Cancer clinical trials.....	133
4.7 AVPI and recruitment to clinical trials	135
4.7.1 Introduction.....	135
4.7.2 Evaluation of studies aimed at increasing recruitment to clinical trials	135
4.7.2.1 Generally.....	135
4.7.2.2 Cancer setting	136
4.7.3 Why AVPI might be of value in increasing cancer clinical trial recruitment rates.....	139
4.8 Limitations of previous work	141
4.9 Summary of Part III - AVPI	141
4.10 Summary of the literature review: Parts I - III (Chapters 2-4)	144
4.11 Aims of the study.....	146
4.12 Hypotheses	146
4.12.1 Hypothesis.....	146
4.12.2 Null Hypotheses	146
 CHAPTER FIVE: METHODS	 147
5.1 Introduction	147
5.2 Study design	147
5.2.1 Design.....	147
5.2.2 Threats to validity	148
5.2.3 Context of study	149
5.2.4 Intervention.....	149
5.2.4.1 Control arm.....	149
5.2.4.2 Intervention arm.....	150
5.2.5 Primary endpoint	150
5.3 Co-ordination of the study	150
5.4 Sample	151
5.5 Raising awareness	152
5.6 Patient recruitment	152
5.6.1 Timeframe and targets	152
5.6.2 Recruitment process.....	154
5.6.3 Screening	155

5.6.3.1 Exclusions	156
5.6.3.2 Patients not approached for the AVPI study	156
5.6.4 Consent	157
5.6.5 Refusal to the AVPI study	158
5.6.6 Recruitment challenges	159
5.6.7 Recruitment summary	160
5.7 Patient randomisation	161
5.8 Data collection	163
5.8.1 Measures/instruments	163
5.8.1.1 Log sheet	164
5.8.1.2 Knowledge questionnaire (Questionnaire: Patient Understanding of Research).....	164
5.8.1.3 Assessment of anxiety (STAI-S)	164
5.8.1.4 Clinical Trial Decision Questionnaire	167
5.8.2 Process	167
5.8.3 Data entry.....	169
5.9 Analysis.....	170
5.9.1 Primary endpoint: clinical trial refusal rates.....	170
5.9.2 Knowledge/understanding	170
5.9.3 Anxiety	171
5.9.4 Reasons for accepting and declining clinical trial participation	171
5.9.5 Patients' perceptions of usefulness of the AVPI.....	171
5.10 Ethical considerations.....	171
5.10.1 Protocol approval.....	171
5.10.2 Patient information and support	172
5.10.3 Questionnaires	173
5.10.4 Confidentiality	173
5.11 Timescales	174
5.12 Costs and funding	174
5.12.1 Costs	174
5.12.2 Funding	174

CHAPTER SIX: DEVELOPING THE INTERVENTION.....175

6.1 Introduction	175
6.2 Background	175
6.3 Development of the AVPI	177
6.3.1 Content of the AVPI	177
6.3.2 Logistics and organisational issues	178
6.3.3 Patient involvement	179
6.3.4 Ethics	181
6.3.4.1 Ethics review	181
6.3.4.2 Consent.....	181
6.3.4.3 Protection of images.....	181
6.3.5 Finance	182
6.3.6 Script	182
6.3.6.1 Content and writing.....	182
6.3.6.2 Presentation and delivery	183
6.3.7 Filming.....	184
6.3.7.1 Clinical setting	184
6.3.7.2 Localising the production	185
6.3.8 Editing	186
6.3.9 Copyright/intellectual property rights.....	186
6.4 Discussion.....	187

6.4.1 Challenges	187
6.4.2 Opportunities	189
6.5 Conclusion	189

CHAPTER SEVEN: DEVELOPING AND TESTING A QUESTIONNAIRE TO ASSESS PATIENT UNDERSTANDING ABOUT RESEARCH191

7.1 Introduction	191
7.2 Background	191
7.2.1 Challenges in assessing understanding	191
7.2.2 Assessment of understanding	192
7.2.2.1 Studies to assess patient understanding for informed consent	193
7.2.2.2 Assessment of the quality of informed consent	195
7.2.2.2.1 Cancer setting	195
7.2.2.2.2 Non-cancer trial setting	196
7.3 Aims of the QD study	197
7.4 Development of the questionnaire	198
7.4.1 Introduction and content of the questionnaire	198
7.4.2 Patient involvement	198
7.4.3 Professional consultation and review	198
7.5 Testing of the questionnaire	199
7.5.1 Sample	199
7.5.2 Measures	199
7.5.2.1 Questionnaire: Patient Understanding of Research	199
7.5.2.2 Assessing acceptability of Questionnaire: Patient Understanding of Research	200
7.5.3 Data collection and recruitment	200
7.5.3.1 Patients	200
7.5.3.2 Nurses	202
7.5.4 Analysis	203
7.5.5 Ethical considerations	203
7.5.6 Results	204
7.5.6.1 Demographics	204
7.5.6.2 Testing of the questionnaire	205
7.5.6.3 Acceptability of the questionnaire	207
7.5.7 Discussion	208
7.5.8 Limitations of the study	211
7.5.9 Conclusion	211

CHAPTER EIGHT: RESULTS213

8.1 Introduction	213
8.2 Participant flow	213
8.3 Demographics and baseline patient characteristics	215
8.3.1 Patients and trials	215
8.3.2 Type of intervention	220
8.4 Primary endpoint – clinical trial refusal rate	221
8.4.1 Refusal rate/clinical trial entry	221
8.4.2 Association between demographics/patient characteristics and clinical trial entry	222
8.5 Knowledge and understanding	224
8.5.1 Knowledge questionnaire	224
8.5.2 Demographics/patient characteristics and knowledge scores	229

8.5.2.1 Association of demographics/patient characteristics and baseline knowledge score	229
8.5.2.2 Association of demographics/patient characteristics and change in knowledge score	232
8.6 Anxiety	232
8.6.1 STAI-S Questionnaire	232
8.6.2 Association between demographics/patient characteristics and anxiety	234
8.7 Clinical trial decision making	235
8.7.1 People who patients discussed their decision with.....	236
8.7.2 Reasons for accepting/declining a clinical trial	236
8.7.3 Consent process.....	239
8.7.4 Acceptability of the AVPI	243

CHAPTER NINE: DISCUSSION, CONCLUSIONS AND RECCOMENDATIONS245

9.1 Introduction	245
9.2 Refusal rates	245
9.2.1 Statistical power	246
9.2.2 Relation between refusal rates and knowledge/understanding	247
9.2.3 Interaction	250
9.2.4 Information content.....	251
9.2.5 Summary of possible reasons why refusal rates were not reduced in this study	252
9.3 Knowledge and anxiety	253
9.3.1 Knowledge/understanding	253
9.3.2 Assessment of understanding	257
9.3.3 Influence of demographics and patient characteristics.....	258
9.3.4 Relation between knowledge and anxiety	258
9.4 Non-rational, social and process factors that affect decision making	259
9.4.1 Social relationships/influence of others.....	260
9.4.2 Most important reasons to patients.....	262
9.5 Parameters of the informed consent process	264
9.5.1 Timing	264
9.5.2 Acceptability of the intervention	265
9.6 Implications and recommendations	266
9.6.1 Implications for practice	266
9.6.2 Recommendations for further research.....	268
9.7 Study limitations	270
9.8 Conclusions.....	271

REFERENCES.....273

APPENDICES303

TABLES	PAGE	
Table 2.1	Outline summary of Chapter 2	16
Table 2.2	Summary of literature search: recruitment – cancer	18
Table 2.3	Summary of literature search: recruitment – non-cancer	18
Table 2.4	Phases of clinical trials	19
Table 2.5	Central concepts in understanding health-related behaviour (Morrow <i>et al.</i> 1994)	27
Table 3.1	Outline summary of Chapter 3	55
Table 3.2	Summary of literature search: informed consent	57
Table 4.1	Outline summary of Chapter 4	109
Table 4.2	Summary of literature search: audiovisual patient information	110
Table 4.3	Key points from the literature review	145
Table 5.1	Patients not approached for the AVPI study	157
Table 5.2	Reasons for AVPI study refusal	159
Table 5.3	Schedule of events	168
Table 5.4	Study work plan	174
Table 5.5	Costs	174
Table 6.1	Roles of nurses directly involved in developing the intervention	179
Table 7.1	Demographic details of the sample (patients and nurses)	204
Table 7.2	Response to questions by group	205
Table 7.3	Patient acceptability of knowledge questionnaire (Questionnaire: Patient Understanding of Research)	208
Table 8.1	Demographic and baseline patient characteristics	216
Table 8.2	Age	217
Table 8.3	Characteristics according to clinical trial	219
Table 8.4	Interventions used by patients in the study	220
Table 8.5	'Other' reasons that patients were not entered into clinical trials	221
Table 8.6	Proportion of patients that subsequently entered into clinical trials	222
Table 8.7	Association between demographics/patient characteristics and trial entry	223
Table 8.8	Distribution of the within-patient changes	226
Table 8.9	Questions in knowledge questionnaire	227
Table 8.10	Percentage correct for each question in the knowledge questionnaire at each time point	228
Table 8.11	Comparison of change between study arms, per individual question	229
Table 8.12	Association between demographics/patient characteristics and anxiety at baseline	235
Table 8.13	Patients' who 'strongly agree'/'agree to some extent' to statements which may be related to whether or not they agreed to take part in the clinical trial offered to them	237
Table 8.14	Questions corresponding to the most important reasons given by patients for agreeing or not agreeing to take part in a clinical trial	239
Table 8.15	Patients' perceptions of their understanding of trial information received, in terms of effect on clinical trial entry	240
Table 8.16	Patients' perceptions of their understanding of trial information received, in terms of effect of the study arm	240
Table 8.17	Patients' perceptions of time, prior to decision making	242
Table 8.18	Numbers of patients who read the clinical trial written information sheet	242
Table 8.19	Numbers of patients who found the written information sheet useful	242

Table 8.20	Patients' perceptions of effect of information sheet on the clinical trial decision	243
Table 8.21	Numbers of patients who watched the AVPI	243
Table 8.22	Numbers of patients who reported finding the AVPI useful	244
Table 8.23	Patients' perceptions of effect of the AVPI on the clinical trial decision	244

FIGURES	PAGE	
Figure 2.1	Conceptual model of the factors affecting patients' decisions about clinical trials (Albrecht <i>et al.</i> 2003)	40
Figure 3.1	Degrees of autonomy of intentional actions (Faden and Beauchamp 1986, p239)	65
Figure 3.2	Summary of informed consent (modified from Verheggen <i>et al.</i> 1996)	74
Figure 5.1	Monthly recruitment targets	153
Figure 5.2	Recruitment summary	160
Figure 5.3	Patient pathway through randomisation	162
Figure 7.1	Recruitment summary for patients in a previous clinical trial	201
Figure 7.2	Recruitment summary for non clinical trial patients	202
Figure 7.3	Recruitment summary for clinical research nurses	203
Figure 7.4	Patients' and nurses' percentage scores based on all 13 questions	206
Figure 7.5	Patients' and nurses' percentage scores based on 6 questions with corrected item total correlations >0.4	207
Figure 8.1	Participant flow through the AVPI study	214
Figure 8.2	Distribution of percentage knowledge score for patients completing questionnaires at both time points	225
Figure 8.3	Within-patient differences in knowledge score between the two time points	225
Figure 8.4	Change in knowledge level and clinical trial entry	226
Figure 8.5	Association between various patient characteristics and knowledge score at baseline	231
Figure 8.6	Association of education and stage of cancer with baseline knowledge	232
Figure 8.7	Distribution of percentage anxiety score for patients completing questionnaires at both time points	233
Figure 8.8	Within-patient differences in anxiety between both time points	234
Figure 8.9	People with whom patients discussed their decision to take part in the trial	236
Figure 8.10	Objectively assessed and subjectively assessed understanding	241

APPENDICES	PAGE	
Appendix 1.1	Publications written as a result of the study	304
Appendix 1.2	Clinical trial patient pathway at The Beatson West of Scotland Cancer Centre	333
Appendix 2.1	Literature search: recruitment to clinical trials	334
Appendix 3.1	Literature search: informed consent	336
Appendix 4.1	Literature search: audiovisual patient information	337
Appendix 5.1	Study team	338
Appendix 5.2	Randomised clinical trials open in lung, breast and colorectal cancer during the period of AVPI study recruitment	339
Appendix 5.3	Patient information sheet	341
Appendix 5.4	Consent form	344
Appendix 5.5	Registration form	345
Appendix 5.6	Recruitment log sheets	346
Appendix 5.7	Letter to GP	348
Appendix 5.8	Knowledge questionnaire (Questionnaire: Patient Understanding of Research)	349
Appendix 5.9	Spielberger's State-Trait Anxiety Inventory – State Scale	353
Appendix 5.10	Clinical Trial Decision Questionnaire	355
Appendix 5.11	Record of returned questionnaires	357
Appendix 5.12	Correct answers to knowledge questionnaire	358
Appendix 6.1	Video-script used in filming	360
Appendix 7.1	Initial knowledge questionnaire (prior to testing)	370
Appendix 7.2	Questionnaire to assess acceptability of knowledge questionnaire	374
Appendix 7.3	Patient information sheet for exploratory testing of knowledge questionnaire	375
Appendix 7.4	Consent form for exploratory testing of knowledge questionnaire	377
Appendix 8.1	Monthly numbers of patients recruited to AVPI study in relation to each clinical trial	378

CHAPTER ONE: INTRODUCTION AND BACKGROUND TO THE STUDY

1.1 Introduction

1.1.1 Introduction to the thesis

This thesis reports on a study designed to test the impact of an audiovisual patient information intervention on recruitment to randomised cancer clinical trials. It was hypothesised that by increasing patient understanding of the information given, clinical trial refusal rates would be reduced, and that any increase in understanding would not be associated with an increase in anxiety.

Clinical trials are the only safe and effective way to improve treatment of cancer. However, small numbers of patients are recruited to cancer clinical trials every year for several reasons, including issues around the patient (e.g. treatment preference, uncertainty, knowledge and understanding), the clinician (e.g. communicative behaviour, attitudes, difficulty with the consent procedure), the trial itself (e.g. study design, complexity) and system/organisation factors (e.g. organisation infrastructure, additional time required for consent requirements). Aspects of informed consent are apparent in all four domains. Few trials have been undertaken of interventions designed to improve trial recruitment, and those that have been carried out are small in scale and difficult to generalise. Further research is much needed to determine effective interventions to increase clinical trial recruitment (McDaid *et al.* 2006).

A study of the recruitment literature demonstrated that patient refusal is the main reason that clinically eligible patients are not recruited to clinical trials. However, it is not always clear why patients refuse. Although a proportion of clinical trials report their refusal *rates*, the *reasons* why patients refuse are often not reported. Where reasons have been reported, they are as cited above: for example, a patient's difficulties in understanding trial information such as randomisation, and factors associated with the clinician, such as

perceptions of trust. Meanwhile, the results of studies that have focussed solely on the issue of why patients refuse clinical trials are very similar to those reported in the general recruitment literature. As with recruitment in general, patient refusal often appears to be associated with issues centred around the consent process.

Patient refusal was chosen as the primary endpoint for this study because reducing refusal was considered to be a potentially effective way of increasing recruitment. This is because of the relatively large impact it has on clinical trial recruitment rates, and also because some of the factors associated with refusal appear to be amenable to change, for example correcting misconceptions and improving patient understanding as was the focus in this study. Patient understanding was identified in the recruitment and patient refusal literature as being influential on refusal rates. Poor understanding was mainly due to misinterpretation and misconception of clinical trial information, particularly in relation to the concept of randomisation. In view of the fact that a number of issues integral to the consent process are implicated in patient refusal, and the key role of understanding as the target of the intervention, and also as the fundamental underpinning of informed consent as identified from the literature, informed consent became a major focus for this study.

The informed consent process was reviewed in the literature, from both a theoretical and empirical perspective, in order to determine the aspects that are important and amenable to change, prior to developing the intervention. This resulted in the identification of patient understanding as integral to all dimensions of informed consent: what the patient needs to know (*information*); how that information is conveyed to optimise understanding (*disclosure*); the extent to which the patient understands the information conveyed (*understanding*); and the extent to which the patient's consent meets the criteria for decision making in this context – competence and voluntariness [understanding is key to both competence and voluntariness] (*decision making*). This provided further justification for focussing on patient understanding both in terms of the main study endpoint as a

potential way of reducing clinical trial refusal rates, and also in terms of patient understanding in its own right as a key component of informed consent.

The theoretical underpinning for the study is taken mainly from the work of Faden and Beauchamp (1986), and to a lesser extent, Manson and O'Neill (2007). Patient understanding is considered the basis for autonomous action (Faden and Beauchamp 1986), which is fundamental in the consent situation. Understanding *that* you are being asked to decide about taking part in a trial, and understanding *what* is communicated about the trial, are the key parts of understanding that are important in informed consent. Other factors essential for autonomous action are competence and voluntariness, which are also linked to patient understanding. Evaluation of informed consent is challenging in the absence of an accepted definition, and as a result there has been a fragmented approach to measurement. Evaluation has included assessment of satisfaction with the process, assessment of competence/capacity to consent, and assessment of patient knowledge and understanding. Because of the importance of understanding in terms of both consent and recruitment, this study focussed on evaluating informed consent in terms of patient understanding. Due to the lack of suitable tools identified in the literature, relevant to the randomised cancer trial setting, a new questionnaire was developed, and is discussed in detail in Chapter 7.

The rationale for including anxiety as a secondary outcome measure was the need to ensure that any intervention designed to increase patient understanding did not have a detrimental effect on anxiety. Consistent with previous literature associated with patient information interventions, the aim was for the intervention not to increase anxiety, with the hope that, by providing the patient with information they could understand, anxiety might even be reduced.

There is a small volume of literature suggesting that patients who have more knowledge, and better understanding, of clinical trial information are more likely to enrol; however, the evidence is not conclusive and this study aimed to add to the literature in this area, specific to the randomised cancer trial setting.

Various approaches to improving knowledge and understanding in cancer (and other specialist areas) have been studied. These include the use of audiovisual methods. Audiovisual patient information (AVPI) has been shown to increase knowledge, influence behaviour and assist patients with decision making. However, limited information is available on the effect of these methods in the cancer clinical trial setting, in terms of both consent and recruitment. AVPI was chosen as the intervention for this study because of: (i) the evidence outwith the clinical trial setting - its effectiveness in increasing knowledge without increasing anxiety, improving the decision making process, and in some cases influencing the decision itself; (ii) the small body of evidence on its effectiveness in the clinical trial setting; and (iii) its effectiveness as a tool for cancer patient education. The literature appears to suggest that AVPI has the potential to improve knowledge and understanding of clinical trials (without increasing anxiety), and to increase clinical trial recruitment by reducing refusal rates. As confirmed in the literature, patient understanding of the concept of randomisation poses particular challenges, so the decision was taken to focus on this issue, in the wider context of clinical trials. Other important features designed to improve understanding (again identified in the literature), such as tailoring, and aspects of information presentation, were incorporated. In order to meet the informational requirements in an audiovisual format, a video/DVD/CD-ROM had to be developed for this purpose: this process is described in detail in Chapter 6.

The final area of interest in this study was the basis for the patient's decision to participate (or not) in clinical trials. Patients' reasons for consent or refusal were not part of the main focus of the study; however, because the literature is limited in this area, there was the

opportunity to add to this knowledge, specifically in the case of randomised cancer trials. The aim of this part of the study was to better understand the factors affecting patients' decisions. It was intended that this would also help to determine future areas for research, taking into account the results of the other aspects of this study. This is obviously a very brief summary of the justification for the study, and a more detailed discussion is provided in Chapters 2, 3 and 4.

The structure of the thesis is as follows. The remainder of this chapter will focus on the clinical and political context within which the study was undertaken. Chapters 2, 3 and 4 comprise the literature review, and discuss the wealth of relevant literature concerning recruitment to clinical trials, informed consent, and audiovisual patient information. Chapter 5 focuses on the methodology employed in the main randomised study, with Chapter 6 describing the development of the intervention. The development and testing of a new questionnaire to assess understanding of randomised clinical trials is discussed in Chapter 7. Full results are reported in Chapter 8, which is followed by discussion, conclusions and recommendations for practice and research in Chapter 9. Some of the chapters incorporate material from papers, based on the study, which have already been published; these are shown in full in Appendix 1.1. For simplicity, this study will be referred to as the AVPI study.

1.1.2 Background to the study

Prior to reviewing the literature, this chapter will now describe the context within which the research was undertaken. Background information will be given on the clinical setting, as well as the political context in relation to cancer care, clinical trial recruitment and informed consent.

1.2 Clinical setting

1.2.1 Overview of The Beatson West of Scotland Cancer Centre

The study was carried out at The Beatson West of Scotland Cancer Centre (BWoSCC). The BWoSCC is the lead centre for the delivery of non-surgical cancer care for the West of Scotland (WoS). It serves a population of 2.6 million and has clinical links with 16 hospitals in four surrounding health board areas. It is Scotland's largest cancer centre, and the second-largest in the United Kingdom. Each year, over 8,000 new patients are seen, and more than 15,000 courses of chemotherapy and 6,500 courses of radiotherapy are administered. All radiotherapy treatments and the majority of chemotherapy treatments in the WoS, are given in the centre.

1.2.2. Clinical trials at The Beatson West of Scotland Cancer Centre

Chemotherapy is administered routinely according to standard chemotherapy protocols at the BWoSCC for all cancers, in addition to being administered as part of a clinical trial. This includes the populations under study - breast, lung and colorectal cancer. Other standard and clinical trial treatments given at the BWoSCC for these cancers are radiotherapy and hormone therapy.

Over the past 10-20 years the BWoSCC has been developing its research profile, and has become well established as a centre of excellence for cancer clinical trials. Over 1000 patients are entered into clinical trials every year at the centre, and there are approximately 80 clinical trials running at any one time. These include all types of clinical trials, with a particular focus on early stage testing (phase I), which is the first time a drug or treatment is given to people. This follows on from laboratory and animal testing of a new drug or treatment. In cancer care, phase I trials are carried out on people with cancer rather than on healthy volunteers, as would be the case for medicines applicable to other illnesses. This is due to the potentially toxic nature of cancer treatments, and because it is necessary to determine metabolic effects of the disease and treatments. Although

there is a substantial focus on phase I trials at the cancer centre, there is an equally substantial commitment to randomised phase III clinical trials, where a new treatment is compared with the standard current one. This accounts for the largest number of clinical trials running at the cancer centre, as well as the largest numbers of patients taking part in trials. It is from this group of trials that the study population was taken. The pathway for a patient being considered for a clinical trial at The Beatson West of Scotland Cancer Centre is shown in Appendix 1.2

The cancer centre has seven in-patient wards, a radiotherapy department, and a large out-patient and day case unit, in addition to the Clinical Research Unit, which specialises in early phase clinical trials. Patients undergoing treatment as part of a randomised clinical trial are usually seen in the out-patient department and day case area. Some will receive their treatment in one of the in-patient wards.

1.2.3 West of Scotland context

Local WoS hospitals give routine chemotherapy for colorectal, lung and breast cancer, including treatment within clinical trials according to specific protocols. The clinical trials aspect is coordinated by a Scotland-wide clinical trials network called the Scottish Cancer Research Network (SCRN). The SCRN is divided into 3 smaller networks, to link with the three regional cancer groups in Scotland. The WoS arm of the SCRN is based at the BWoSCC. Although other hospitals in the WoS could have contributed to the study sample, for practical reasons all of the patients in this study were seen at the BWoSCC, and received their treatment there too. One of the eligibility criteria was that the patient had to be receiving treatment at the cancer centre.

1.3 Political context

1.3.1 Cancer care

Over the last 10 years cancer has become one of the national health priorities in the United Kingdom (UK), bringing an increase in financial investment.

In England, the *NHS Cancer Plan* (Department of Health 2000) set out the action needed over a ten-year timeframe to improve cancer prevention and screening services, cut cancer patient waiting times, enhance treatment and palliative care services, and boost cancer research. Since then, substantial progress has been made, and a follow-up document, the *Cancer Reform Strategy* was published in December 2007 (Department of Health 2007a).

The Scottish Cancer Strategy, *Cancer in Scotland: Action for Change*, was published in July 2001, by the Scottish Executive (now the Scottish Government) setting out a clear direction for the improvement of cancer services in Scotland (Scottish Executive 2001a). It identifies a wide range of measures necessary to prevent, detect and improve treatment and care for people with cancer. Substantial financial support was ring-fenced to support these measures. A follow-up document, *Cancer in Scotland: Sustaining Change*, was published in May 2004 reporting on progress since 2001 and the next steps to ensure continuing improvement in cancer services (Scottish Executive 2004). One of the cornerstones for taking forward the strategy was the establishment of three Regional Cancer Advisory Groups (RCAGs) in Scotland. Cancer Managed Clinical Networks (MCNs) were also established and incorporated into the new structures, the majority of them being regional (national for rare cancers). Further guidance on the structure and function of RCAGs was provided by the Scottish Executive in the NHS HDL (2001)71, which included the requirement to establish MCNs for all cancers (Scottish Executive 2001b). The MCNs in each region are brought together within the RCAG, which functions as an overarching supra-regional body. Clinical trials are important in all of the cancer

MCNs. The Scottish Cancer Group, coordinated by the Scottish Government, was established to oversee the implementation of the Scottish Cancer Strategy via the RCAGs. The Scottish Cancer Group continues to require RCAGs to monitor progress and provide six monthly progress reports.

1.3.2 Recruitment to clinical trials

As a result of the high political profile of cancer care, and the publication of national cancer plans which included cancer research, there has been an increasing interest in clinical trials, particularly in relation to the challenges of increasing the numbers of patients recruited. This is an international issue, discussed in Chapter 2. Since the publication of the cancer plans, there have been several UK ministerial announcements pledging millions of pounds to further develop the infrastructure and integration of cancer research. Following this, funding was made available, and monitoring plans put in place to ensure that targets were met.

In Scotland, the Scottish Cancer Research Network (SCRN) (reporting into the WoS RCAG), was the result of the substantial investment from the Scottish Executive. It was designed to provide patients with access to clinical trials in their local hospital, and to help meet the government's target: 10% of cancer patients being recruited to clinical trials. Indeed, the initial objective of the SCRN was to double accrual to trials within a three-year period, from a baseline of less than 3% in 2001. This target was achieved within the timeframe as a result of the additional infrastructure of dedicated research nurses and data managers. Now, with the networks established, the focus has shifted to sustaining recruitment to clinical trials.

A similar initiative – the National Cancer Research Network - had been established in England in April 2001 by the Department of Health, again with the aim of increasing recruitment to cancer clinical trials. It had similar targets to the Scottish initiative, and also

achieved doubling of recruitment within a three year period. The revised *Manual of Cancer Services* (Department of Health 2007b) is an integral part of the NHS Cancer Plan and modernisation of cancer services in England. Research is a fundamental part of this, with *Cancer Research Network Measures* having recently been included in the Manual (March 2007), which has the aim of improving the quality and standards of cancer research and integrating research networks with the generic cancer structures.

In addition to the SCRN and the NCRN, an overarching clinical trial initiative was launched in April 2001, known as the NCRI, the National Cancer Research Initiative. Its main aim was to bring together the major funders of research to allow a more strategic approach to identifying and supporting cancer research. NCRI is a partnership between the Government, charity and industry, and promotes co-operation in cancer research among the 20 member organisations for the benefit of patients, the public and the scientific community. Among the member organisations involved are: Department of Health (England); Scottish Government; Northern Ireland Research and Development Office; Wales Office of Research and Development; Association of the British Pharmaceutical Industry (ABPI); Medical Research Council (MRC); Cancer Research UK; Macmillan Cancer Support and Marie Curie Cancer Care. The NCRI has a central role in the integration of research and care to provide accessible, high quality patient-centred cancer services. It consists broadly of two research Networks: the National Translational Cancer Research Network (NTRAC), which leads on translational research, and the National Cancer Research Network (NCRN) (includes the SCRN), which provides infrastructure for large, multicentre clinical trials. Both Networks collaborate to provide scientific support and an evidence base for cancer care.

One of the key targets for the NCRI is to increase recruitment to clinical trials, and one means of achieving this was the establishment of a network of accredited trials units in the UK to deliver high quality cancer clinical research. The BWoSCC is part of this, in

collaboration with the Information Services Division (Edinburgh), as an NCRI accredited trials unit. The aims of the network are to ensure cohesion and coverage of NCRI trials activity, to strengthen links with the NCRI Clinical Studies Groups, to respond to changing research governance and regulatory frameworks, and to integrate laboratory-based research into trial activity.

With an increased focus on improving recruitment rates, leading to more patients consenting to clinical trials, it is even more important to ensure that ethical standards are not being compromised as a result of the focus on increasing recruitment.

1.3.3 Ethical issues and informed consent

The ethical issues associated with informed consent will be discussed in detail in Chapter 3. However, within the policy context it is useful here to highlight the European Union Directives in relation to clinical trials and the subsequent changes in UK law, as well as national and local developments in relation to consent.

1.3.3.1 *European Union Directives*

The European Union (EU) Directives represent one of the major initiatives to address issues of quality and standards in clinical trials. First came the *EU Clinical Trials Directive* in 2001 (2001/20/EC); it was followed by the *EU Good Clinical Practice Directive* in 2005 (2005/28/EC).

The EU Clinical Trials Directive (2001/20/EC) was developed to 'simplify and harmonise the regulation of clinical trials across the European Union, thereby facilitating the internal market in medicinal products while protecting participants and public health' (Woods, 2004). The EC Clinical Trials Directive (2001/20/EC) focuses on the conduct of clinical trials of medicinal products conducted on people, in particular the implementation of *Good Clinical Practice*. Good Clinical Practice is a set of internationally recognised ethical and

scientific quality requirements, developed by the International Conference of Harmonisation (ICH). These requirements must be observed when designing, conducting, recording and reporting clinical trials that involve human subjects (ICH Guidelines for GCP 1996). Included in this is guidance on the content of clinical trial patient information, and the key elements/process of informed consent. Compliance with this good practice provides assurance that the rights, safety and well-being of trial subjects are protected, and that the results of the clinical trials are credible.

The Medicines and Healthcare products Regulatory Agency (MHRA) is the regulatory body that was responsible for drafting the UK legislation in response to the EU Directives. In 2004, this resulted in the *Medicines for Human Use (Clinical Trials) Regulations* (S.I. 2004/1031) (Department of Health 2004). UK law was amended in August 2006 to incorporate the EU Good Clinical Practice Directive (2005/28/EC), and resulted in the *Medicines for Human Use (Clinical Trials) Amendment Regulations* (Department of Health 2006). Patient consent to research is integral to these directives and the current UK law.

1.3.3.2 Consent

In addition to the EU directives, there are local and national developments aimed at improving standards in clinical trials. The 2000 NHS Plan in England pledges that proper consent must be sought from all NHS patients and research subjects. To achieve this goal, the Department of Health set up the *Good Practice in Consent* initiative, and enlisted an advisory group made up of patient representatives, carers, clinicians, academics and NHS managers. Part of the work of this group included the publication of a *Good Practice in Consent Implementation Guide*, which focuses on consent to examination and treatment (Department of Health 2001a). This was widely promoted via the Health Service Circular, *Good Practice in Consent* (Department of Health 2001b). There is a distinct lack of reference to research in this guide; the only area covered is consent to tissue sampling, in a small section. However, the principles for consent to research are the same as for

consent to examination or treatment, and the document has similar content to the guidance given specifically for clinical trials (e.g. ICH GCP 1996; local clinical trial consent forms; Scottish Executive 2001c). The *Mental Capacity Act* (MCA) came fully into force on 1 October 2007. Although it is a wide-ranging piece of legislation, some of its provisions are relevant to consent. Consequently, the Department of Health plan to amend its consent guidance, and the model policy and consent forms, to reflect the provisions of the MCA.

In Scotland, the Scottish Executive set up a working group to develop guidelines for writing patient information in the research context. These were published in 2001, and offer comprehensive guidance concerning the key information to be included for patients (Scottish Executive 2001c). The Scottish Government also addresses issues of consent to research in the *Research Governance Framework for Health and Community Care in Scotland* (Chief Scientist Office 2006), which is an updated version of the initial research governance framework published in 2001.

At an individual health board/organisation level, there has been an increase in awareness of requirements for patient consent both within and outwith the research setting, and many organisations now have formal policies in place. In NHS Greater Glasgow and Clyde (the organisation where the research was undertaken), there is a formal policy governing all aspects of patient consent, which also reflects the Scottish Executive Guidance (2001c). NHS Greater Glasgow and Clyde has also recently established an e-learning module on consent which is available to any member of staff wishing to undertake it. This is actively encouraged for staff involved with patients in clinical trials.

1.4 Summary

In summary, the research was undertaken at The Beatson West of Scotland Cancer Centre, which is the second largest cancer centre in the UK. It has a large, well

established clinical trials profile, and is well connected within the UK clinical trials networks. The study was undertaken in the context of cancer as a national priority, and the substantial political pressure to increase clinical trial recruitment rates. During this time, there was a focus on improving the quality and integration of clinical trials across Europe, which resulted in changes to UK law. Also of relevance were the developments in both the cancer and the non-cancer local and national agendas in relation to consent policy, focussing professionals' attention on the paramount importance of *informed* consent. In addition to the literature, which will be discussed in the following three chapters, all of the factors discussed in this chapter contributed to reasons for undertaking the research, and to the design and conduct of the study itself.

As discussed at the beginning of this chapter, the study was designed to test the impact of an audiovisual patient information intervention on recruitment to randomised cancer clinical trials. The literature review will now highlight patient refusal, in the wider context of clinical trial recruitment, as a potentially useful focus for increasing patient recruitment. It will highlight the lack of effective interventions for increasing recruitment and the lack of research into reasons for patient refusal. Chapter 2 identifies the key factors in the informed consent process in terms of recruitment, and highlights patient understanding as being particularly important. This is continued in Chapter 3, where theoretical aspects of informed consent are discussed prior to a review of the empirical literature, and patient understanding is identified as being fundamental to the concept. Chapter 4 then discusses audiovisual patient information as a means of improving patient understanding, and potentially consent rates, in the randomised cancer trial setting.

CHAPTER TWO: INTRODUCTION TO THE LITERATURE REVIEW AND PART I - RECRUITMENT TO CLINICAL TRIALS

2.1 Introduction to the literature review

This literature review was conducted in three main areas to provide justification for the study, which was to investigate the effect of an audiovisual patient information intervention on informed consent and recruitment to cancer clinical trials. Although there was substantial overlap across the three areas, it was useful to address them individually owing to the large literature base, and in order to ensure that important papers were not missed. Three separate literature searches were carried out and are discussed in detail in Chapters 2-4 as shown below:

- Chapter 2 (Part 1 of literature review) - *Recruitment to clinical trials* (including barriers, influencing factors, patient refusal);
- Chapter 3 (Part 2 of literature review) - *Informed consent* (including key components and measurement);
- Chapter 4 (Part 3 of literature review) - *Audiovisual patient information* (including its role in the clinical trial setting).

These are then brought together in the summary at the end of Chapter 4, leading to a statement of the aims and hypotheses for the study. The main theoretical underpinning for the study is discussed in Chapter 3 in relation to informed consent theory.

PART I – RECRUITMENT TO CLINICAL TRIALS

2.2 Introduction to recruitment to clinical trials

This chapter focuses on recruitment to clinical trials. Firstly, there will be a discussion of the search strategy which will be followed by discussion of the key areas of relevance for this study. An overview of clinical trials in cancer will be provided, with a particular focus on randomised trials. This will be followed by a discussion of clinical trial recruitment rates and the factors affecting recruitment in relation to the clinician, the patient (including refusal rates and reasons), the trial and the organisation. Next, the influence of socio-economic and socio-demographic factors will be outlined. Finally, there will be a focus on strategies and interventions aimed at increasing clinical trial recruitment rates, which will be followed by a summary of Part I. An outline of the issues covered in this chapter is given in Table 2.1.

Table 2.1. Outline summary of Chapter 2

Literature search		
Clinical trials in cancer		
Randomised clinical trials		
Recruitment to clinical trials		
Challenges with the literature reporting recruitment rates		
Recruitment rates to cancer trials		
Factors affecting clinical trial recruitment		
Patient factors		Health behaviour theory
		Patient refusal
		Reasons for patient refusal
		Randomisation
		Relationship with physician
Clinician factors		
Trial		
Organisational/system factors		
Summary of factors		
Socio-demographic and socioeconomic factors		
General literature		Age and education status
Cancer		Age
		Gender, education and disease stage
		Socioeconomic status
		Minority groups
Strategies to increase clinical trial recruitment		
		General literature
		Cancer clinical trials
Summary of recruitment		

2.3 Literature search

The literature in relation to clinical trial recruitment was searched using the following five concepts: 1) clinical trials; 2) recruitment to trials; 3) influencing factors; 4) cancer and 5) willingness/refusal/barriers. Electronic databases searched were: Ovid MEDLINE(R) (mesz), Ovid MEDLINE(R) In-Process and Other Non-Indexed Citations (prem), CDSR (coch), ACP Journal Club (acp), DARE, CCTR, British Nursing Index (brni), CINAHL (nursing), EMBASE (emez), PsycINFO (psyf). The search strategy was devised with the input of an experienced medical librarian. Additional references were located by searching the bibliographies of related papers, examining conference proceedings, and using the Google search engine. The combination of keyword (searched for specific words and phrases in titles and abstracts) and MESH subject heading resulted in the retrieval of large search sets, which then needed to be manually sorted; but this was the preferred strategy so as not to exclude any potentially relevant material.

Due to the large number of potentially relevant articles identified, grouping was then carried out into 'cancer' and 'non-cancer' trials, and limits applied accordingly. The cancer group were limited to English language and the last 20 years. This resulted in a total of 1579 articles whose abstracts were then assessed for relevance by the librarian who was familiar with the proposed research. The majority of those excluded were papers discussing trials and their results, not the design/methodological aspects of the trial. Other excluded papers were comments/letters/editorials/abstracts from conferences and studies focussed on paediatrics or neonates. A final total of 293 abstracts were identified for further consideration.

The 'non-cancer' literature was restricted to English language, the last 10 years and to review articles. When duplicates already identified by the cancer recruitment search were removed, this resulted in 336 which, following assessment, led to a final total of 86 abstracts for further consideration.

Full details of the search strategy are shown in Appendix 2.1. Summary information is presented in Tables 2.2 and 2.3. The line number corresponds with that in the full search strategy in Appendix 2.1.

Table 2.2. Summary of literature search: recruitment – cancer

Combination of Terms	Number of Hits
Line 16 = clinical trials + recruitment + cancer and influencing factors or willingness/refusal/barriers	2384
Line 20 = limited to last 20 years, English language, duplicates removed	1579
Line 21 = final total following assessment	293

Table 2.3. Summary of literature search: recruitment – non-cancer

Combination of Terms	Number of Hits
Line 21 = clinical trials + recruitment + influencing factors	5843
Line 26 = clinical trials + recruitment + willingness/refusal/barriers	4398
Line 32 = line 21 or line 26, limit to last 10 years and English language, duplicates removed	2760
Line 33 = additional duplicates already identified in 'cancer' search removed	2190
Line 35 = limited to review papers	336
Line 36 = final total following assessment	86

Full papers were obtained for the majority of the selected 86 non-cancer review abstracts and the 293 cancer related ones. Following some context setting about clinical trials, the main areas in relation to recruitment which are of relevance to this study will be discussed.

2.4 Clinical trials in cancer

Clinical trials in cancer are essential to develop new treatments to improve patient care. There are well established processes in drug development which consist of four distinct phases of clinical testing. These are briefly summarised in Table 2.4., to provide information on the context within which phase III cancer trials are carried out. Each phase of testing builds on information from the previous phase. Each new drug or treatment will undergo pre-clinical testing and then go through phases I - III, with some also undergoing additional evaluation (after being licensed) in phase IV.

Table 2.4. Phases of clinical trials

Type of Trial	Function / Description
Phase I	Examine the new treatment's safety. Side-effects are identified and the appropriate dose determined.
Phase II	Continue the testing carried out in phase I and determine the new treatment's effect against particular cancers.
Phase III	The drug or treatment looks promising from phase I and II testing and is expected to be at least as good as, hopefully better than the standard treatment available for a particular group of patients with cancer. Phase III trials determine the effectiveness of the new treatment, and how well it works compared to older treatments. In some situations it may be appropriate to have a placebo or 'supportive care' as one of the randomisation arms.
Phase IV	These trials are carried out after the drug is licensed, often to monitor long term effectiveness/side-effects.

2.4.1 Randomised clinical trials

Randomised clinical trials - the focus of this research - are predominantly carried out at the phase III stage of clinical testing, although occasionally randomisation is also carried out in phase II. Although there are scientific and ethical challenges in each phase of clinical research, the randomised clinical trial has been shown to be particularly problematic in relation to misinterpretation and poor understanding of patient information

(Appelbaum *et al.* 1987; Sutherland *et al.* 1990; Snowdon *et al.* 1997; Featherstone and Donovan 2002). In addition, relatively high rates of patient refusal have been shown (Kotwall *et al.* 1992; Klabunde *et al.* 1999), compared with earlier phase studies (Gordon and Daugherty 2001; Cox 2002). Phase III trials comprise the largest component of clinical research, in terms of the number of trials and number of patients involved. These trials are therefore the major contributor to the worldwide problem of low recruitment rates to cancer clinical trials.

2.5 Recruitment to clinical trials

Recruitment to clinical trials generally, is a challenge both within and outwith the cancer setting, with various recruitment rates reported across specialties. Owing to the wealth of information specific to cancer and the particular challenges of recruiting to cancer clinical trials (vulnerable patients, complex terminology), this section will focus predominantly on the cancer literature. However, information will be drawn from the non-cancer literature as appropriate, in relation to the barriers to recruitment, and influencing factors. There is much less literature focussing on interventions designed to increase recruitment, and the health care literature generally will be referred to in this section since much of the 'non-cancer' work is potentially relevant to the cancer setting.

2.5.1 Challenges with the literature reporting recruitment rates

It is difficult to compare rates across studies owing to the different interpretation of 'recruitment rates'. Some investigators consider the actual number of patients recruited within the context of the general population of those with the condition being studied. Others report rates as those patients that meet the inclusion criteria for the trial (all eligible patients), or the proportion of patients who are actually enrolled (all eligible patients who consent). Ideally the percentage of the population that is eligible for recruitment and the percentage of eligible subjects that participate, should be described (Richardson *et al.* 1998). The majority of studies focus on newly diagnosed patients with cancer, as the data

on these cases is often easier to collect. However, it should be acknowledged that substantial numbers of previously diagnosed or established cancer patients are also potentially eligible for clinical trials and do participate. An example of this is the study by Hunter *et al.* (1987) who reviewed community physician logs in order to understand selection factors in clinical trials. They found that 20% of all log entries (cancer patients who were potentially eligible for clinical trial participation) were previously diagnosed or established patients with cancer. Despite reporting this percentage, previously diagnosed or established patients with cancer were not included in their analysis. Concurrent with much of the literature, they focussed on new patients. It is unclear why this was the case, but it appears to be as a result of incomplete data for established patients with cancer.

Several studies of recruitment report hypothetical clinical trial situations where attitudes and intentions to participate are assessed (Llewellyn-Thomas *et al.* 1991; Llewellyn-Thomas *et al.* 1995; Ellis *et al.* 1999b; Trauth *et al.* 2000; Comis *et al.* 2003; Solomon *et al.* 2003). Some of the review papers have included these studies and some have not. It is recognised that it is more helpful to consider actual rates, since what patients think they might do is not always what they actually do when faced with a real life situation. However, information from these studies will be drawn upon in relation to the barriers and interventions, as there are implications for the general education of the public in relation to clinical trials (Comis *et al.* 2003).

2.5.2 Recruitment rates to cancer trials

The following figures are mainly taken from review papers to give an overview of recruitment rates in cancer clinical trials. It is commonly reported that less than 5% of patients with cancer are recruited worldwide into clinical trials each year (Lara *et al.* 2005; Leitch *et al.* 2005; Du *et al.* 2006; Fayter *et al.* 2006). Approximately 2.5-3% of patients newly diagnosed with cancer in the United States (USA) are enrolled into clinical trials each year despite estimates that 12-44% of patients with cancer are eligible for entry into

protocols (Gotay 1991; Morrow *et al.* 1994; Lara *et al.* 2001). Similar figures are reported in the UK usually on the basis of small scale studies, however, in a larger regional study in England in 2000/2001, the enrolment rate was also low at 3.5% (Corrie *et al.* 2003). In a fairly recent report of the National Cancer Research Institute (NCRI) in the UK, the recruitment rate from the National Cancer Research Network was reported at 10.9% of incident cancer cases (NCRI 2004). Prior to this, as discussed in Chapter 1, there was a major political focus on cancer clinical trials and additional government investment. This has resulted in a better infrastructure, better organisation of trials and, as anticipated, increased recruitment rates.

It is common for clinical trials not to reach their initial recruitment targets, and to require an extension to the recruitment period, because they have not recruited the number of patients required to answer the study question. This is confirmed by the review, carried out in the UK, of multicentre studies undertaken by the Medical Research Council and the Health Technology Assessment Board (McDonald *et al.* 2006). They looked at 114 trials between 1994 and 2002 and found that less than one third of trials achieved their original recruitment target, with half being granted an extension (McDonald *et al.* 2006). Low recruitment rates are of concern because of the need to progress scientifically, but also because of the threat to clinical applicability and generalisation of results (Britton *et al.* 1999).

Recruitment to clinical trials varies for several reasons. Some are potentially modifiable, some are not. Many barriers to recruitment have been identified in the literature and fall into four main groups – issues around the patient, clinician, organisation and the trial itself. In addition, there are other factors that may have an influence on recruitment, such as socio-demographic and socioeconomic characteristics, which will be discussed in Section 2.7.

2.6 Factors affecting clinical trial recruitment

Much has been written about factors affecting recruitment, with most of the work focussing on *barriers* to enrolment in clinical trials. This has been both generally (Prescott *et al.* 1999; Ross *et al.* 1999; Afshar *et al.* 2005; Abraham *et al.* 2006; Mills *et al.* 2006) and in trials specific to cancer (Gotay 1991; Ho 1994; Morrow *et al.* 1994; Klabunde *et al.* 1999; Lara *et al.* 2001; Mills *et al.* 2006; Tournoux *et al.* 2006). In the cancer literature, studies have focussed on barriers to recruitment generally, in relation to specific cancer sites (with the majority of work in breast cancer), with respect to a specific location (e.g. cancer centre, regional network), or in the context of a particular trial.

The majority of the studies have investigated doctor or patient perceptions of clinical trial recruitment, with a major focus on barriers. Doctors' perceptions have been studied mainly via interviews and/or survey questionnaires (Hjorth *et al.* 1996; Langley *et al.* 2000; Lara *et al.* 2001; Baum 2002; Kornblith *et al.* 2002; Leitch *et al.* 2005). Patients have also been surveyed (Brown *et al.* 2000; Jenkins *et al.* 2000; Lara *et al.* 2001; Kemeny *et al.* 2003, Avis *et al.* 2006) and interviewed (Mills *et al.* 2003) to elicit their views. Other approaches included interviewing Clinical Research Associates (CRAs) via focus groups, in Canada (Grinfeld *et al.* 2002; Wright *et al.* 2002), and surveying nurses in the USA (Burnett *et al.* 2001). The vast majority of cancer studies have focussed on cancer treatment trials, although there is also relevant work specific to cancer screening and prevention trials, which have produced similar findings in relation to barriers.

Two major reviews of note will be highlighted prior to discussion of specific studies in relation to factors associated with trial recruitment. The Mills *et al.* (2006) study is the only review that has looked specifically at patient reported barriers to cancer trials, and also attempted to quantify the importance of the issues. The other review of note was undertaken by Fayter *et al.* (2006) and is particularly thorough, and again is specific to participation in cancer clinical trials.

Mills *et al.* (2006) analysed 12 qualitative studies (n=722) and 21 quantitative studies (n=5452) in a recent systematic review and meta-analysis of patient-reported barriers to participation in cancer clinical trials. They estimated the frequency with which patients identified particular issues by pooling across the reviewed studies which had presented data on barriers as proportions. A coding template was developed by the authors, which categorised barriers to participation as a) protocol-related, b) patient-related or c) physician-related. The data was then pooled to show the proportions of participants who noted concern for specific barriers identified in the template under these three headings. The most common reasons cited as barriers included: dislike of randomisation; general discomfort with the research process; complexity and stringency of the protocol; presence of a placebo or no treatment group; potential side-effects; being unaware of trial opportunities; the idea that clinical trials are not appropriate for serious diseases; fear that clinical trial involvement would have a negative effect on the relationship with their physician; and their physicians' attitudes towards the trial. It must be acknowledged, however, that the quantitative studies they assessed identified only a few of the barriers compared with qualitative studies, and that due to the small numbers of studies pooled, it is difficult to determine a sense of relative frequency. The authors believe that the majority of concerns identified in their study can be alleviated with directed educational strategies (Mills *et al.* 2006).

A comprehensive review of the barriers to participation, as well as the modifiers and benefits involved in participation in cancer clinical trials, was carried out by the Centre for Reviews and Dissemination at the University of York (Fayter *et al.* 2006). This review included studies over ten years, from 1996, building on an earlier general clinical trials review by Prescott *et al.* (1999). Fayter *et al.* (2006) identified a total of 12,816 references from literature searches, and selected 56 studies reported in 58 papers for the review. They grouped studies according to their perspective – patients or health care professionals (included doctors, nurses and clinical research associates). This was a

thorough review which also assessed the quality of the research, and included unpublished work. All types of study designs were included as long as they provided relevant outcomes. Findings were reported as a narrative summary and in tabular form with data extraction tables and quality assessment tables.

Fayter *et al.* (2006) reported difficulties assessing the quality of several of the studies due to lack of information about recruitment methods, study design and piloting. There were also problems with data collection procedures with many of the studies, including the potential for the introduction of bias, the extent of which they found difficult to quantify. Owing to the methodological limitations of the studies as identified by the review, Fayter *et al.* (2006) are cautious about what should or should not be interpreted as a barrier. They recommend instead that the particular interplay of barriers, modifiers and benefits relevant to participation in cancer trials should be prospectively identified by clinical investigators in light of the 'themes' identified by the review, and they provide checklists to assist with this task. The themes were identified from two perspectives: the patient and the health professional. From the patient perspective, these were:

- issues of treatment preference
- the uncertainty patients feel about participating in trials
- the role of knowledge and information
- the need to time the request for trial participation more carefully.

From the health professional perspective, the themes were:

- a range of system-related and organisational barriers
- barriers inherent in a trial's design
- barriers connected with the attitudes of individual health professionals.

(Fayter *et al.* 2006).

As well as being identified in the reviews, the factors comprising these themes have been consistently identified in both the general and cancer treatment and screening literature. These can be broadly grouped into four categories: 1) the patient; 2) the clinician; 3) the trial; 4) and the organisation. An important additional factor, which has reportedly affected recruitment in the USA, is insurance coverage. However, insurance coverage is becoming less of an issue in some states in the USA due to policy and legal changes related to medical insurance (Martel *et al.* 2004). Since the UK has a different system of health care, medical insurance is not of relevance to the clinical trial setting in the UK.

In order to support and expand on findings from the two reviews already discussed (Fayter *et al.* 2006; Mills *et al.* 2006), relevant research will now be discussed in relation to the identified four categories: patient factors; clinician factors; the trial; and organisational factors

2.6.1 Patient factors

Several patient factors have been identified, by both health care professionals and by patients themselves, as being important in patients' decisions about whether or not to participate in a clinical trial. The majority of research in this area does not have any theoretical foundation, with the exception of a small number of papers that link trial recruitment to theories of health behaviour (Morrow *et al.* 1994; Sutherland *et al.* 1998; Verheggen *et al.* 1998). This review of patient factors will begin with these studies.

2.6.1.1 *Health behaviour theory*

Morrow *et al.* (1994) reviewed the literature on recruitment to oncology trials and developed a framework for integrating information about oncology trial accrual in relation to four core concepts implicated in patient-related health behaviour as shown in Table 2.5. These are based on the central concepts from four theories of health-related behaviour:

the Health Belief Model, Subjective Expected Utility Theory, Protection Motivation Theory, and the Theory of Reasoned Action (Morrow *et al.* 1994). From the literature, the authors organise the patient and physician factors thought to influence patient enrolment in clinical trials into the four behavioural concepts shown in Table 2.5.

Table 2.5. Central concepts in understanding health-related behaviour (Morrow et al. 1994)

The <i>probability</i> that an unwelcome health event will happen to a patient
The <i>severity</i> of that event if it does occur
The <i>effectiveness</i> of a particular behaviour such as taking part in a clinical trial
The <i>cost</i> of adopting that behaviour

It must be noted that their ideas do not appear to have been tested in a prospective clinical trial situation, although aspects of them have been taken forward in relation to specific theories.

Verheggen *et al.* (1998) carried out a hospital-wide survey in The Netherlands to provide more insight into the socio-psychological determinants of patient participation in clinical trials, and used an extended form of the Health Belief Model (HBM) to explain clinical trial participation. In relation to explaining health actions, the HBM hypothesises that behaviour depends mainly on 1) the desire to get well if ill (or to avoid sickness if well) and 2) the belief that a specific health action will restore health, or prevent or improve illness (Verheggen *et al.* 1998). To be able to do this, the 'cue of action' must be evoked to trigger the decision-making process. An individual's personal perception and motivation, or information provided by the clinician, can evoke this cue of action (Veheggen *et al.*

1998). Verheggen *et al.* apply this theory to the decision about participation in clinical trials, and postulate that the decision may be explained by the extent to which a patient perceives a threat to his or her health, and the extent to which a patient believes that trial participation will be effective in reducing this threat, given the perceived effectiveness of standard treatment. In addition to these original features of the HBM, Verheggen *et al.* (1998) assessed 'subjective norm' which focussed on the self reported influence that important others may have on behaviour, locus of control, and a number of general health values and orientations of patients. Using questionnaires, they interviewed 198 patients after they had made their decision about whether or not to participate in the trial, and claim that patients make a personal balance account when deciding about participation. This includes the physical and emotional added value that patients hope to gain from the trial treatment, as compared with the non-trial treatment, minus the risks they expect in the trial and the extra time they expect the trial to take. They suggest that the extent to which patients feel physically threatened by their illness, and their opinions about medical care and care-givers in general, will also affect their decision (Verheggen *et al.* 1998).

The Theory of Reasoned Action, which predicts that personal attitudes and 'subjective norm' are influential in determining intention to undertake a behaviour, was used as a conceptual framework for developing a questionnaire to elicit beliefs and attitudes about participating in a hypothetical chemotherapy trial (Sutherland *et al.* 1998). Sutherland *et al.* hypothesised that such a questionnaire could serve as a decision aid for patients deciding whether or not to take part in a clinical trial. The main purpose of the study was to understand the underlying beliefs of patients with cancer about taking part in clinical trials. Two types of beliefs were identified – universal beliefs and trial-specific beliefs. Another group of beliefs – individual-specific beliefs - were not identified by the questionnaire, although they were highlighted by patients in the study as being important. The authors acknowledge that individual-specific beliefs could have had a substantial

influence on attitudes and intention to participate (Sutherland *et al.* 1998). They found that, although there was support for the theory, once attitude was taken into account, 'subjective norm' had only a small contribution to make. Patients' decisions on the whole did not appear to be influenced by the questionnaire, which in turn did not appear to contribute to the decision-making process. Patients seemed to have made their decision about participation soon after first hearing about the trial. However, it must be noted that a major limitation of this study was that actual behaviour (i.e. clinical trial participation) was not studied, only intention to perform the behaviour.

Curbow *et al.* (2004) hypothesised that knowledge and beliefs play a central role both in patient understanding of the informed consent process and in their decision to accept participation in a trial. They tested an intervention which increased knowledge but this was not associated with a change in beliefs. Beliefs are often hypothesised to be determinants of behaviour either directly (Health Belief Model) or through attitudes (Theory of Reasoned Action) (Curbow *et al.* 2004). It has been suggested that pre-existing knowledge can bias the processing of new information in a negative or positive way and that a high level of knowledge can stabilise beliefs, making them more likely to be associated with behaviours (Eagly and Chaiken, 1993 in Curbow *et al.* 2004). Unfortunately, the authors did not investigate the effect on actual consent rates.

In cancer screening, models of health behaviour have been shown to be poor at consistently predicting behaviour (Bish *et al.* 2000 in cervical cancer, Yarbrough and Braden 2001 in breast cancer). It is unclear how useful these models are at explaining or predicting behaviour within the cancer clinical trial setting, since as discussed, the research in this area is very limited. Specific health beliefs, rather than the combination of factors within the models themselves, appear to be important in relation to clinical trial recruitment.

The literature shows a trend for patients with particular health beliefs to be more likely to participate:

(1) patients with higher concern about their illness (Harth *et al.* 1992 in terms of parents' status in paediatric trials; Gorkin *et al.* 1996 in cardiology; and O'Connell *et al.* 2002 in HIV).

(2) patients who were sicker or had advanced disease (Schwartz and Fox 1995 in MS; Gorkin *et al.* 1996 in cardiology; Charlson and Horwitz 1984 and Britton *et al.* 1999 in general health studies).

As a way forward in health behaviour research, it is suggested that theory comparison is essential, as is the recognition of the similarity of health behaviour constructs (Noar and Zimmerman 2005). From the four models of health behaviour commonly tested in health research studies (previously discussed at the beginning of this section), two of the core common concepts are the probability that an unwelcome health event will happen to a patient, and the severity of that event if it does occur (Morrow *et al.* 1994). 'Higher concern about their illness' is consistent with the probability concept, and 'patients who were sicker or had advanced disease' is consistent with the severity concept.

More recently, Leventhal's Common Sense Model of self-regulation (CSM) has received substantial attention in the literature and has been widely used to understand responses to illness (Marteau and Weinman 2006). It has also been suggested to be useful in understanding risk information and behaviour (Cameron 2003, in Marteau and Weinman 2006). There are two parallel components to the model: the cognitive processing of how people regulate their responses to illness danger, and the person's regulation of emotional control (Hale *et al.* 2007). Illness representations or lay beliefs about disease integrate with the existing, normative guidelines that people hold, to allow them to make sense of their symptoms and guide any coping actions (Hale *et al.* 2007). The five key domains of illness representations have been established as identity, cause, timeline, consequences

and control/cure (Leventhal *et al.* 2001). *Identity* is the name given to conditions and symptoms; *cause* relates to a personal perception based on experience as well as professional information; *timeline* includes how long condition will last, acute v's chronic; *consequences* reflect the personal belief of the physical and social impact from the condition; and *cure/control* is concerned with the personal beliefs about cure and control and the person's perception of their influence over this. Cameron *et al.* (2005) used the CSM in their study of the role of illness beliefs, emotion regulation factors and socio-demographic characteristics in decisions to participate in a group support program for patients with breast cancer. They found that participation appeared to be guided by cognitive and affective factors identified by the CSM. However, the model does not appear to have been used in relation to the clinical trial participation decision. For the CSM to be used effectively it would be necessary for researchers to be clear whether they were trying to influence trial participation in its own right or whether they saw trial participation as an intermediary to helping people manage their cancers.

Because the majority of studies on clinical trial recruitment have no theoretical basis and do not address the complex relationship between knowledge, attitudes and behaviours, Fayter *et al.* (2006) suggest that future research uses a theoretical underpinning similar to that used by Vergheggen *et al.* (1998) (which was not specific to cancer), with an extended form of the HBM. However in view of the lack of compelling evidence, health behaviour theory was not used as the main theoretical underpinning for this study, although specific components of health behaviour models, such as the severity of disease, were assessed.

2.6.1.2 Patient refusal

In many studies, patient refusal accounts for the largest proportion of clinically eligible patients not entered into trials (Kotwall *et al.* 1992; Klabunde *et al.* 1999; Lara *et al.* 2001). Although it is considered good practice to collect data on eligible patients who were not

entered into a trial (Altman 1996), including the proportion of patients who decline to participate, this is not always done and is often omitted from the study publication. This is an important issue which can result in difficulties determining representativeness of the results to the relevant patient population. It is also difficult therefore to generalise about refusal rates for different types of trials.

In the non-cancer literature, varying refusal rates have been reported: 35% in a sample of 400 patients for a cardiac arrhythmia study (Gorkin *et al.* 1996), 67% in a sample of 789 women considering a trial of oestrogen for stroke (Corbie-Smith *et al.* 2003), and 36% (n=871) of elderly patients (n=2403) in a trial of pharmacy practice research (Petty *et al.* 2001).

In cancer trials, similar rates have been reported: 28% (Jenkins and Fallowfield 2000); 40% (Klabunde *et al.* 1999); and 49% (Lara *et al.* 2001). Higher rates are typically reported in chemotherapy prevention/risk counselling studies, when compared with treatment trials; for example, in a trial of breast cancer risk counselling, this figure was 53% (Rimer *et al.* 1996). It has been suggested that the perceived likelihood of having, or being at risk of developing, cancer may be the determining factor on a patient's decision about whether or not to participate in a cancer prevention trial (Morrow *et al.* 1994). Due to the severity of cancer and the negative connotations of the disease, it could be anticipated that this would be a powerful motivator for participation in prevention/risk counselling trials. It is interesting, then, to note that refusal rates are typically higher in these trials, a finding which challenges the idea that severity of illness is likely to increase participation in trials. This may be as a result of 'optimism bias', where people believe that they are invulnerable and consider their own chance of ill health to be below average (Weinstein 1982). Unrealistic optimism was present in cancer screening studies for prostate cancer and for breast cancer, in the majority of elements of the health behaviour models (Clarke *et al.* 2000). Patients were interviewed about their risk of getting the disease, perceived

severity of the disease, and benefits of and barriers to having screening (mammogram for breast cancer, PSA testing for prostate cancer). Self-ratings were compared with mean scores for the ratings of others. For example, in breast cancer, for 'risk', women were asked to estimate the percentage risk of getting breast cancer, giving a figure between 1 and 100%. They estimated this at 25.7% for self and 44% for others (mean scores) which show unrealistic optimism in relation to perceived risk (Clarke *et al.* 2000). Similar results were found in all HBM variables for prostate cancer and almost all for breast cancer (the exception was general barriers associated with having a screening mammogram) (Clarke *et al.* 2000).

Some trials have asked participants to respond to hypothetical situations; these have reported refusal rates of 40% in chemotherapy trials (Sutherland *et al.* 1990) and 58% for a chemotherapy trial specific to colorectal cancer (Llewellyn Thomas *et al.* 1991). However, the limitations of trials that ask about hypothetical situations cannot give confidence that this is reflective of patients actually faced with the decision (Cassileth *et al.* 1982).

An English cancer research network had one of the lowest refusal rates in the literature, at 19%, which was in the context of a relatively high overall recruitment rate of 10% in 2002 (Corrie *et al.* 2003). There may be several reasons for this. This network is part of the National Cancer Research Network, which was set up, with investment, to increase recruitment to cancer clinical trials, predominantly by increasing the infrastructure to support clinical trials; as a consequence it may be that patients are better supported and that their informational needs are better met. It is difficult to know, as this was not discussed, and data was not collected on reasons for patient refusal.

2.6.1.3 Reasons for patient refusal

There are many reasons contributing to patients' decisions to decline a clinical trial. Unfortunately, the literature is limited in this area and only a minority of clinical research papers report reasons for refusal. The data has often been collected from clinicians or data managers, resulting in the question of how closely this would reflect reasons given directly by patients themselves. Cox and McGarry (2003) reviewed the literature in relation to why patients don't take part in cancer trials, and found a paucity of in-depth information from the perspectives of patients themselves about the underlying decision making processes and reasons why patients don't participate.

Most of the research that has been done directly with patients is in a hypothetical trial situation, where their attitudes or opinions are assessed in relation to clinical trial decision making. Much has been learned from this work about attitudes and opinions, but, as already stated, it must be acknowledged that hypothetical situations are not always representative of real-life experience, and research has shown that patients can act differently when making personal decisions (Cassileth *et al.* 1982; Trauth *et al.* 2000).

Surveys focussing on patients only, via self-report, will give good information about patients' perceptions of the reasons they refused or accepted a trial. However, this approach may miss important reasons affecting the decision that patients themselves are not aware of, such as poor understanding of the information. A small number of studies have looked qualitatively at reasons why patients accepted or refused to participate in a clinical trial, and issues relating to information and understanding were identified (Paskett *et al.* 1996; Featherstone and Donovan 2002).

Taking into account the limitations of the literature, reasons for patient refusal include lack of trust in medical research, negative attitudes and beliefs towards clinical trials (from clinicians as well as patients), preference for treatment, additional demands of the trial, worry caused by uncertainty, concerns about information and consent, including difficulty understanding trial information and issues around randomisation (Gotay 1991; Morrow *et al.* 1994; Lovato *et al.* 1997; Klabunde *et al.* 1999; Ross *et al.* 1999; Lara *et al.* 2001; Cohen-Mansfield 2003, Curbow *et al.* 2006). Practical barriers included transport, cost and time (Fayter *et al.* 2006).

Jenkins and Fallowfield (2000) surveyed both patients who agreed and those who declined clinical trial entry about the reasons influencing their decision. Two hundred and four patients completed a 16-item questionnaire designed for the purposes of the study. Altruism and trust in the doctor were reported as the main reasons for taking part. Trust in the doctor was also cited as a main reason for declining participation; but, as acknowledged by the authors, in the absence of detailed interviews, it was not possible to know how this phrase was interpreted by patients, or the effect of the perceived benefits of standard treatment. Another main reason given by patients for declining the trial was worry about randomisation. As noted by the authors, it is not clear whether this is because patients did not understand the concept, or because they did.

The type of trial, as well as, good communication with the clinician, were also powerful motivating factors for participation (Jenkins and Fallowfield 2000). Another important factor is whether or not a placebo or 'no treatment' arm is involved (Jenkins and Fallowfield, 2000). In the Jenkins and Fallowfield (2000) study, 35 different oncology trials were reviewed involving 17 medical clinicians in the UK. A significantly higher acceptance rate for trials providing active treatment in every arm (80.6%) was reported, as compared with those trials with a 'no treatment' arm (60.5%). Refusal has been shown to be higher

among patients offered adjuvant phase III protocols (37%) compared with non-adjuvant protocols (29%) (Hunter *et al.* 1987). Refusal was also higher for cancer trials involving chemotherapy and radiotherapy, as compared with hormone therapy where there was a high acceptance rate of 85.5% (Jenkins and Fallowfield 2000). However, Spiro *et al.* (2000) reported a refusal rate of 73.5% of potentially eligible patients to a lung cancer trial running in two centres in London. The trial involved patients receiving their primary treatment (surgery, radiotherapy or best supportive care) and then being randomised to either receive or not receive three courses of chemotherapy. The high refusal rate could have been due to the very different treatment arms and patients having a preference for or against chemotherapy. It could also be due to lack of understanding of equipoise and/or the information provided. However, it is difficult to know since limited information was collected on reasons for patient refusal, with 44% of patients declining without giving a reason (Spiro *et al.* 2000).

In some trials family members were found to influence patients against trial participation (Paskett *et al.* 1996 in breast cancer; Camerini *et al.* 1999 in breast cancer chemoprevention trials; Spiro *et al.* 2000 in lung cancer; and Wilt *et al.* 2003 in prostate cancer). Reasons for this are not clear in the literature.

2.6.1.4 Randomisation

Patient understanding of the concept of randomisation is further discussed in Chapter 3. However, the focus here will be the effect on recruitment of poor understanding, acceptance and attitudes towards randomisation.

Challenges with understanding the concept of randomisation, reluctance to be randomised, and attitudes to randomisation have all been associated with poor recruitment. Reluctance to be randomised, was a major barrier for patients with breast

cancer who were surveyed about their attitudes to complementary and alternative medicine clinical trials (Melisko *et al.* 2005). Understanding and acceptance of clinical equipoise were key to participants' consent to randomisation in a prostate cancer trial (Mills *et al.* 2003). Attitudes to randomisation have been studied by Fallowfield *et al.* (1998a), using a self report questionnaire: The Attitudes to Randomised Trials Questionnaire. This tool discriminated between three different patient groups:

- Those who seem comfortable with the concept of randomisation.
- Those with some concerns who, with fuller explanation of the concept, are willing to consider randomisation.
- Those firmly against randomisation and participation in clinical trials, regardless of what information is provided.

Out of 315 patients completing the questionnaire, only 141 (44.8%) would agree to participate in a trial if it was randomised. When patients were given further information about randomisation, 119 (68.4%) of the 174 who initially said no to randomisation, or who were unsure, reported that they would change their minds and take part (Fallowfield *et al.* 1998a). This suggests that by improving communication about, and understanding of, randomisation, clinical trial recruitment rates could be increased. This view is supported by Harrison *et al.* (2007), who studied patients' and doctors' willingness to participate in a hypothetical trial for rectal cancer. Dislike of randomisation was a common reason for patient refusal.

2.6.1.5 Relationship with physician

The relationship between the patient and the physician (or clinician) is becoming of increasing interest to researchers studying clinical trial recruitment. Several factors have been shown to be important. Mistrust in the clinician is often cited by patients as a barrier to participation: Abraham *et al.* (2006), in a review of surgical randomised trials, and Mills

et al. (2006), in a review of HIV drug trials. The converse has also been shown to be the case. 'Trust in the clinician' was identified as an important motivator for participation in a clinical trial for patients with prostatic disease (Featherstone and Donovan 2002) and in early anticancer drug trials (Cox and Avis 1996). In gynaecology, the patient-physician relationship has been shown to be important to patients considering clinical trial participation. Patient level of familiarity with the physician-investigator was considered the most important factor affecting clinical trial participation when gynaecology patients entering clinical trials were compared with gynaecology patients not entered (Luck *et al.* 2005).

Patients' perceptions of the health care professional, or the recommendations made by them, have been shown to be important in the patient's treatment decision (Paskett *et al.* 1996; Ellis *et al.* 1999b [both studies carried out in hypothetical conditions with a major focus on patients with breast cancer]; Grant *et al.* 2000). Other factors affecting the doctor-patient relationship are discussed in the following section – clinician factors – in relation to communicative behaviour of clinicians.

2.6.2 Clinician factors

Clinician factors affecting clinical trial recruitment have been reported as: attitudes towards trials; motivations for participation; time constraints; worry about effect on doctor-patient relationship; lack of staff and training; concern for patients; lack of professional autonomy; preference for treatment and difficulty with the consent procedure (Gotay 1991; Morrow *et al.* 1994; Klabunde *et al.* 1999; Prescott *et al.* 1999; Ross *et al.* 1999; Lara *et al.* 2001; Abraham *et al.* 2006; Castel *et al.* 2006). Physicians' attitudes were considered to be the principle physician-related barriers according to CRAs (Grunfeld *et al.* 2002). These included their own personal beliefs about the trial, or their attitudes towards the suitability of a patient for a specific trial, despite meeting the eligibility criteria, for reasons such as anticipated logistic problems, or the belief that the patient would not understand

the information, or was too old to cope. Fallowfield *et al.* (1997) also studied clinicians' attitudes to clinical trials of cancer therapy and found that there were differences between professional groups within oncology: medical oncologists placed more emphasis on research than clinical activities, felt more pressure to take part in trials, and were more likely to value the resulting higher profile, nationally and internationally, of clinical trial participation, as compared with clinical oncology and surgical colleagues (Fallowfield *et al.* 1997). Other factors cited in the literature are reluctance to refer patients for clinical trials (Siminoff *et al.* 2000), and health professional gate keeping of a trial due to personal biases towards or against a study arm (Hjorth *et al.* 1996; Ellis *et al.* 1999a; Langley *et al.* 2000; Westcombe *et al.* 2003). In some situations there is also a lack of awareness of ongoing clinical trials, on the part of health care professionals (Siminoff *et al.* 2000; Fayter *et al.* 2006).

Health care professionals as modifiers of clinical trial participation are becoming more frequently studied and discussed. Ruckdeschel *et al.* (1996) reported that one of the major factors determining whether patients will be successfully accrued to trials is the quality of the communication between the physician and the patients (and family members if present). Communicative behaviour of clinicians has been reported by patients in several studies as influencing their decision about whether or not to take part in a trial. Grant *et al.* (2000) found that, for patients who said 'yes' to a cancer trial, physicians communicative behaviours and patient satisfaction were important factors in their decision. For patients who said 'no', the motivations were less clear. Rapport, awareness and understanding of randomised clinical trials were important reasons for patients with prostate cancer accepting a clinical trial (Eng *et al.* 2005). Physicians who are supportive and responsive to patients' concerns are likely to be the most effective at enrolling patients in studies (Albrecht *et al.* 2003). It follows, then, that understanding patients' decisions about trials, and improving the communication process, are key to improving clinical trial recruitment (Albrecht *et al.* 2003).

Albrecht *et al.* (2003) developed a model to explain patient decision making about clinical trials which is shown in Figure 2.1. This model posits that 1) the characteristics of the physician, 2) the nature of the trial protocol itself, 3) predisposing factors of the patient, and of the patient's family member or significant other, affect a patient's decision to enrol in a clinical trial. The impact of all of these variables on the actual participation decision is mediated by the kind of communication that occurs between the individuals (Albrecht *et al.* 2003).

This model has not been widely tested to date, but a federally funded study is currently underway in the USA, to fully evaluate the model and to determine the extent to which all the components, as incorporated into a more elaborated structural equation model, independently and collectively explain patient perceptions of the physician and patient decisions regarding trial treatment (Albrecht *et al.* 2003).

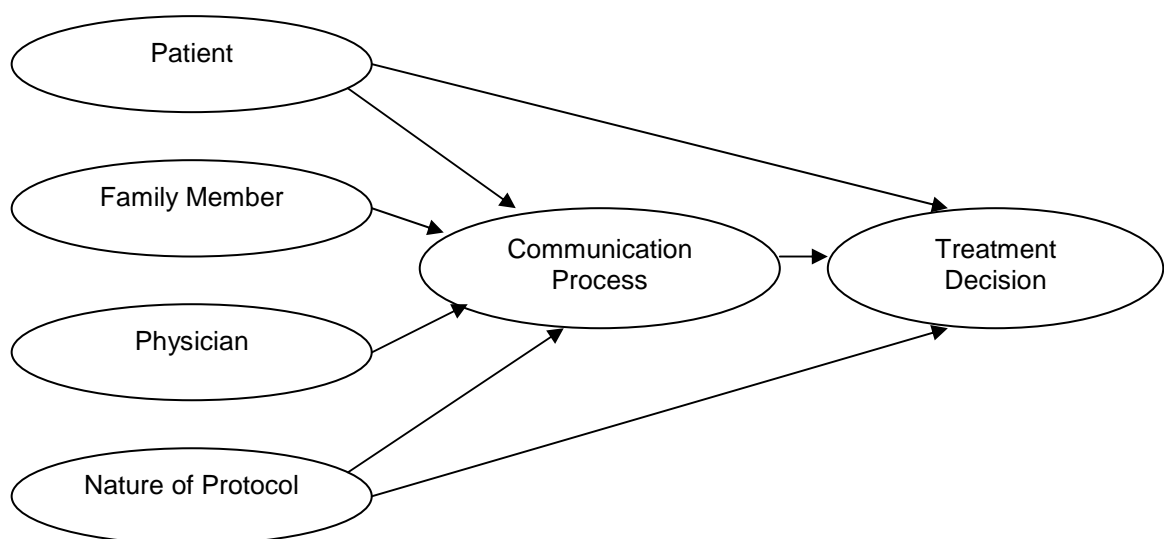


Figure 2.1. Conceptual model of the factors affecting patients' decisions about clinical trials (Albrecht *et al.* 2003)

The importance of the interaction between the patient and the clinician, as highlighted in the literature, is consistent with Manson and O'Neill's (2007) thinking in relation to

informed consent. Manson and O'Neill discuss the transactional or interactive character of successful communication as being crucial to informed consent (p69); their argument will be discussed more in Chapter 3. This is consistent with ideas from a number of decision analysis perspectives, that it is the communication transaction that appears to be important.

2.6.3 Trial

There are a number of factors affecting recruitment which are associated with the trial itself. These include: availability of trial, restrictive eligibility criteria, complicated trial design and challenges with the informed consent procedures, including the mode of presentation of information (Gotay 1991; Morrow *et al.* 1994; Klabunde *et al.* 1999; Lara *et al.* 2001; Fayter *et al.* 2006). The scientific rationale of the trial is important in engaging health care professionals (Ellis *et al.* 1999a; Baum 2002; Wright *et al.* 2002; Westcombe *et al.* 2003; Fayter *et al.* 2006), with 'insufficiently interesting research question' identified as a barrier in the review by Prescott *et al.* (1999).

2.6.4 Organisational/system factors

Most of the issues in relation to organisational factors focus on the resource-intensive nature of running clinical trials, and the need for an adequate infrastructure and resources. In some cases, the consequence will be that the clinical trial will not take place at all. In others, the trial will be initiated, but will recruit low numbers of patients or none at all. Lack of resources was identified by medical oncologists, radiation oncologists and surgeons as one of the major barriers to participation in breast cancer trials in Australia (Ellis *et al.* 1999a). Similarly, in Germany inadequate infrastructure was identified as the main reason that German institutions do not take part in ovarian cancer trials (Sehouli *et al.* 2005). Somkin *et al.* (2005) investigated organisational barriers to clinical trial recruitment in the USA, highlighting the need for infrastructure, intra-organisational communication, and consideration of trial impact on internal health plan resources. Furthermore, according to

Clinical Research Associates, 'systems barriers' were the main issues negatively affecting clinical trial accrual in Canada, specifically the impact of greater demands in a climate of decreasing health care resources (Grunfeld *et al.* 2002).

In the UK, infrastructure and resources are substantial challenges, although this is improving due to the political investment in clinical trials discussed in Chapter 1. The additional time involved discussing the trial, and obtaining consent, has been highlighted as a substantial component of the extra work generated by a clinical trial (Grunfeld *et al.* 2002; Kornblith *et al.* 2002; Wright *et al.* 2002). Other institutional issues that have been identified are trials competing for the same patient population (Skeel *et al.* 1998; Goodwin *et al.* 2000).

2.6.5 Summary of the patient, clinician, trial and organisational factors

It is difficult to quantify the extent of influence of individual factors discussed, as the majority of studies do not address this. As Fayter *et al.* (2006) point out, what is important is knowledge of these as potential issues for any trial, and a good assessment prior to initiation of the trial. The relative importance of barriers will vary according to the context and the setting (Fayter *et al.* 2006).

It is essential to address the barriers wherever possible, to optimise patient recruitment. Importantly, issues around patient information and communication, understanding and informed consent are identified in all four 'barrier' areas (patient, clinician, trial, organisational/system). This is one domain that *is* potentially modifiable and will be further discussed in Chapter 3. This is especially important since many of the socio-demographic and socioeconomic factors discussed in the next section, whilst of interest, are not amenable to change and therefore not typically influenced by interventions to increase accrual (Morrow *et al.* 1994).

2.7 Socio-demographic and socioeconomic factors

There are inconsistencies and conflicting findings, in both the general and the cancer literature, in relation to the influence of socio-demographic (SD) and socioeconomic (SE) factors on clinical trial recruitment rates. Much of the research is from the USA and it is difficult to know how this compares with other countries. In addition, it has been suggested that differences in SD and SE characteristics between clinical trial populations, compared with real world populations, may impair extrapolation of results (Connolly and Low 2000). As a result of the potential selection bias, there may be a predictive nature between SD characteristics and measured trial data points, such as treatment compliance, trial dropout, adverse event reporting and resource utilisation, which may impair a trial's operational integrity and efficiency (Connolly and Low 2000). This is in addition to the potential influence on recruitment rates. SD and SE factors should be considered in the planning stages of a trial; however, it is acknowledged that this needs to be on a trial-specific basis, taking into account the clinical context, due to the inconsistencies in the literature across studies.

2.7.1. General literature

2.7.1.1 *Age and education status*

In the general literature, studies showed no difference in recruitment rates with age (van Stuijvenberg *et al.* 1998, parents' status in paediatric trials); gender (Ethier *et al.* 1999 in HIV); or education (Gorkin *et al.* 1996 in cardiology; Corbie-Smith *et al.* 2003 in stroke). The influence of education status on recruitment is unclear, with conflicting results from studies. Better educated patients consented to trials for anxiety (Rapaport *et al.* 1995), HIV (Hankins *et al.* 1998) and a non-pharmacological intervention in the elderly (Whelton *et al.* 1997). Poorly educated patients were more likely to consent in an HIV trial (Bartholow *et al.* 1997) and paediatric trials (parents were consenting) (Harth *et al.* 1992). A large cardiology study showed no difference in education status of participants;

however, patients with a high understanding of the trial information were more likely to participate (Gorkin *et al.* 1996).

2.7.2 Cancer

In relation to cancer trials, the influence of socio-demographic and socioeconomic factors is also inconclusive.

2.7.2.1 Age

Despite conflicting findings, the majority of studies in cancer showed no difference in age (Llewellyn-Thomas *et al.* 1991 in colorectal cancer; Jenkins and Fallowfield 2000 in general oncology; Kemeny *et al.* 2003 in breast cancer; Movsas *et al.* 2007 for radiotherapy patients). Interestingly, although the study by Kemeny *et al.* (2003) showed no difference in participation as a result of age, both age and stage of cancer were predictors of whether a patient was offered a trial (fewer older patients were offered). Movsas *et al.* (2007) also found that type of cancer was not predictive of enrolment in trials for radiotherapy patients.

A trend in both directions for the influence of age has been reported in large scale studies. In an Ocular Melanoma study, older patients were more likely to participate (Diener-West *et al.* 2001). In contrast, a study of breast cancer patients in Scotland found that older patients were less likely to participate (Twelves *et al.* 1998). For newly diagnosed patients with a wide range of cancers, younger age was also a predicting factor for participation (Hunter *et al.* 1987). Melisko *et al.* (2005) explored attitudes towards complementary and alternative medicine (CAM) clinical trials in patients with breast cancer, and found that attitudes were significantly affected by patients' age and stage of disease. Older people and those with earlier stage disease had more negative attitudes towards CAM trials. However, treatments given in CAMS trials are different to more aggressive anticancer treatments given in the majority of cancer clinical trials, for reasons including side-effect

profile and anticancer effect. Caution should therefore be exercised in generalising results outwith the CAM trial setting.

2.7.2.2 Gender, education, and stage of disease

Similar to the more general literature, there was also no difference in gender (Hunter *et al.* 1987 in newly diagnosed cancers; Llewellyn-Thomas *et al.* 1991 in colorectal cancer), or education (Llewellyn-Thomas *et al.* 1991) in relation to the participation decision. There was the same trend as in the general literature for patients who were more unwell: patients with more symptoms were more likely to participate (Diener-West *et al.* 2001).

Interestingly, in trials of cancer prevention, screening and risk counselling, there is a trend for younger, married, more educated clients with a high perceived severity or disease risk, to participate (Mettlin *et al.* 1985; Rimer *et al.* 1996; Nijs *et al.* 1997). These trials are intrinsically different to cancer treatment trials, which form the largest component of clinical cancer research, and involve patients *without* cancer. Morrow *et al.* (1994) explains the distinction between the two types, discussed as 'cancer treatment trials' and 'cancer control trials', in relation to key concepts from models of health behaviour. Issues of disease probability and severity have much more importance in prevention and screening trials (Morrow *et al.* 1994). Despite the distinction, generalisations are being made from these studies to cancer clinical trials as a whole, by authors such as Kotwall *et al.* (1992). This can result in an inaccurate picture of the influence of socio-demographic and socioeconomic factors in cancer clinical trials.

2.7.2.3 Socioeconomic status

SE status does appear to be related to recruitment to cancer clinical trials. Sateren *et al.* (2002) considered 24,332 patients accrued to NCI sponsored cancer treatment trials in the USA over a 12 month period, and found that geographical areas with high SE levels had higher levels of clinical trial accrual. Conversely, older women with breast cancer with

low SE status were less likely to take part in a trial (Gross *et al.* 2005). Conflicting findings were reported in a study of patients with sarcoma (n=103) where there was no influence of socioeconomic status on recruitment rates (Barofsky and Sugarbaker 1979). It must be acknowledged that this was a small scale study, with a specific patient group.

2.7.2.4 Minority groups

Research focusing on minority groups is not widely evident in the UK literature, although there is substantial work from the USA in relation to minority groups as a whole (Guiliano *et al.* 2000) and also focussing specifically on African Americans (Shavers *et al.* 2001), Asian-Americans (Nguyen *et al.* 2005), Latinos (Herman and Larkey 2006), Chinese American (Tu *et al.* 2005), American Indians and Alaskan Natives (Hodge *et al.* 2000). Much of what is reported is specific to cancer screening, with less research specific to cancer treatment trials. It has been suggested that minority groups are less likely to enrol in cancer trials (Murthy *et al.* 2004). Similar issues to those identified as barriers to participation in non-minority groups have been identified – lack of knowledge, communication challenges, fear, mistrust, attitudes and beliefs, financial costs, low socioeconomic status as well as cultural characteristics (Guiliano *et al.* 2000). Trust in the physician was an important theme influencing recruitment in several of the studies (Shavers *et al.* 2001).

There have been several successful initiatives in the USA to increase recruitment in minority groups. For example, the Eastern Cooperative Oncology Group in California introduced clinical trials education programmes for patients, families and clinicians (Pinto *et al.* 2000). Brown *et al.* (2000) used culturally targeted mass mailings and media presentations, based on acquiring an understanding of the minority community, to increase recruitment of minority women in cancer screening, prevention and treatment trials.

2.8 Strategies to increase clinical trial recruitment

Due to the complexity of barriers that need to be addressed to improve recruitment to clinical trials, the interventions that have been tested have been diverse (McDaid *et al.* 2006). There are a number of good systematic reviews that summarise the evidence in this area.

2.8.1 General literature

Within the general clinical trial setting, Mapstone *et al.* (2007) reviewed strategies to improve recruitment to research studies focussing on RCTs and Quasi RCTs. They found 15 eligible trials, which included a total of 33,719 participants. Trials of monetary incentives, additional questionnaire at invitation, and treatment information on the consent form all demonstrated benefit. However, the authors acknowledge that these specific interventions from individual trials are not easily generalisable. They conclude that it is not possible to predict the effect most interventions will have on recruitment (Mapstone *et al.* 2007).

Watson and Torgerson (2006) carried out a systematic review of recruitment intervention studies from 1996 - 2004. Hypothetical and 'mock' trials were excluded, and included studies had to have used random allocation. They identified 14 papers with 20 interventions and reported similar findings to the Mapstone review. Effective interventions included telephone reminders, questionnaire inclusion, monetary incentives, using an open rather than a placebo design, and making trial material culturally sensitive (Watson and Torgerson 2006).

Another systematic review investigated interventions to improve research participants' understanding during the informed consent process (Flory and Emanuel 2004). Hypothetical or simulated studies were included in the review, with the main outcome of

interest being improved understanding, although data on willingness to participate in clinical trials was also reported. Forty-two studies were included: 12 reporting multimedia interventions; 15 enhanced consent forms; 5 extended discussion; 5 of test/feedback interventions (where participants were tested on the information they received and received feedback on incorrect answers); and another 5 were classed in a miscellaneous category. Twelve studies reported accrual or willingness to participate as a secondary aim of the study, and there was a willingness to join a randomised trial in 3 of these. However, these were all simulated scenarios with unknown relevance to a real situation. The authors recommend that further studies avoid using hypothetical scenarios.

2.8.2 Cancer clinical trials

A high quality systematic review of interventions to increase participation of cancer patients in randomised controlled trials (RCTs) was recently carried out by the Centre for Reviews and Dissemination at the University of York (McDaid *et al.* 2006). They reviewed studies of any intervention to improve cancer patient participation in RCTs which reported participation rates. Eight studies were identified, with the majority concerned with some aspect of the consent process. Only three were concerned with interventions implemented within a UK context (McDaid *et al.* 2006). In the first study, Donovan *et al.* (2002) used qualitative research to successfully increase recruitment (from 40% - 70%) in a treatment trial for prostate cancer by changing the nature and emphasis of information and presentation to patients. They carried out in-depth interviews to explore patients' interpretation of study information, and tape-recorded recruitment appointments to enable scrutiny of content and presentation of study information by recruiters. Results showed that recruiters had difficulty discussing equipoise and presenting treatments equally, and unknowingly used terminology that was misinterpreted by participants. This information was then used to determine changes to content and presentation of information, namely changes to the order of presenting treatments to encourage emphasis on equivalence,

avoidance of misinterpreted terms, redefining of the non-radical arm, and a more convincing presentation of randomisation and clinical equipoise. In the same trial, reported in a separate paper, Donovan *et al.* (2003) found that nurses and urologists were equally effective at recruiting patients with nurses being more cost effective. In the other study, doctors were provided with information about patient preferences for information and their attitudes towards trials, before they discussed the trial with the patient. Trial participation rates were then compared between this group of patients and a comparison group where doctors did not receive prior information. No difference in recruitment rates was found (Fleissig *et al.* 2001).

McDaid *et al.* (2006) concluded that there is not a strong evidence base for interventions that increase cancer patient participation in clinical trials, and that good quality RCTs are needed in this area. Another important point highlighted by this review was that due to the dangers of coercion, research involving interventions targeted at the informed consent process as a means of increasing trial participation should not be considered in isolation from the quality of the informed consent process (McDaid *et al.* 2006).

2.9 Summary of Part I - Recruitment

There is no shortage of studies investigating the problems of low recruitment to clinical trials, with many identifying lists of barriers in relation to the patient, clinician, trial and the organisation. The literature is unclear about the effect of age, gender and education status, but suggests that higher socioeconomic status and poorer prognosis/unwell patients are more likely to consent to a cancer clinical trial.

Few trials have been undertaken of interventions designed to improve trial recruitment. Those which have attempted to address some of the barriers to recruitment are generally small scale and difficult to generalise. A recent review assessing effectiveness of

interventions to increase recruitment in randomised cancer treatment trials concluded that there was no effect in any of the studies reported, but that the evidence was not of sufficient quality to conclude that the interventions do not work (McDaid *et al.* 2006). Further research in this area is much needed to determine effective interventions.

Patient refusal is the most common reason for potentially eligible patients not participating in cancer trials. However, there is a lack of high quality research addressing the reasons why patients refuse. Lists of reasons have been cited by patients and clinicians as being important influencers; however, further work is necessary to determine the relative importance of individual factors from a patient perspective, but also to investigate other reasons that may influence refusal that patients themselves are unaware of, for example lack of understanding of clinical trial information and concepts such as randomisation. Issues around patient understanding and informed consent were widely identified as factors negatively affecting recruitment and contributing to patient refusal rates. This will be further discussed in Chapter 3 in relation to informed consent and clinical trial decision making.

Major conclusions from the literature

Conclusion 1

There is a need to develop effective interventions to increase the numbers of patients recruited to cancer clinical trials.

Study implications

- This study uses an experimental design to evaluate an intervention designed to specifically address this issue.

- It is important to evaluate AVPI against standard practice, and with an experimental design, so that any effect is likely to be as a result of the intervention. A randomised design with a 'standard practice' control arm was employed in the study.
- To minimise selection bias, studies examining recruitment should focus on all potentially eligible patients as was the case in this study.

Conclusion 2

Patient refusal is the most common reason that clinically eligible patients do not take part in clinical trials but there is limited research into the reasons why this is the case. Reasons for patient refusal should be evaluated from the patient's perspective and also to determine factors that patients may be unaware of, such as lack of understanding of what is required in the trial.

Study implications

- Patient refusal was the primary endpoint in this study.
- Reasons for refusal from a patient perspective were evaluated.
- Patient understanding was objectively assessed via a knowledge test, as well as via patient self-report.

Conclusion 3

Issues around patient understanding and informed consent (such as difficulty with the concept of randomisation) have been identified as contributing to low recruitment in terms of factors affecting the patient; clinician; trial; and the organisation.

Study implications

- Patient understanding is a key focus for this study.
- The concept of randomisation is addressed in detail in the intervention.

- Patients' understanding and acceptance of randomisation is assessed in the knowledge and the clinical trial decision questionnaires.

Conclusion 4

Factors associated with the clinician such as trust, communicative behaviour, quality of the interaction, have also been associated with both consent and refusal to clinical trials.

Study implications

- Although factors associated with the clinician was not a major focus in the AVPI study, personal perceptions of influencing factors on the clinical trial participation decision were assessed by patient self-report and included issues such as trust and the influence of the doctor.

Conclusion 5

The literature is inconclusive in terms of the effects of socio-demographic (SD) and socioeconomic (SE) factors in clinical trial recruitment. An exception to this is SE status in cancer trials, where high SE levels were associated with higher recruitment and conversely patients with low SE levels were less likely to take part in a trial. In addition, patients with a higher concern about their illness, and those who are sicker or have advanced disease appear to be more likely to participate in a clinical trial.

Study implications

- Patient characteristics assessed at baseline included SD and SE factors - age, gender, education status and deprivation category.
- Analysis tested for associations between patient characteristics and clinical trial entry.

- Data were collected on tumour type and whether the patient had limited or advanced disease, to determine whether there was any association between these factors and clinical trial entry.

CHAPTER THREE: LITERATURE REVIEW PART II – INFORMED CONSENT

3.1 Introduction to informed consent

From Chapter 2, it appears that recruitment can be increased by improving informed consent, particularly by improving patient understanding. The aim of this chapter is to examine the informed consent process from both an ethical and practical perspective; to determine its key components, and specifically to examine the role of understanding; to review interventions aimed at improving the process; and to identify effective measures for evaluating informed consent. It will be argued that informed consent can be viewed as an autonomous action, and that patient understanding is fundamental to it. There are substantial challenges in evaluating informed consent, and it will be demonstrated that focussing on patient understanding is an appropriate way of doing this.

Informed consent is a complex, difficult concept, but at a basic level incorporates at least four dimensions:

- What the patient needs to know [or understand] (*information*)
- How that information is conveyed [to maximise understanding] (*disclosure*)
- The extent to which the patient understands the information conveyed (*understanding*)
- The extent to which the patient's consent meets the criteria for decision making in this context – competence and voluntariness [understanding is essential for competence and voluntariness] (*decision making*).

These four dimensions will guide the discussions in this chapter and it will be shown that patient understanding, in addition to being the explicit content of the third dimension, is crucial to the other three. In view of the breadth of information covered in this chapter, Table 3.1 is intended to provide clarity on the structure of the chapter.

Table 3.1. Outline summary of Chapter 3

Literature search		
Definitions		
Ethical and legal background		
THEORETICAL PERSPECTIVE		
Autonomy		
Autonomous actions	Understanding	
	Noncontrol	
	Competence	
Beneficence		
Justice		
Informed consent as part of a wider ethics of communication		
Implications of theory		
EMPIRICAL LITERATURE		
Introduction		
Information	Overview	
	Randomisation	
	Equipoise	Clinical equipoise v personal equipoise
		Patient-centred equipoise
		Therapeutic misconception
Disclosure	Overview	
	Medium	
	Interaction	
Understanding	Overview	
	Knowledge and understanding	
	Knowledge and anxiety	
Decision making	Within context of informed consent	Decision aids
		Shared decision making
	Voluntariness	
	Consent capacity/competence	
Measure of informed consent	Overview	
	Measures	
Chapter summary		

This chapter will draw on much of the literature concerning informed consent in clinical trials. The cancer literature, in terms of consent and treatment decision making, will also be referred to where relevant. Following the literature search, definitions of informed consent will be given, followed by the ethical and legal background, in order to set the context for the subsequent discussions. The focus will then be on the theoretical

perspectives and models shaping current thinking. Following this, the empirical literature will be discussed in terms of the four dimensions of information, disclosure, understanding and decision making, referring to the theory as relevant. Attention will then be given to the measurement of informed consent, with reference to further discussion of the measures in Chapter 7. The chapter will conclude with a summary.

3.2 Literature search

The main purpose of the literature search was to:

- Identify the principles and processes of informed consent, and determine the role of patient understanding;
- Review measures of informed consent.

In view of the large literature base, two searches were initially undertaken. The differences between the searches were that one included 'measures' as a key word and the other did not. The first search involved the following five concepts: 1) clinical trials; 2) consent (including choice); 3) understanding/knowledge/anxiety; 4) measures and 5) cancer/non-cancer. The second search focused on 1) clinical trials; 2) consent (including choice); 3) understanding/knowledge/anxiety; and 4) cancer. These were expanded upon in various ways, as shown in the full details of the search strategy, and then combined (Appendix 3.1). The informed consent literature searches were undertaken after the searches for part I (recruitment) and part III (audiovisual patient information); duplicates already identified in these two searches were consequently removed from this one. Relevant papers are, however, included in the discussion of the literature.

Electronic databases searched were: Ovid MEDLINE(R) (mesz), Ovid MEDLINE(R) In-Process and Other Non-Indexed Citations (prem), CDSR (coch), ACP Journal Club (acp), DARE, CCTR, British Nursing Index (brni), British Nursing Index Archive (bnib), CINAHL (nursing), EMBASE (emez), PsycINFO (psyf). The search strategy was devised with the

input of an experienced medical librarian. Additional references were located by searching the bibliographies of related papers, examining conference proceedings, and using the Google search engine. Terms were combined as shown in Table 3.2. The line number corresponds with the full details of the search strategy in Appendix 3.1.

Table 3.2. Summary of literature search: informed consent

Combination of Terms	Number of Hits
Line 16 = clinical trials + consent/choice + understanding/knowledge/anxiety + measures	3612
Line 17 = cancer + clinical trials + consent/choice + understanding/knowledge/anxiety + measures	819
Line 16 or 17	3388
Line 25 = limit to English language, last 10 years, duplicates removed	1888
Line 26 = cancer + clinical trials + consent/choice + understanding/knowledge/anxiety	1152
Line 30 = limit to English language, last 10 years, duplicates removed	342
Line 25 or 30	380
Final total with duplicates removed	337

As shown in the table, the search was limited to the last 10 years. This was owing to the large volume of literature, and it is acknowledged that there will have been relevant papers prior to this time. However, it was anticipated that important papers would be identified in the review articles, and that they would also be referred to in the more current papers. In addition, the researcher had a large volume of literature on informed consent which had been collected over several years, some of which is also referred to in this chapter.

Full articles were requested for the majority of the final 337 abstracts. Papers that were identified in the search but later excluded were about informed decision making in cancer prevention, genetic counselling, and screening, rather than consent to treatment or research. Others included those concerned with paediatrics, neonates and parental consent.

3.3 Definitions of informed consent

There have been various definitions of informed consent, with most reflecting the decision making component in addition to the informational one. Most of the literature refers to the concept in terms of its components. There is general agreement that the four key elements of informed consent are: disclosure, comprehension, voluntariness, and competence (Bosk 2002), with a fifth - consent/decision making - also often cited (Beauchamp and Childress 2001, p79). Faden and Beauchamp (1986) define an informed consent as.... "an autonomous action by a subject or a patient that authorises a professional either to involve the subject in research or to initiate a medical plan for the patient (or both).....Informed consent is given if a patient or subject with (1) substantial understanding and (2) in substantial absence of control by others (3) intentionally (4) authorises a professional to do..." (Faden and Beauchamp 1986, p278). This is the traditional, most common way of considering informed consent, with an emphasis on autonomy, which will be discussed later in the chapter.

Other writers claim that informed consent is broader than this, and that the context is important (for example, Manson and O'Neill 2007). Although definitions of informed consent have traditionally emphasised respect for autonomy, the meaning and values on which informed consent is based are grounded in society and in the practicalities of social relationships (e.g. shifting boundaries in the doctor-patient relationship, developments in information technology, and increasing bureaucratic regulation of informed consent) (Miller and Boulton 2007). An example should help to illustrate this point. Ethics

committees now sometimes insist that patients are not approached initially by the researcher but rather by their clinician, in a gatekeeper-type approach. Although this is done in an attempt to protect the patient's privacy, it can distort the basis of informed consent by linking the researchers to individuals and organisations with whom patients already have a relationship (Miller and Boulton 2007).

Boulton and Parker (2007) summarize the biomedical ethics literature and, within the context of current regulations and guidelines, identify three criteria by which the validity of consent could be assessed. First, potential research participants must be given all the information relevant to their decision about participation, and understand it. Second, the decision about participation must be voluntary and made without any form of coercion. Third, the person giving the consent must be competent to do so. These criteria give rise to obvious questions, such as: How much and which types of information are essential for consent? What constitutes undue coercion? Who should judge if a person is competent to make such a decision, and how should this be done? (Boulton and Parker 2007). These questions have been the subject of much debate, and remain unresolved, although there is guidance in the literature which helps researchers to address some of the issues, and which will be discussed throughout the chapter.

3.3.1 Informed consent and informed choice

As already discussed, 'informed consent' is a well established concept, used to describe the process in which patients are first informed and then invited to make a decision about whether to undergo a treatment, or enter a clinical trial. 'Informed choice' is another concept used in the literature to denote the information-giving and patient decision making process, but it is almost exclusively referred to in relation to consent for screening, rather than consent to clinical trials. Jepson (2005) argues that the difference between the two concepts is a matter of population, context and setting, although both are concerned with promoting patient autonomy by providing information on the risks and benefits of an

intervention or treatment/trial. In screening, healthy individuals are usually sent a letter inviting them to attend for screening; hence they make an informed choice about whether or not to attend. In informed consent, the patient is actively seeking, or is encouraged, to have some form of treatment, which may be part of a clinical trial. Despite the widespread use and acceptance of the term 'informed consent' rather than 'informed choice' in the clinical trial setting, both in the literature and in practice, the 'choice' component of the process in clinical trials – in terms of whether a patient chooses to accept or refuse the trial – is important, and will be discussed more in Section 3.15.

3.4 Ethical and legal background to informed consent

3.4.1 Ethical background

Informed consent is the ethical underpinning of clinical research. The concept has an interesting ethical and legal history, and remains one of the most controversial issues in the ethics of medical research. The idea of informed consent surfaced in the early part of the nineteenth century and challenged the paternalistic view set out in the Hippocratic Oath (Edwards *et al.* 1998). It is based on the notion that 'a person of competent mind has a right to determine what is done to him/her and the right to determine what is not done' (Edwards *et al.* 1998). Informed consent as a concept was only really accepted in medicine in the mid-twentieth century, as a result of case law (Faden and Beauchamp 1986, p101).

Ethical codes or statements focussing on the protection of research participants have been established over the years to offer guidance to clinical researchers on the ethical conduct of clinical trials, and include informed consent as a key component. One of the most important early statements of ethical principles for research was the Nuremberg Code in 1947. This was established as a result of the Nazi war crimes tribunals, and the exploitation of prisoners of war who were forced to take part in medical experiments, often

with horrific consequences. The Nuremberg Code consisted of ten principles to govern ethical research, of which 'voluntary consent' is central.

Since then, the most well known and established ethical code to be developed is the Declaration of Helsinki, which was constituted, from within the profession, by the World Medical Association in 1964, and has undergone several amendments since. The Declaration of Helsinki remains an integral part of research guidance today, and specifies consent to be a central requirement of ethical research. Helsinki 2004 requires researchers to use *explicit* written and documented procedures in requesting and obtaining consent, and to seek *specific* consent to research (Manson and O'Neill 2007). This includes information about the aims of the study, methods, sources of funding, conflicts of interest, institutional affiliations of the researcher, and anticipated benefits and risks. It has been suggested that these standards may demand too much, since many patients fail to understand common features of trial design, such as randomisation and placebos. Their consent will then not meet Helsinki standards (Manson and O'Neill 2007). Patient understanding is discussed in more detail in Section 3.14.

3.4.2 Legal position for informed consent

The legal position on informed consent has been predominantly concerned with informed consent to treatment, rather than research, and became more formalised in the USA in 1972 when a new judicial standard was introduced: the reasonable person standard, under which "the decision about whether a patient should have been informed of a risk is based on whether a reasonable person in that patient's position would want to be informed" (Mazur 2003). Prior to this, the professional standard of consent to treatment had been adopted, whereby, in a court case, another professional would be called into the court and asked for his/her opinion on what they would have done in a similar situation. In the USA, both the professional standard and the reasonable person's standard are currently followed, depending on the specific American state; Mazur (2003) estimates that

an approximately equal number of states have adopted each condition. In the UK, adequacy of information in law is assessed by the Bolam test, whereby “whether the act or omission complained of accorded with what a reasonable body of professionals would have done at the material time” (Powers 2003). In terms of clinical research, the European Directives discussed in Chapter 1 have influenced the legal context in many countries, including the UK. As reported by Boulton and Parker (2007), informed consent is now a well-established concept which has been incorporated into national legislation in most industrialised countries.

THEORETICAL PERSPECTIVE

3.5 Introduction

The theoretical underpinnings of informed consent have been derived mainly from bioethics, and especially research ethics (Corrigan 2003). Much of this section is influenced by the writings of Tom Beauchamp and Ruth Faden, eminent professors in the field of biomedical ethics. Faden and Beauchamp (1986, p4) discuss two foundational frameworks in terms of informed consent: a legal approach and a moral approach. The legal approach has been almost exclusively concerned with consent in clinical contexts (and was briefly described in Section 3.4.2), whereas the moral approach has been more influenced by the research agenda. Since the law relies on moral principles and test cases to shape its development, in this section the focus will be on the ethical framework for informed consent.

Faden and Beauchamp (1986) argue that three broad ethical principles - respect for autonomy, beneficence and justice - are sufficiently comprehensive to provide an analytical framework for informed consent. It is acknowledged that there is sometimes conflict between the principles, and that there is no consensus about whether autonomy is the only, or even the primary, justification for informed consent requirements. When principles conflict, they need to be weighed against each other (sometimes called

balancing ethical principles), and a judgement must be made about which one should take precedence. However, O'Neill (2003) argues that a more important issue (than autonomy) in informed consent is the need for patients and others not to be deceived or coerced. She asserts that consent procedures should be designed to give others control over the amount of information that they receive, and also the opportunity to rescind consent that they have already given. Although O'Neill offers this as an alternative view of informed consent, it does not seem that the approaches are mutually exclusive. Surely what O'Neill proposes is also a fundamental part of acting autonomously?

3.6 Autonomy

The principle of respect for autonomy broadly refers to the right of self-determination, self-governance, freedom and choice, and is the most commonly cited ethical principle in relation to informed consent. However, there are different interpretations of the concept, and no obvious consensus as to its scope. Faden and Beauchamp (1986, p9) believe that autonomy within the context of informed consent incorporates the right to privacy and the principle of veracity; that is, wherever a moral right to privacy, or the principle of veracity is invoked, it is treated as either reducible to, or a derivative from, an autonomy right.

Most existing analyses take as central the autonomous *person*, someone who has the capacity to act independently and make his/her own personal choices, based on past experiences, values and beliefs. However, Faden and Beauchamp prefer to talk about autonomous *actions*, a concept which they take to be more central than the concept of an autonomous person.

3.7 Autonomous actions

The distinction between autonomous persons and autonomous actions is important. Faden and Beauchamp (1986, p235) discuss informed consents as "acts of autonomous

authorising". Autonomous actions are often performed by autonomous persons but can also be performed by non-autonomous persons. Faden and Beauchamp (1986) believe that "informed consents and informed refusals are particular actions; the goal of informed consent requirements is to enable patients and subjects to perform these actions, that is to make substantially autonomous choices about whether to authorise a medical intervention or research involvement". But what is a 'substantially autonomous choice'?

There is no widespread agreement in the literature about what constitutes an autonomous person or what constitutes an autonomous action. Faden and Beauchamp (1986, p237) suggest that the autonomous person has the capacity for, and frequently exhibits, autonomous action - which would include resistance to social conformity and coercion, as well as reflectiveness, understanding and insight. A generally autonomous person may sign a consent form without reading it; or, in the cancer trial setting, he/she may be very distressed after receiving a diagnosis of cancer, and consequently not be able to act autonomously. These examples suggest that being a generally autonomous *person* is not always sufficient. What is more significant is whether a particular *action* can be considered autonomous.

Faden and Beauchamp (1986, p238) suggest that the three conditions necessary for autonomous action are intentionality, understanding, and without controlling influences, which they refer to as noncontrol (other authors refer to noncontrol as voluntariness). These three conditions are logically different. As far as intentionality is concerned, patients actions are either intentional or not (a dichotomous variable). However, 'understanding' and 'noncontrol' are continuous variables. This is best illustrated by Faden and Beauchamp's continuum, which shows understanding and noncontrol in terms of autonomous actions (Figure 3.1).

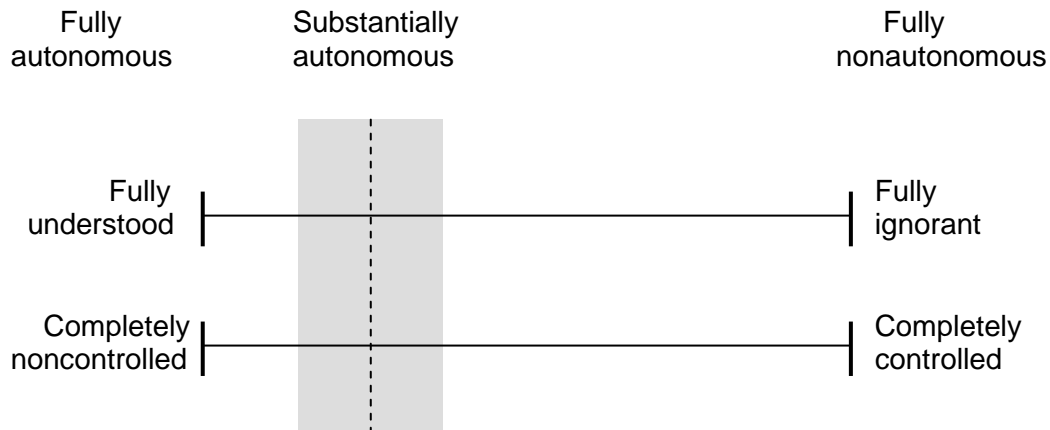


Figure 3.1. Degrees of autonomy of intentional actions (Faden and Beauchamp 1986, p239)

The main difficulty here is the area designated ‘substantially autonomous’. Although ‘fully autonomous’ would be the ideal, in reality, in most areas of practice – including the clinical trial setting – this is very unlikely for the reasons already discussed. ‘Substantially autonomous’ would be a reasonable compromise, so what is meant by substantial is of particular importance. There is no conceptual guidance in this area, and it will depend on the clinical and social context as to how much understanding and noncontrol is acceptable. For all three conditions, understanding is necessary if the patient’s decision is to be intentional and voluntary. However, ‘understanding’ is also something that must be examined independently.

3.7.1 Understanding

As noted above, in informed consent theory, understanding is emphasised as a key condition of autonomous actions; it is therefore one of the main endpoints in the AVPI study described in this thesis. However, the view that understanding should have such a prominent position is not unanimous, and it has been argued that disclosure is more important, and that understanding should not be a condition of informed consent at all (Screenivasan 2003). This is partly due to the challenges in achieving understanding on

the part of the patient, and in particular an understanding of risks and benefits. In the discussion that follows, it is acknowledged that full understanding is an ideal that is difficult, if not impossible to achieve; it will be suggested, however, that it is possible, and important, for a substantial degree of understanding to be present prior to patient decision making about participation.

According to Faden and Beauchamp (1986, p299), if the understanding condition of informed consent is satisfied, the conditions of intentionality and authorisation will usually also be satisfied as a consequence of meeting the condition of understanding. Another important consideration is that the more information a person understands, the greater the likelihood of autonomous action (Faden and Beauchamp 1986, p239). As already discussed, substantial autonomous action is dependent on the condition of substantial understanding. But what is this, and how can it be achieved? Faden and Beauchamp (1986, p303) believe that substantial understanding requires apprehension of *important* descriptions (those that are important to the person's decision from their perspective, but not necessarily decisive), but not *all* the *relevant* or *possible* descriptions. 'Relevant descriptions' are those that contribute in any way (even a minor way) to the apprehension of a situation. A person could therefore be completely ignorant of relatively trivial or unimportant, but nevertheless relevant, propositions about a proposed trial, but still give an informed consent to the trial.

Understanding is a complex concept, and it has been suggested that there are three main types which are set out below (Faden and Beauchamp 1986, p250):

- 1) Understanding *how* (to do something) is equated with knowing how;
- 2) Understanding *that* (something is true). This is a propositional knowledge claim where understanding is reducible to the analysis of knowledge; for example, understanding that I am being asked to consent to this trial; and
- 3) Understanding *what* (has been said); for example, what the trial entails.

For informed consent, understanding *that* you are being asked to decide about taking part in a trial, and understanding *what* is communicated about the trial, are the key parts of understanding that are important. Faden and Beauchamp (1986, p308) believe that substantial understanding is best achieved with a core disclosure of the key facts, followed by a more personal discussion which is focussed on what the patient needs or wants to know. The core disclosure is often determined by regulatory requirements and would consist of: information usually considered important in trial decisions; what the professional thinks is important; and information about the purpose of seeking consent as an act of authorisation (Faden and Beauchamp 1986, p308).

With such a major focus on individual autonomy, the issue of patients having false beliefs is important and puts pressure on the investigator/clinician to address this, wherever possible, by correcting misconceptions. If understanding is based on false beliefs, then understanding will be 'less than correct', and the action (for example, to consent to a trial) cannot be autonomous (Faden and Beauchamp 1986, p253). It is difficult sometimes to judge whether or not a belief is false, and Faden and Beauchamp (1986, p254) discuss the justified belief standard as a potential solution to this problem.... "the justified belief standard captures the common sense conception of reasonable (even if not true) belief and assertion that underlies ordinary social agreements about what is veridical" They do however acknowledge the limitations to this, in that there is little agreement about what makes a belief 'justified'

3.7.2 Noncontrol

In Faden and Beachamp's theory of autonomous action, noncontrol is fundamental. This means that the person is acting independently, with no external controls on his/her action. In the literature, noncontrol has been linked to voluntariness, which has also been discussed within the context of autonomy; however, Faden and Beauchamp (1986, p258) prefer to discuss coercion, manipulation and persuasion as the influences on control, and

to avoid the term 'voluntariness' because of its wide and varied usage. They provide definitions for 'coercion', 'manipulation' and 'persuasion', but acknowledge that it is difficult to define what degree of noncontrol is needed for an autonomous decision, partly because of the subjective nature of the issues and the fact that people are very different in how they respond to these influences.

3.7.3 Competence

Competence is important for autonomous action, and hence informed consent. Competence is also referred to in the literature as 'capacity to consent' or 'decision-making capacity' and much has been written about the concepts, particularly in relation to how they are assessed. It has been suggested that competence can also be portrayed as a continuum, from incompetent to fully competent (Faden and Beauchamp 1986, p290). A threshold would then need to be established, representing the point on the continuum where a person is considered competent enough to consent or refuse a trial. A patient considering clinical trial participation would need to understand the information, and the implications of it, in order to be competent to make the decision about participation.

Assessment of competence is a difficult challenge as will be discussed in Section 3.15.3. It is essential to address assessment, in order to determine whether a person is considered competent to make the decision about clinical trial entry. As Berghmans and Widdershoven (2003) assert, the current dominant approach towards decisional capacity is cognitive and rational. This means that choices are made according to logical procedures of rational thinking. Berghmans and Widdershoven (2003) report that the literature identifies assessment of decision making capacity as having four criteria: "the capacity to make a choice; the capacity to understand relevant information; the capacity to evaluate the character of the situation and possible consequences; and the capacity to handle information rationally." They suggest alternatives to this which consider the relevance of emotion and mood, meaningfulness to the patient, and promoting the patient-

physician interaction to discuss values (personal to patient, and values of treatment). These factors should also be considered when capacity to consent is being assessed.

3.8 Other relevant ethical principles

3.8.1 Beneficence

The principle of beneficence is a key principle of medical ethics, and is concerned with maximising good and promoting the welfare of others. It includes the following four elements: “(1) one ought not to inflict evil or harm; (2) one ought to prevent evil or harm; (3) one ought to remove evil or harm; and (4) one ought to do or promote good” (Faden and Beauchamp 1986, p10).

In terms of consent to research, the investigator would be expected to adopt this principle, primarily in relation to the patient, but would also have beneficence responsibilities to future patients and the population as a whole, the employing authority, and the study sponsor. Details of the risks and benefits involved in the clinical trial should be fully disclosed to patients. Patients need to have an appreciation, and an understanding, of these risks and benefits.

3.8.2 Justice

“A person should be treated according to what is fair, due or owed” (Faden and Beauchamp 1986, p14). Faden and Beauchamp give the example, within the clinical trials setting, of the controversy surrounding the use of prisoners as subjects in research, and questions whether it is right or ‘just’ to do this. Even if the principles of beneficence and autonomy are met, which in this case it could be argued that they are (there is likely to be benefit to society as a whole, and the subjects have autonomously given their consent to participate), there is still an issue about the principle of justice. But should the principle of autonomy take precedence? Although Faden and Beauchamp discuss justice as relevant to informed consent, they are very clear that the most important principles are autonomy

and beneficence; and they claim that the major ethical and conceptual problems with informed consent are not justice-based. However, an important consideration is the inclusion of marginalised groups in research: ethnic minorities, people living in remote communities, people with communication impairment. This further highlights the importance of the social context in informed consent.

3.8.3 Balancing the principles in informed consent

Prior to the introduction of informed consent in the mid-twentieth century, the beneficence model was overwhelmingly dominant in medical ethics and health care practice. With the introduction of informed consent and the focus on the patients' right to self-determination, the principle of autonomy is becoming increasingly important. It is generally believed that autonomy is the most important ethical principle in informed consent, and that this should never be overridden, regardless of the context or circumstances (Kottow 2003). Faden and Beauchamp (1986, p19) do not support this view, although they do support enabling autonomous choice as the goal of informed consent requirements. They do not believe that autonomous choice, or the underlying principle of autonomy, *always* outweighs other ethical considerations. They acknowledge that in some situations, beneficence and justice, as well as role responsibilities (such as providing the best professional care), may have sufficient weight to override respect for autonomy (Faden and Beauchamp 1986, p19).

3.9 Informed consent as part of a wider ethics of communication

Manson and O'Neill (2007, pp. xi and 40) challenge traditional thinking on informed consent, and contest the claim that appeals to autonomy provide justification for informed consent procedures. They argue that informed consent is best thought of as a wider ethics of communication, and discuss eight key aspects of communication that they claim tend to be 'obscured or ignored' by the current heavy reliance on conduit and container metaphors, which they claim shape the way we think about informed consent. These eight key aspects suggest that informing is: (1) context-dependent, (2) norm-dependent, (3)

propositional, (4) rationally evaluable, (5) referentially opaque, (6) inferentially fertile, (7) a type of rational action, and (8) audience-specific (Manson and O'Neill 2007, p41). The 'conduit' metaphor refers to, for example, transferring the content of information, and the 'container' metaphor implies the idea that information is contained, for example, in the human mind, email, or text. Information that exists in one container is transferred to another. If information is then viewed as content rather than action, as per the conduit/container model, it is likely that some elements of information and communication, such as knowledge, will be emphasized, while many significant features of communication that depend on agency, such as context and relationships, will be downplayed or ignored (Manson and O'Neill 2007, p48).

Manson and O'Neill (2007, p69) suggest that the agency model of communication provides a framework for recognising the interactive or transactional nature of successful communication, emphasising what is said and what is done by both parties. They claim that this approach allows a deeper and more plausible justification of informed consent than autonomy-based justifications that centre on disclosure for decision making. Informed consent is thought of as a communicative transaction between agents. As communication transactions, informed consent transactions must respect the norms that are required for successful communication: intelligible, relevant, accuracy and truth/truthfulness (Manson and O'Neill 2007, p85).

In some cases a patient may base his/her decisions on his/her background knowledge - that "certain kinds of communicative action, or reason-giving or forms of respectful behaviour", have taken place - and not on the content of the informed consent disclosure (Manson and O'Neill 2007, p32). This fits with understanding the role of information as making people feel involved, and helping to manage expectations rather than being used to making choices, *per se*. Faden and Beauchamp (1986, p307) also advise that professionals should move their emphasis away from the traditional focus on disclosure,

and focus more on the communication aspect of the relationship to determine the specific needs and concerns of the patient, and to encourage a setting where the patient is comfortable to ask questions. There is still an important role here in optimising patient understanding of the clinical trial information.

Corrigan (2003) suggests that the traditional bioethical model of consent, whose core foundation is autonomy, can be equated with an 'empty ethics' model in which the context is not considered and the consent process becomes a rational-choice model of action. She emphasises the importance of considering informed consent in its clinical and social context, and offers her study of patients in clinical drug trials as evidence. Corrigan (2003) asserts that informed choices, based on an adequate understanding of the clinical trial information, and consideration of the potential benefits and risks, are difficult to achieve in practice because of the importance of the type of illness a patient is suffering from, anxiety, treatment expectations, and trust in the doctor and medical science (Corrigan 2003). It is acknowledged that adequate or substantial understanding is difficult to achieve in practice, as has been highlighted by Corrigan; however, it can still be argued that it is an important aim, that it is possible to secure it in the clinical and social context, and that it can be optimised when taking these individual factors into account.

3.10 Implications of the theory

It would seem, from reviewing the theoretical perspectives, that maximising opportunities for autonomous actions, based on understanding, is important for informed consent, but that this needs to take account of the individual context and the communicative transaction. Other important areas for autonomous action are noncontrol (voluntariness) and competence to consent (decision making capacity), both of which depend on patient understanding.

Informed consent theory is implicated in all four dimensions of informed consent as discussed at the beginning of this chapter – information, disclosure, understanding and decision making. The theoretical context was not formally discussed under these headings so as not to fragment the main focus of the argument, which is centred on informed consents as autonomous actions, with the key component being patient understanding. However, it is important to clarify the link with the four dimensions, as these will form the basis of the discussion for the empirical literature. Understanding is obviously the basis for the *understanding* dimension, but is also implicated in the *information* dimension, in terms of understanding ‘what’ is important (e.g. randomisation, equipoise, voluntariness of consent), and also the *disclosure* dimension, since factors such as the medium and clinician/patient interaction can have a positive or negative effect on the patient’s understanding of the information disclosed. The other conditions for autonomous actions - noncontrol (voluntariness) and competence (capacity) to consent - require patient understanding in order to be fully met, and are integral to the *decision making* dimension.

The empirical literature will now be discussed in terms of the four key dimensions, linking back to theory as appropriate.

EMPIRICAL LITERATURE

3.11 Introduction

Much of the empirical literature discusses ‘barriers’ to informed consent. However, following a strategy akin to the one used by Verheggen *et al.* (1996) in their review of informed consent in clinical trials (Figure 3.2), this review assesses the relevant research in two key domains: *informed* and *consent*. The difference from the Verheggen model is that within the *informed* domain, information disclosure is split into two categories: ‘information’, including content, volume and presentation, and ‘disclosure’, the information-giving process. Comprehension (understanding) is the third component of the *informed* domain. The *consent* domain consists of decision making and motivation to participate

(Figure 3.2). 'Decision making' and 'motivation to participate' will be combined in order to make the model consistent with the four key informed consent dimensions identified at the beginning of this chapter: information, disclosure, understanding and decision making. Motivation to participate is not discussed in this chapter since it has already been addressed in Chapter 2.

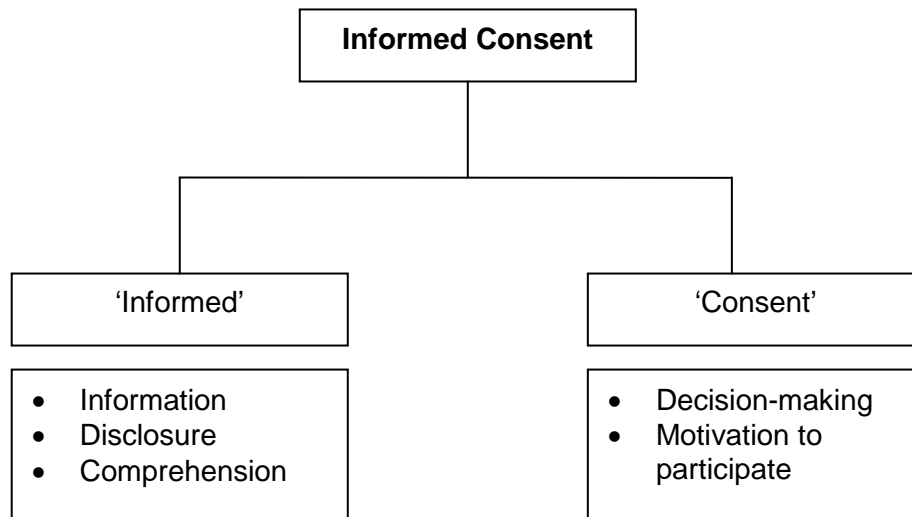


Figure 3.2. Summary of informed consent (modified from Verheggen et al. 1996)

On a practical level, patients must receive appropriate information that they can understand, to enable them to make decisions about whether or not to take part in a clinical trial. The informed consent process is “an opportunity to provide accurate and non-judgemental information regarding trial procedures and potential risks and benefits, correct any misconceptions and allay any unfounded fears, and provide sufficient time and resources to facilitate the thoughtful consideration necessary for the best possible personal decisions” (Barrett 2002).

Various interventions have been developed with the aim of improving informed consent, many of which will be referred to in the relevant subsequent sections of this chapter.

Interventions aimed at improving informed consent focus on different aspects of the process, with the majority centred on the information-giving process or on increasing patient understanding.

3.12 Information

3.12.1 Overview

Content, volume, readability and presentation have all been shown to be important in optimising informed consent procedures in terms of understanding. These, together with public knowledge about clinical trials, are briefly discussed here.

Information content for patients being considered for clinical trials is governed, to a large extent, by regulations and guidelines (e.g. ICH Good Clinical Practice Guidelines (1996) and Research Governance Frameworks), as discussed in Chapter 1. Faden and Beauchamp (1980) (in Fureman *et al.* 1997) suggest that, in medical settings in which the subjects are less familiar with the treatment options (which would be the case in randomised cancer trials), information provided may have a proportionately greater effect on decision making. Furthermore, as already discussed, informed consent theory suggests that in addition to the core components identified in guidelines, and what the professional believes to be important, there should be a focus on the specific informational needs of the individual, to ensure that personal issues are addressed in the consultation (Faden and Beauchamp 1986, p308). Particularly difficult for patients to both understand and to accept, in randomised clinical trials, are the concepts of randomisation (Featherstone and Donovan 1998; Hietanen *et al.* 2000) and clinical equipoise (Mills *et al.* 2003; Madsen *et al.* 2007). As a consequence, these will be addressed separately, later in the chapter (Sections 3.12.2 and 3.12.3).

There are different views on the volume of information necessary for informed consent in clinical trials, with the majority of studies showing that patients are satisfied with what they

receive (Ferguson 2002). Edwards *et al.* (1998) carried out a review of informed consent in clinical trials and found that there seems to be an optimal level of information about side-effects, a level which avoids overburdening with detail, but which provides enough information for the most important risks to be understood. Studies which have compared simple, shortened or 'easy to read' consent forms with the standard more complex version found that more information was retained with the shortened versions (Dresden and Levitt, 2001) and that more patients reported reading the shortened versions (98% v 68%) (Dresden and Levitt 2001). Anxiety was lower, and satisfaction was higher, with the easy to read version (Coyne *et al.* 2003). In the non-clinical trial setting (the injection of intravenous contrast material into patients for radiological purposes), brief information reduced patient anxiety, whereas detailed information increased it, as assessed by the Spielberger State-Trait Anxiety Inventory (Yucel *et al.* 2005). Comparably, in consumer decision making for hospital choices in the USA, a 'less is more' approach to information about health care quality, with the important information highlighted, led to better understanding and better decision making, especially for those lower in numeracy (Peters *et al.* 2007).

A number of studies have investigated the readability of clinical trial consent forms, many specific to oncology trials, and have consistently found them to be aimed at too high a reading level, and to be too difficult to understand (Morrow 1980; Grossman *et al.* 1994; Sharp 2004). If the written information is not being understood by patients, then this puts pressure on the investigator/clinician, and requires greater emphasis on the quality of the interaction with the patient and the effectiveness of communication, to ensure that consent is genuinely informed.

Information can be presented in different ways. For example, linguistic analysis followed by changes in information leaflets, improved readability and understanding in a Danish clinical drug trial (Bjorn *et al.* 1999). Framing information positively (for example,

focussing on chance of survival over time rather than chance of death over time) is associated with higher levels of understanding, and increased likelihood of consent to treatment (Armstrong *et al.* 2002). Tailoring information (for example to specific situations, patient groups, individual preferences or requirements) was shown to be effective in a meta-analytic review of the literature (Noar *et al.* 2007). Further discussion on the effects of framing and tailoring information can be found in Chapter 4, focussing on audiovisual patient information, as was relevant to the AVPI study.

Several authors have emphasised the value of the population being more aware of clinical trials (Edwards *et al.* 1998; Trauth *et al.* 2000; Apolone and Mosconi 2003; Fisher 2006). Public knowledge about clinical trials is known to be poor (Apolone and Mosconi 2003; Comis *et al.* 2003; Fisher 2006), and Manson and O'Neill (2007, p67) argue that all communication is rooted in background knowledge and inferential competences. This would suggest that, by improving the general public's baseline knowledge of clinical trials, it may be possible to enhance the communication process in informed consent. In addition, the more that people know before they are invited to take part in a trial, the better equipped they are to cope with the informed consent procedure (Edwards *et al.* 1998). Although this was not an aspect that was addressed in the AVPI study, patients' past experience of clinical trials was assessed within the context of their baseline knowledge of clinical trials. Patients who had had previous experience of clinical trials would be expected to have additional knowledge in this area.

3.12.2 Randomisation

Randomisation means that trial participants have an equal chance of receiving any one of the treatment arms in a clinical trial. Randomisation is considered optimal in experimental design on effectiveness, with ethical justification dependent on the acceptance of equipoise. However, randomisation is frequently misunderstood (Appelbaum *et al.* 1987; Sutherland *et al.* 1990; Snowdon *et al.* 1997; Edwards *et al.* 1998; Ellis *et al.* 1999b;

Hietanen *et al.* 2000; Madsen *et al.* 2007). Even when patients (or potential research participants) do understand it, many of them find it difficult to accept (Featherstone and Donovan 1998, 2002; Robinson *et al.* 2005; Madsen *et al.* 2007). The effect on recruitment has already been discussed in Chapter 2, Section 2.6.1.4. This section discusses randomisation in the context of informed consent.

Despite being given information about randomisation (a necessary requirement of written patient information for research governance), and an explanation of the process (although what this entails varies), many patients still believe that the doctor chooses the treatment for them (Ellis *et al.* 1999b; Hietanen *et al.* 2000). In a UK study investigating how oncologists explain randomised trials to their patients, Jenkins *et al.* (1999) found that verbal information from doctors about randomisation was variable; and, while there was much discussion about proposed treatments and side-effects, reasons for randomising treatment were kept to a minimum (Jenkins *et al.* 1999). Over the last few years, UK guidance has been developed with the aim of improving the content and readability of trial information, and this has been incorporated into multicentre research ethics application procedures; so there is now some degree of standardisation for written information (Kerr *et al.* 2004). In terms of randomisation, the guidelines advocate the description: “The groups are selected by a computer which has no information about the individual”.

Poor understanding of randomisation raises concerns that patients may be giving consent without understanding what is involved, and is an area that has attracted substantial research interest over the last ten years. Research questions focus mainly on whether patients understand the concept, and on whether they accept it. There has been a mix of quantitative and qualitative approaches to studying randomisation, with the majority of studies asking patients directly, either by interview or questionnaire. There has also been some work with lay people, with similar study outcome measures (Kerr *et al.* 2004; Robinson *et al.* 2005). Another approach has been to determine patients’ preferences for

different descriptions of the term randomisation. A recent study involving 600 patients with cancer showed the CancerBACUP description to be the most preferred, and the more technical description of randomisation, from the National Cancer Institute in America, to be least liked (Jenkins *et al.* 2005).

Kerr *et al.* (2004) gave leaflets to 130 adults attending a UK further education college, giving them scenarios illustrating randomisation, and interviewed 12 of the sample to gain a deeper understanding of understanding and acceptability of the concept. Findings from both the quantitative and qualitative data showed that the majority of participants were able to judge when the allocation methods were random, but they did not find the method of random allocation acceptable. In general, participants did not appreciate the scientific value or purpose of the method, a finding which is supported by other studies: Robinson *et al.* (2004) with adult students; Featherstone and Donovan (1998) with clinical trial patients (prostatic disease); and Stead *et al.* (2005) with diabetes clinical trial patients. In Kerr *et al.*'s (2004) study, when information about the scientific value of randomisation was given to the participants, acceptability of only one method - allocation by computer - was increased. This supports the current UK guidelines, as noted above. When informing patients about randomised trials, Kerr *et al.* (2004) recommend focussing on the scientific purpose of random allocation.

Featherstone and Donovan (2002) carried out a qualitative study of patients' experiences in randomised trials. They interviewed 33 men with lower urinary tract symptoms related to benign prostatic disease, exploring their recall and understanding of trial information and how they were allocated to a treatment. They found that while most patients recalled major aspects of trial design, including allocation by chance, they also had other views about their treatment allocation, which were sometimes contradictory. The patients were trying to understand it in relation to their own beliefs, recall and actual experiences of the

trial (Featherstone and Donovan 2002). The resultant outcome was either the placing of trust in the clinician, or the development of distrust (Featherstone and Donovan 2002).

3.12.3 Equipoise

Clinical equipoise is an important ethical and scientific justification for randomisation. In patient information for trial participation, equipoise is usually expressed in terms of uncertainty about which treatment is best, or about the benefits of a new treatment. Equipoise has been discussed as a precondition to an ethical trial (Olson 2002). It has also been said that the ethical recruitment of patients to trials requires the presence of clinical equipoise (Mann and Djubegovic 2003). Most research on equipoise has focused on participants' awareness of this uncertainty (Robinson *et al.* 2005), and both qualitative and quantitative approaches have been used. Interestingly the term 'equipoise' has been replaced by 'indifference' by Veitch (2002 and 2007), a term which appears to be a clearer, more comprehensive way of referring to equipoise. Veitch speaks of "indifference about which treatment's expected benefit/harm package is preferred", and further asserts that "one may be quite uncertain about some set of scientific facts, and still be very clear that one has a preference for one treatment over an other".

Equipoise is important to both patients and investigators, and different types of equipoise are discussed in the literature, the main difference being whose view of equipoise is taken to be definitive. The main types identified are: scientific (community) equipoise, also referred to as theoretical equipoise (Freedman 1987), clinical (community) equipoise (Veitch 2002), individual clinician (personal) equipoise (Veitch 2007), and patient (centred) equipoise (Olson 2002), also referred to as individual subject indifference (Veitch 2002). Scientific equipoise is when scientists must be uncertain about which treatment is scientifically best. This can be different to clinical equipoise; this is determined by clinicians, who will have a broader perspective, as it concerns their patients and includes the effect of very different treatment options, side-effects and life-style costs, among other

considerations (Veitch 2007). The literature focuses predominantly on clinical equipoise, which is the most popular view.

3.12.3.1 Clinical equipoise v personal equipoise

Problems can arise if a trial has been developed by a team of experts who believe it to have clinical or communal equipoise, and the clinician-investigator at a certain study site is expected to recruit to the trial, but does not personally share the uncertainty, and so does not have personal equipoise. The frequency of this situation is unknown. Jenkins *et al.* (1999) reported that, whilst oncologists expressed uncertainty about treatment decisions in nearly all of the consultations studied, in only 14.6% was this uncertainty personal. It cannot be assumed, however, that personal equipoise existed only for oncologists involved in these 14.6% consultations, since this number may be higher as a result of oncologists not disclosing their opinions to patients. This could be non-intentional (an omission), or could be deliberate, so as not to negatively affect the doctor-patient relationship. In situations where the clinician is lacking in personal equipoise, Alderson (1996) and Freedman (1987) both advise accepting the communal equipoise view. The individual clinician may not have access to all the data, may only have experience with a small skewed sample of patients, or may have personal values which influence assessment of benefits and harms (Veitch 2002).

As with randomisation, patients find it difficult to accept and believe in equipoise (Mills *et al.* 2003). Mills *et al.* (2003) interviewed 21 men with localised prostate cancer from three UK clinical centres and found that, although recall and understanding of the major principles of the randomised design were good, clinical equipoise caused difficulty and influenced trial consent rates; patients who found equipoise acceptable tended to consent, whereas those who could not accept it tended to refuse participation. In another study, involving 355 adult students, approximately half were reluctant to accept that the doctor might genuinely not know which treatment is best (Robinson *et al.* 2004).

Although the widespread view is that clinical equipoise is of both scientific and ethical importance, this view is not unanimous. Indeed, it has been suggested that equipoise is irrelevant, and that only the subject's evaluation of the options is morally relevant (Veitch (2007)). According to Veitch (2002) it is rare for a clinician to be indifferent between two treatment options. It has also been questioned whether equipoise in a strict sense is possible to achieve (Meran 2003).

3.12.3.2 Patient-centred equipoise

Despite claims that equipoise is irrelevant, Veitch (2002) appears to argue for patient-centred equipoise as one of the moral conditions for RCTs. He claims that individual subjective indifference provides the moral justification for randomisation, and should replace other types of equipoise as the basis for justifying randomisation (Veitch 2002).

On a similar note, Olson (2002) argues for 'patient-centred equipoise' and asserts that, since the decision to enrol is the patient's and it is their interests that should be advanced, it is not relevant what the investigator thinks. A trial would then be in equipoise for a patient when enrolling gives them the same chance of a good outcome as not enrolling. However, Olson does not appear to mean that the patient makes the judgement about whether enrolling/non-enrolling will give them the same chance of a good outcome, but rather that clinical trials inherently provide this opportunity. Olson (2002) argues that for most trials, this will be the case because:

- "1) patients in trials receive superior care,
- 2) trial enrolment minimises the risk of being a victim of a therapeutic disaster and
- 3) health professionals make mistakes, and a 50% chance of receiving the worse treatment until a trial reports is always better than any chance of receiving the worse treatment indefinitely" (Olson 2002).

It is difficult to accept these justifications and the blanket approach, since patients will not always receive superior care in a trial; and due to the nature of cancer, life expectancy is often poor, with trials often taking several years to complete enrolment, prior to reporting. Although Olson appears to support the idea of patient centred equipoise, her description of it is unconvincing. For patient-centred equipoise to be meaningful, it would seem more appropriate to support Veitch's (2002) perception of individual subject indifference, and to consider patients own personal values and their perceptions of the influences on the consent decision, as the fundamental requirement. It is therefore the patient's judgment that is important, based on their understanding, in terms of whether or not a trial is in equipoise for them.

3.12.3.3 *Therapeutic misconception*

A denial of both equipoise (patient assumes that the doctor knows what is best for them) and randomisation (patient assumes the doctor will choose a treatment for them) can result in the therapeutic misconception (Robinson *et al.* 2005): the belief that “every aspect of the research project...was designed to benefit (one) directly” (Appelbaum *et al.* 1987, p20). Patients assume that they are allocated to a particular treatment based on their individual need. The therapeutic misconception has been highlighted as an issue affecting the ethics of randomised trials and informed consent by a number of authors (for example: Snowdon *et al.* 1997; Featherstone and Donovan 1998; Daugherty *et al.* 1999; Screenivasan 2003). A way of addressing the therapeutic misconception is to improve patient understanding and acceptance of randomisation and clinical equipoise.

3.13 Disclosure

3.13.1 Overview

Although information and disclosure are closely linked, disclosure here will focus on the information giving *process*, building on the previous section, which was concerned with the content and volume of information. The timing of the decision-making process, the

time allowed for it, and the presence of family and friends during the process, will be briefly discussed, prior to a consideration of the medium and professional/patient interaction.

The timing of the process, along with the time afforded to patients to consider the information and hence their decision, are important in clinical trials. The timing of the process is difficult to address in cancer RCTs, since the trial treatment has to be initiated soon after the initial clinic consultation, since it is often part of a therapeutic treatment plan for the disease. There is therefore limited scope for varying the timing, and the challenges of discussing trial participation with cancer patients are well documented (Tabak 1995; Daugherty 1999; Huizinga *et al.* 1999).

Studies have shown that patients need varying amounts of time to make an autonomous decision about participation. For example, Hietanen *et al.* (2000) found that only 68% of 255 patients felt they had enough time to decide about a randomised trial of adjuvant therapy for breast cancer, and that less educated and older patients needed more time. Morrow *et al.* (1978), in a randomised trial, found benefits of increased understanding in radiation oncology patients taking their consent form home prior to signing, compared with patients who signed at the clinic. Presumably this is due to the additional time afforded to these patients for reading and digesting the contents of the consent form, and also perhaps as a result of family involvement and support.

It is generally agreed that where possible, as well as acceptable and desired by patients, family and friends should be involved in the process, as they can be a substantial source of support. Caution should be exercised, however, as they can influence the patients' actual decision, as discussed in Chapter 2, Section 2.6.1.3. It is difficult to know whether the presence of family and friends influences the patient by persuasion, or even coercion, or whether it assists them in the decision-making process by helping them to understand

the research information, and to reduce anxiety by their presence. It is likely that both can and do occur, depending on the context and relationships involved.

3.13.2 Medium

The medium in which the information is given is also important for patient understanding. A variety of methods for delivering patient information have been studied, in different situations. Trevena *et al.* (2006) carried out a systematic review on communicating with patients about evidence, and found that communication tools in most formats (written, verbal, video, provider delivered and computer based) will increase patients' understanding, but are more likely to do so if structured, tailored and/or interactive. Chelf *et al.* (2001) reviewed ten years of evaluation of cancer patient education, and found that one of the most effective mediums, in terms of increasing knowledge and understanding, is audiovisual. Faden and Beauchamp (1986, p324) also support the use of audiovisual aids, and suggest that these methods may be particularly helpful in achieving substantial understanding, as discussed in Section 3.7.1. As the intervention in this study, audiovisual patient information is the focus of the next chapter, and so will be discussed in no more detail here.

3.13.3 Interaction

The main factors in clinician-patient interaction which have been studied and shown to be important are physicians' behaviour and communication skills (Albrecht *et al.* 1999; Grant *et al.* 2000). Albrecht *et al.* (1999) found that patients were more likely to take part in research when their physician discussed with them, face to face, the items normally included in the consent form, and when they behaved in a 'reflective, patient-centred, supportive and responsive manner'. The importance of clinicians' attitudes and interaction, in terms of decision making and recruitment, has already been discussed in Chapter 2. Here, the focus will be on the informed consent process, rather than on the decision itself.

There is a wealth of literature on interaction and communication in the general cancer setting, including a useful review of physicians' communication behaviour by Arora (2003), and papers reporting effective interventions, such as training packages, to improve communication skills, attitudes and behaviours of oncology clinicians (Fallowfield *et al.* 2002; Jenkins and Fallowfield 2002; Fallowfield *et al.* 2003). There is much less literature specific to the cancer research setting, although it is a growing area of interest.

Albrecht *et al.* (2005) examined the cancer research literature to determine the extent to which effective communication occurs during the informed consent process. Despite the increasing interest in the 'interaction' aspect of the consent process, and the widespread agreement that the personal interaction between health care providers and patients is an important part of the process, Albrecht *et al.* (2005) found that little is known about the actual ways in which treatment and clinical trial information is explained by oncologists and other health care providers to patients and their significant others. They highlight the benefits of using video as a research tool to capture the depth of the communication process. This would build on previous studies, which, although having provided useful data (Brown *et al.* 2004, as discussed below), are limited by being audio-taped.

There have been a number of interventions designed to improve the doctor-patient interaction in the cancer clinical trial setting. These have predominantly been targeted at the doctor, usually involving communication skills guidance or training (Fallowfield *et al.* 1998b; Fleissig *et al.* 2001; Brown *et al.* 2004; Jenkins *et al.* 2005; and Hietanen *et al.* 2007).

Brown *et al.* (2004) developed a set of 'communication strategies' to assist doctors in discussing RCTs with patients. These communication strategies were underpinned by ethical, linguistic and psychological theory, and were informed by research involving 26 consultations with 10 oncologists. The themes identified were:

- shared decision making (at the patient's preferred level of involvement);
- sequence of moves in the consultation (includes the order of information given and the structuring of patient and doctor input to promote patient understanding, ensure equal weight of standard and trial treatment, and avoid coercion);
- type and clarity of the information provided (for example, avoiding jargon, using analogies and summaries);
- disclosure of controversial and potentially coercive information (such as information that is often not revealed to patients, for example, financial incentives for doctors) (Brown *et al.* 2004).

These themes were identified as being important in seeking consent to clinical trials, and were the four key areas in communication strategies developed to assist doctors in communicating with their patients. The authors have recently reported an evaluation of a training programme (one day workshop) which was based on these strategies (Brown *et al.* 2007). The evaluation involved 10 oncologists from 3 Australian cities, and 90 patients. Ninety informed consent consultations were audio-taped, before and after the training, and then transcribed. Patients and doctors also completed satisfaction questionnaires. Some benefits of the intervention were identified; for example, doctors used less coercive behaviour and used more aspects of shared decision-making behaviour. However, several areas were not improved, such as the structure of the consultation; doctors did not structure their consultations in the recommended fashion, as taught in the workshop. Further work is now underway to evaluate an extended training programme, incorporating these communication strategies, in a larger randomised controlled trial (Brown *et al.* 2007).

There is a lack of research on patient outcomes (such as understanding) as a result of improving the communication skills of clinicians and clinician/patient interaction. In a

Finnish prospective case-controlled intervention study, Hietanen *et al.* (2007) investigated the effect of a one-day communication skills training course (for physicians and research nurses), designed to improve the quality of the informed consent process, which they assessed by giving patients the Quality of Informed Consent Questionnaire (QuIC) (described in Chapter 7, Section 7.2.2.2.1). They found a significant increase in satisfaction and understanding among the patients in the intervention group, and recommended that similar types of training be included in the clinical trial planning process (Hietanen *et al.* 2007).

Another intervention study designed to improve communication in the randomised cancer trial setting involved examining patient information preferences, and attitudes to trials, prior to seeing their doctors. The doctors were then either shown these questionnaires (intervention) or not (control) (Fleissig *et al.* 2001). Findings showed that patient and doctor satisfaction, and length of consultation (as well as trial accrual), were not associated with the intervention. However, limitations of the study, as noted by the authors, include: the doctors rarely referred to the questionnaires during the consultation; a formal evaluation of doctors' views was not performed (although anecdotal evidence suggests that they did find the questionnaires useful); and the Preference for Information Questionnaire did not discriminate between patients in terms of their information preferences (Fleissig *et al.* 2001). This is an important issue, as the study was designed to allow the doctors to tailor the explanations given to each patient according to their information preferences. Although the questionnaire did not discriminate, it did show that patients with cancer want specific details about their illness and treatment (Fleissig *et al.* 2001). Question prompt sheets have been used effectively to increase patient involvement in the cancer consultation process (Brown *et al.* 1999) and, as noted by Fleissig *et al.* (2001), this may be worth further investigation in the cancer trial setting, along with questionnaire interventions such as that described in Fleissig's own study.

Communication skills needed by physicians caring for people with cancer are discussed by Back *et al.* (2005) in terms of the disease trajectory, with a section focussing on offering clinical trials to patients. This article provides useful practical guidance, drawing from the general cancer literature. The authors also discuss some of the newer, (interactive) approaches to communication skills training (mainly targeted at doctors), which have been developed in cancer care, and which are reported to have improved communication skills of clinicians (for example, Fallowfield *et al.* 1998b; Back *et al.* 2003). Since this publication, there have been other interesting studies published on teaching communication skills in the cancer trial setting. Of note is the work by Jenkins *et al.* (2005), who evaluated the Cancer Research UK training programme, which aimed to improve health care professionals' communication with cancer patients in the context of randomised trials. This is an intensive training programme using video and interactive exercises. The evaluation involved 33 clinicians and 68 research nurses throughout the UK. Communication (with actors) was videotaped before and after the intervention, and the actor and participant were both asked for their assessment of the communication, in addition to an objective evaluation of the videotape against pre-set key criteria for good communication, and compliance with ethical and informational standards. Results showed that the intervention improved participants' confidence and competence when communicating about RCTs.

Although there is useful guidance in the literature about clinician-patient interaction during the consent process, some of which has been discussed, it is clear that further work is necessary to understand more about the process and patient outcomes, and to design effective interventions to improve it.

3.14 Understanding

3.14.1 Overview

As discussed throughout this chapter, understanding is a key component of informed consent. Understanding is sometimes referred to as 'comprehension' in the literature (Faden and Beauchamp 1986, p301), and the terms have been used interchangeably. For clarity, in this thesis the term 'understanding' will usually be used rather than 'comprehension', since this is consistent with the terminology of much of informed consent theory. Where 'comprehension' is used in relation to specific studies, it can be considered to be synonymous with 'understanding'. Recall, on the other hand is different to understanding. Recall is "the function of the access one has to the stored memory of an event and it can be influenced by the salience of information and the passage of time" (Reynolds and Nelson 2007). Reynolds and Nelson (2007) point out that the understanding of some aspects of informed consent may be equivalent to recall, but that this is not the case with every aspect.

Many authors advocate the need to improve patients' understanding of clinical research (Hunter *et al.* 1987; Jenkins and Fallowfield 2000; Barrett 2002; Brown *et al.* 2004), and it is known that misconceptions about clinical trials (for example those surrounding randomisation, equipoise, placebo and an overestimation of the effect of standard treatment), exist among patients and the public (Hietanen *et al.* 2000; Joffe *et al.* 2001a; Featherstone and Donovan 2002; Comis *et al.* 2003; Stead *et al.* 2005). This is particularly worrying in view of the fact that decisions about trial entry may be based on incomplete or incorrect information. Several authors have highlighted the difficulties of defining and measuring understanding (Barrett 2005; Sugarman *et al.* 2005; Cohn and Larson 2007). This lack of clarity, and a generally disjointed approach, has led to slow progress in learning more about, and subsequently improving, patient understanding and the informed consent process.

Despite this, several reviews of informed consent have identified useful findings in terms of understanding. Sugarman *et al.* (1998) reviewed consent in older adults, and found that diminished understanding was associated with older age and fewer years of education. Schaeffer *et al.* (1996) looked at the impact of disease severity on the informed consent process, and found that the information that patients retained was related to disease severity; for example, severely ill phase I trial patients retained the least information about risks and side-effects compared with other groups, including healthy volunteers who retained the most. Interestingly, the consent form was also rated less useful by subjects with more advanced disease (Schaeffer *et al.* 1996). Cox *et al.* (2006) also found in their review that understanding was poor for patients consenting to phase I trials.

Various suggestions have been made to improve patient understanding, such as improving national guidance and pre-testing information sheets (Stead *et al.* 2005), using audiovisual patient information (Chelf *et al.* 2001), telephone based nursing interventions (Aaronson *et al.* 1996), corrected feedback (Wirshing *et al.* 1998; Dunn and Jeste 2001), simplified consent forms (Dunn and Jeste 2001), informed decision making checklists (Verheggen *et al.* 1996) and communication skills training for health care professionals (Hietanen *et al.* 2000). Although individual intervention studies have shown benefits in understanding (for example, Aaronson *et al.* 1996; Cull *et al.* 1998; Danino *et al.* 2005), Cohn and Larson (2007), in their review, reported that no single intervention strategy was consistently associated with improved understanding. They analysed studies published in the previous ten years, with the aim of identifying promising interventions. Given the lack of clarity in the literature about 'knowledge' and 'understanding', and the fact that different authors have used the terms synonymously (see next Section – 3.14.2), a substantial limitation to Cohn and Larson's (2007) study is that they did not include 'knowledge' as a key word. This would have undoubtedly resulted in potentially relevant studies being missed.

3.14.2 Knowledge and understanding

'Understanding' is a difficult concept to define, and this has led to a lack of clarity in the use of the term and in its relation to 'knowledge'. Considering the context is helpful in clarifying the concept. Based on Faden and Beauchamp's (1986) theory of informed consent, understanding *that* you are being asked to decide about taking part in a trial, and understanding *what* is communicated about the trial, are the key parts of understanding that are important. The literature is unclear about what the differences are (if any) between 'knowledge' and 'understanding', and the terms are frequently used to mean the same thing, with no clear distinction.

The dictionary (Oxford English Reference Dictionary 2002) definitions are as follows:

'Knowledge' – a theoretical or practical understanding of a subject.

'Understanding' – the ability to perceive the meaning of (words, person, a language etc).

It is interesting that 'understanding' forms part of the 'knowledge' definition; and, if knowledge can be thought of as a 'theoretical or practical understanding of randomised clinical trials', then the terms can be regarded as synonymous. It is acknowledged that it may be possible to distinguish between the terms, and that the distinction may prove to be useful and significant. However, because of the lack of clarity in the literature, this study has not attempted to distinguish between the concepts. Here, 'understanding' is based on Faden and Beachamp's (1986) description of understanding *that* and understanding *what*, and is the main term used in the study. Throughout the thesis, the terms are used interchangeably; and in the results chapter, as a matter of terminological convenience, the questionnaire used to assess 'Patient Understanding of Research' is referred to as the 'Knowledge Questionnaire'.

There have been a variety of approaches to assessing knowledge/understanding, both subjectively and objectively. These are discussed in detail in Chapter 7, which justifies

the rationale for developing a new tool to assess understanding in the randomised cancer trial setting.

3.14.3 Knowledge and anxiety

Patient anxiety levels are often high due to a number of factors, including having a recent cancer diagnosis and cancer treatment (Kelly *et al.* 2002). In most cases, anxiety is part of a normal reaction to cancer. There is evidence that situational stress can evoke anxiety states, and strong support for the distinction between state (how one feels at the moment) and trait (how one generally feels). The concepts of state and trait anxiety were first identified through research involving factor analysis in 1961 (as reported in Gaudry *et al.* 1975), and since then there have been several studies to define the concepts and develop procedures for their measurement, such as the Spielberger State-Trait Anxiety Inventory.

Although an appropriate treatment for anxiety is to provide adequate information and support (Kelly *et al.* 2002), the evidence on whether anxiety levels are increased by knowledge/understanding in the clinical trial situation is inconclusive. Some studies have found that patients with better knowledge or understanding were more anxious (Simes *et al.* 1986), but the majority of studies have found patient anxiety to be unchanged or reduced (Edwards *et al.* 1998; Ellis *et al.* 2001; Hewison *et al.* 2001). In the Edwards *et al.* (1998) review of informed consent for clinical trials, high levels of knowledge were significantly associated with less anxiety. There are several well established tools available to assess patient anxiety, and the justification for the approach used in this study forms part of the methodology discussion in Chapter 5.

3.15 Decision making

3.15.1 Decision making in the context of informed consent

In addition to the information given by the clinician, and patient understanding of that information, decision making in the context of informed consent to clinical trials requires voluntariness and competence to consent, both of which will be discussed in this section.

The underlying assumption of researchers evaluating informed consent to clinical trials seems to be that research subjects adhere to basic principles of rational choice (Reynolds and Nelson 2007). Rationality is defined as “decision making consistent with the principles of probabilities”, where a rational choice is “one in which the option with the highest expected utility is selected” (Holmes-Rovner and Wills 2002). In the clinical trial context, patients would understand the required information about a trial, weigh up its importance, and make the decision about participation based on the best expected value of outcomes (Lidz 2006). However, heuristics and biases have been found to influence decision making based on probabilities, with the result that patients’ decisions may not be based on their personal values (Holmes-Rovner and Wills 2002). In addition, one of the key criticisms of rational choice models is the influence of a variety of socio-cultural and affective factors on decision making - for example, information gained from sources other than health care professionals, cultural norms and emotion (Holmes-Rovner and Wills 2002). Since the focus for the theoretical underpinning of the work was informed consent theory, a detailed discussion of the theories of decision making is outwith the scope of this thesis. Nevertheless, it is important to acknowledge this field of work, which will be referred to in the discussion, as a potential area for future research.

Decision making is especially challenging in randomised cancer trials since patients are asked to consider participating in a clinical trial at a time when they have just received a diagnosis of cancer, or have just learned that they need further treatment because their disease has spread or recurred. Information retention and decision-making capacity may

be compromised when patients are already anxious, frightened or upset, and may also be experiencing physical symptoms as a result of their illness. Patients are often required to make the decision about participation within a relatively short period of time (usually one week), because of the urgent need to start anticancer treatment.

Studies have shown that often patients make the decision about whether or not to take part in a clinical trial immediately after receiving information about it. (Huizinga *et al.* 1999, in phase III cancer trials; Länsimies-Antikainen *et al.* 2007, in a trial for patient with a metabolic syndrome). These were both small qualitative studies where almost all the patients reported having made their decision instantaneously. The quality of the decision in this situation is questionable. Decision aids have been suggested as a way of supporting patients more effectively, and of encouraging them to take their time and ask questions.

3.15.1.1 Decision aids

Decision aids have been identified as interventions to help individuals focus on a deliberate choice between two or more treatment options (O'Connor *et al.* 1999; Bekker *et al.* 2003). They typically contain evidence-based information, presented in a simple graphical manner, with the aim of helping patients to clarify their values and to weigh up the pros and cons of the options before making the decision (O'Connor *et al.* 1999; Juraskova *et al.* 2007). It is not clear why they work, but it has been suggested that their effectiveness can be explained in terms of either the facilitation of cognitive strategies or changes to emotional processes (Bekker *et al.* 2003).

Benefits associated with the use of decision aids for health treatment or screening decisions are: less decisional conflict, higher knowledge/understanding scores, more active involvement of patients in decision making and, in some cases, greater satisfaction with the decision-making process, as well as more satisfaction with the decision itself

(review by O'Conner *et al.* 1999; review by O'Conner *et al.* 2003; Whelan *et al.* 2003; Tiller *et al.* 2006; Krist *et al.* 2007; review by Waljee *et al.* 2007). Blank *et al.* (2006) reviewed studies of cancer patients' treatment-related decisions, and found considerable evidence that decision aids can improve the quality of decisions across a range of illnesses, although they do acknowledge that the data for cancer treatment decision making is limited. They also acknowledge that a key area for further research is the participation decision for randomised clinical trials. Decision aids have rarely been evaluated in the context of clinical trials (Juraskova *et al.* 2007). Juraskova *et al.* (2007) have just completed a pilot study of a decision aid (booklet plus personalised worksheets) to help patients decide whether to take part in a large breast cancer trial or to choose the standard care option. Benefits of the intervention include high levels of understanding (both subjectively and objectively measured), and strongly positive attitudes to the trial. Patients liked the booklet, particularly the visual presentation of information. The decision aid is now being evaluated with patients from Australian and New Zealand centres taking part in a large international breast cancer trial (Juraskova *et al.* 2007).

3.15.1.2 Shared decision making

There has been increasing interest in the concept of shared decision making in the cancer setting, which has resulted in interventions being designed to increase patient involvement in the decision making process. An example of this is the study by Brown *et al.* (2006), who tested a package of a patient information booklet and video about treatment decision making (intervention), against a generic cancer patient information booklet (control). The package was designed to facilitate shared decision making, and was administered before seeing the oncologist. The first consultation was audio-taped and transcribed, and patients also completed questionnaires. Results showed that patients receiving the package were more likely than controls to declare their information and treatment preferences in the consultation, as well as their thoughts on costs, side-effects and

benefits of treatment. Considerably more themes were introduced by doctors to patients receiving the package, compared with the controls.

It has been suggested that informed consent and shared decision making are synonymous (Katz 1982 and 1984, in Beauchamp and Childress 2001, pp77-78). However, shared decision making is not common in informed consent. According to Holmes-Rovner and Wills (2002), this is because of the tension between allowing an investigator to take part in the patient's decision making and the danger of coercion. As asserted by Beauchamp and Childress (2001, p78), shared decision making neither defines nor displaces informed consent. According to MacLean (2006, p677), a deliberative model of shared decision making should be the goal of physician-patient relationships (which they view as a consent-giving relationship), because they consider this to be the only model that is suitable for constructing preferences and values. It is unclear if shared decision making improves patient understanding, and the role of shared decision making in informed consent is an area in need of further research, which would benefit from drawing on the preference construction literature (Lichtenstein and Slovic 2006).

3.15.2 Voluntariness

Although Faden and Beauchamp (1986) prefer to avoid the term 'voluntariness' and instead refer to 'noncontrol', (Section 3.1.3.4), 'voluntariness' is widely used in the literature, and is referred to by Beauchamp and Childress (2001, p80), along with 'competence', as a precondition for informed consent. There is little research that specifically examines the voluntariness of decisions to take part in research, and there is a lack of a coherent model, or tools for measuring it (Nelson and Merz 2002). Nelson and Merz (2002) reviewed the literature and assert that voluntariness is viewed as a matter of self-control. Threats to voluntariness can arise from the vulnerability of potential subjects (e.g. diminished capacity, socioeconomic status: prisoners, students, the poor, and other

role constraints such as family influence and poor prognosis), and the characteristics of the researcher and research setting (e.g. the authority of the physician and researcher behaviours such as persuasion, manipulation and coercion) (Nelson and Merz 2002). Potential research subjects need to have an understanding of the research, and what it means to them, in order to have the competence to consent (or refuse) and therefore make a voluntary decision about whether to enrol in a clinical trial.

3.15.3 Consent capacity/competence to consent

In the literature, 'consent capacity' is also referred to as 'competence to consent' or 'decision making capacity to consent'. Competence has already been highlighted earlier in this chapter as a key factor in informed consent theory (Section 3.7.3). Much of the work assessing consent capacity/competence to consent has been carried out with patients who were expected to have impaired capacity, often as a result of their illness or condition; for example, patients with mental illness (Kim *et al.* 2001 with Alzheimer's patients; Palmer *et al.* 2007 with bipolar patients and schizophrenia patients). Wendler (2004) describes consent capacity as having a set of abilities to be able to give valid informed consent. "This set of abilities includes the capability:

- 1) to understand the research in question
 - 2) to appreciate how the research applies to one's own situation, and
 - 3) to make a voluntary decision whether to enrol in the study in light of this understanding"
- (Wendler 2004).

The central role of understanding in this description of capacity is clear.

Studies of instruments designed to assess decisional capacity for clinical research or treatment (1980-2004) were reviewed by Dunn *et al.* (2006). They identified six instruments focussing on understanding of disclosed information, and eleven that assessed understanding, appreciation, reasoning and expression of a choice. They found substantial variation in reliability and validity of the instruments, the degree of

standardisation of disclosures, flexibility of item content, format, and scoring procedures. Limitations of the instruments included a lack of supporting psychometric data and a lack of generalisability across contexts (Dunn *et al.* 2006). Dunn *et al.* (2006) report that the MacArthur Competence Assessment Tools (MacCAT) for Clinical Research and Treatment had the most empirical support, but that other tools may be equally suited or better suited depending on the context. Robinson *et al.* (2005) identified a potentially important aspect that is ignored in Appelbaum and Grisso's (2001) MacCAT procedure – patient understanding about *why* the trial is being conducted in a particular way (for example randomisation). If these gaps in understanding are not noticed, the patient may make his own interpretations, which may lead to important misconceptions (Robinson *et al.* 2005).

Assessing capacity to consent would appear to be important; however, it has been suggested that it may be of more value to assess the actual consent, since people who have the capacity to consent do not always give valid consent (Wendler 2004). Wendler advocates that all potential research subjects should have a formal evaluation of their informed consent. He argues that the best way to determine whether a patient has the capacity to understand, and to give voluntary consent, is to determine, after adequate explanation, whether they do actually understand and give voluntary consent (Wendler 2004). This would seem appropriate, and was one of the reasons that assessment of understanding was chosen for the AVPI study, and the reason why competence/capacity to consent was not assessed.

3.16 Measures of informed consent

3.16.1 Overview

There are several challenges in measuring informed consent. As previously discussed, there is no widely agreed definition of informed consent, although there is some agreement about what the elements of informed consent are. For these elements, there

is a lack of definition about what is meant by the relevant terms, such as ‘understanding’, ‘competence’ and ‘voluntariness’. A variety of different measures have consequently been developed. Some have focussed on the individual elements, whereas others have tried to measure the whole process.

3.16.2 Measures of informed consent

Discussion of the measures and associated studies can be found in Chapter 7, where the justification is provided for developing a new instrument to measure understanding. Measurements of competence have already been discussed in Section 3.15.3 of this chapter. Another approach to measuring informed consent has been to focus on patient satisfaction with the process, often by questionnaires designed for specific studies (Montgomery and Sneyd 1998 in clinical trials for anaesthesia; Sorenson *et al.* 2004 in randomised controlled trials for cancer; Feldman Stewart *et al.* 2007 in prostate cancer). Most of the satisfaction studies report high levels of patients’ satisfaction with the informed consent process and, although an interesting aspect of consent is to determine how patients feel about the process, it was considered important to focus on a more objective measure. Patients satisfied with the process may still not be adequately informed, or understand the implications of their decision. In this study, the decision was taken to focus on ‘understanding’, since it is a key ethical requirement for informed consent, appears to have an effect on recruitment to clinical trials, and was considered to be amenable to improvement by the intervention.

3.17 Summary of Part II - Informed Consent

Informed consent can be viewed as comprising four main dimensions, where patient understanding is integral to all:

- What the patient needs to know [or understand] (*information*)
- How that information is conveyed [to maximise understanding] (*disclosure*)

- The extent to which the patient understands the information conveyed (understanding)
- The extent to which the patient's consent meets the criteria for decision making in this context – competence and voluntariness [understanding is essential for competence and voluntariness] (*decision making*).

Major conclusions from the literature

Conclusion 1

Informed consent can be viewed as autonomous choice and, as a consequence, requires patient understanding as the key component, along with voluntariness and competence. Patient understanding is viewed as understanding *that* you are being asked to take part in a clinical trial, and understanding *what* is communicated about the trial.

Study implications

- Patient understanding is a major endpoint in the study.
- This includes a focus on voluntariness and competence in the content of the video/DVD/CD-ROM. These are assessed via a self-report questionnaire which includes subjective and objective assessment of understanding. Questions include voluntariness of the participation decision (understanding *that*), understanding of freedom to withdraw from the study, and understanding about what happens if they refuse to participate in the clinical trial.
- Understanding *what* includes content as discussed in Conclusion 2, with a focus on aspects identified in the literature as particularly problematic to patients, such as understanding and acceptance of randomisation and clinical equipoise.

Conclusion 2

'Substantial understanding' is essential for autonomous actions, and requires that patients receive (and understand) core disclosure of key facts, as well as important information from their own perspectives.

Study implications

- The standard written information already addresses core information about the trial, according to regulatory requirements, and includes what a body of expert clinicians has deemed important, prior to initiation of the trial.
- The video/DVD/CD-ROM highlights the key generic clinical trial core facts.
- Patients were involved in the development of the content of the video/DVD/CD-ROM and advised on issues that were important to them.
- At an individual level, the patient is advised in the video/DVD/CD-ROM to have a verbal discussion with their doctor about the important issues for them.

Conclusion 3

The context is important for patient understanding and informed consent, in particular the clinician/patient interaction, as well as personal factors according to the patient (e.g. implications of the trial as it affects them).

Study implications

- AVPI as an intervention allows and encourages further discussion with the health care team about issues important to patients in their decision.
- AVPI facilitates and encourages active involvement of family and friends in the information discussion (at home and in clinic).

- Decision questionnaire assesses important reasons for patients in their decision, from a social and practical perspective, as well as specific to the health care setting.
- Patients' perceptions of aspects of the patient/clinician interaction are assessed in the decision questionnaire.

Conclusion 4

Other important ethical principles are beneficence and, to a lesser extent, justice.

Study implications

- Risks and benefits for each clinical trial are disclosed in the study-specific information sheet, which patients routinely receive prior to decision making, and this was retained in the study. There is a clear link via the video/DVD/CD-ROM referring patients to the information sheet for this discussion.
- The audiovisual approach in this study, by its very nature, may be useful for difficult-to-reach patient groups who are often excluded from clinical trials, such as low-literacy individuals and patients with communication impairment.

Conclusion 5

There are substantial challenges in relation to defining informed consent and its various elements, which has led to difficulties in measuring and evaluating it in practice. Despite this, it is clear that patient understanding is crucial and has been integral to most approaches to measuring informed consent. There are a variety of different approaches to measuring patient understanding but none specifically address the issues in the UK randomised cancer trial setting.

Study implications

- Patient understanding is used as the measure of evaluation of informed consent in this study.
- A new questionnaire was developed specifically for patients in randomised cancer trials.

Conclusion 6

There is a lack of clarity in the literature about what constitutes patient knowledge and what constitutes patient understanding. No evident distinction is made, and the terms are used interchangeably. What appears to be important is not the terminology, but whether or not the message is 'received' by the patient

Study implications

After much consideration, no attempt at distinction has been made in this study, so as to avoid adding to the confusion. Both terms are used – 'understanding' mainly in relation to the theoretical discussions, and 'knowledge' in the results chapter, for ease of reporting on the knowledge questionnaire.

Other conclusions from the literature and their implications for the study

Conclusion from Literature	Implication for AVPI Study
Information	
Most consent forms are too difficult in terms of readability.	AVPI can assist with this as a good supplement to written information, to emphasise key points.
Patient understanding is better with shorter, easy to read consent forms.	The AVPI study consent forms were kept short and focussed on key facts. The patient information sheet for the AVPI study underwent assessment for readability.
Tailoring patient information can improve understanding.	Information was tailored in the video/DVD/CD-ROM, as discussed in Chapters 4 and 6.
Baseline public knowledge of clinical trials is important.	Past experience of clinical trials was assessed within the context of patients' baseline knowledge.
Disclosure	
Patients need time to consider their decision about trial participation.	Wherever possible, patients were given at least a week between clinic appointments to consider their decision.
Some patients find benefit from family/friend involvement in their decision.	Close family members are included in consent discussions routinely in the centre, if acceptable to the patient. If randomised to the intervention group, patients were given the video/DVD/CD-ROM home between clinic appointments to view and discuss with family if desired. The decision questionnaire assessed to what extent patients did discuss their decision with their family/friends.
Selection of an appropriate medium for information transfer, is important for patient understanding and consent, with the audiovisual route particularly effective.	Audiovisual route selected as the intervention for this study.
Interaction between patients and clinicians is important in terms of the communication process in informed consent, although not clear how this relates to patient understanding.	Patients asked in questionnaire about some of the factors associated with the interaction process (e.g. trust in the clinician) but interaction is not investigated in any detail, as this would be a study in its own right.

Conclusion from Literature	Implication for AVPI Study
Understanding	
Diminished understanding was associated in the literature with older age, less education and disease severity.	These factors were determined for each patient in the AVPI study at baseline, and compared with levels of understanding
There are a variety of different approaches to measuring understanding but none specifically address the issues in the randomised cancer trial setting, relevant to the UK setting.	A new tool developed for this purpose in the AVPI study.
It is important when increasing knowledge/understanding, not to increase anxiety.	Anxiety was assessed in this study. The tool used was the Spielberger State-Trait Anxiety Inventory which is consistent with previous research and has good reliability and validity in the clinical trial setting
Decision Making	
Decision making about trial participation is particularly difficult for patients in the cancer trial situation	Questionnaires were kept short and no additional patient visits were introduced as part of the AVPI study, compared with routine care. There was continuity in terms of the same researcher seeing the patient at both visits.
Studies about patients' decisions should be in a real patient setting, faced with the actual decision and not in a hypothetical context, as results may be different.	The present study was undertaken in a real life cancer clinical trial setting.
Decision aids appear to be effective in other specialties in improving understanding and assisting patients with decision making, but have not been tested extensively in the cancer trial situation.	AVPI can be considered as a decision aid and patients were asked about its effect on their decision about clinical trial participation.
Voluntariness and competence are important for decision making	These are discussed in the video/DVD/CD-ROM and evaluated via patient questionnaire.

Informed consent will always be a challenge, and will never be perfect in the cancer clinical trial situation, owing to factors that are difficult to change, such as the vulnerability of patients and complex treatments. However, there is a wealth of literature and some well established theory to guide clinical practice and optimise the information-giving and consent process. Increasing patient understanding will improve informed consent, and perhaps increase clinical trial recruitment rates. Audiovisual patient information has been shown to be an effective means of improving patient understanding, and will now be discussed in Chapter 4.

CHAPTER FOUR: LITERATURE REVIEW PART III - AUDIOVISUAL PATIENT INFORMATION

4.1 Introduction to audiovisual patient information

Audiovisual patient information (AVPI) was identified in the previous chapter as worthy of further investigation in the clinical trial setting, in terms of improving informed consent and also clinical trial recruitment rates. This chapter will provide more detailed information about AVPI and explain why this method was chosen as the study intervention.

AVPI has been studied extensively in health care mainly as a tool for patient education, sometimes in relation to improving compliance, but also with the aim of assisting patients with decision making. Several outcome measures to determine its effectiveness have been used, with the majority focussing on knowledge or understanding of a health care procedure. Other areas studied include the effect of AVPI on patient satisfaction, quality of life, management of symptoms and side-effects, anxiety levels, compliance, behaviour, and the effect on the decision itself. Most of the methodologies employed have been structured questionnaires, some of them established tools (for example, to measure anxiety or quality of life), but many being developed for the purposes of the individual study, most commonly in relation to knowledge or understanding.

The literature will be discussed in relation to the types of AVPI, use of AVPI in health care, content and presentation of the information, and AVPI as a tool to improve the consent process and consent rates within the clinical trial setting. Limitations of previous research in this area will be discussed prior to summarising the relevant literature. Table 4.1 provides an outline summary of the chapter.

Table 4.1. Outline summary of Chapter 4

Literature search		
Types of AVPI	Format	
	Comparison of approaches	
AVPI use in health care	Overview	
	Health promotion	
	Screening	
	Surgery and rehabilitation	
	Cancer care	
Content of AVPI	Tailoring information	
	Framing information	
	Tailoring and framing AVPI	
Clinical trials	Clinical trials in health care generally	
	Cancer clinical trials	
AVPI and recruitment to clinical trials	Introduction	
	Evaluation of studies	Generally
		Cancer setting
Limitations of previous work		
Summary of AVPI literature		
Summary of literature review: Parts I-III (Chapters 2-4)		
Aims of the study		
Hypotheses	Hypothesis	
	Null hypothesis	

4.2 Literature search

For the purpose of searching the literature for areas of relevance in terms of audiovisual patient information, the following five concepts were used and expanded upon as shown in the full details of the search strategy (Appendix 4.1).

1. cancer
2. audiovisual (AV) material
3. clinical trials
4. recruitment/participation
5. patient information/education/knowledge/understanding

Electronic databases searched were: Ovid MEDLINE(R) (mesz), Ovid MEDLINE(R) In-Process and Other Non-Indexed Citations (prem), CDSR (coch), ACP Journal Club (acp), DARE, CCTR, British Nursing Index (brni), British Nursing Index Archive (bnib), CINAHL (nursing), EMBASE (emez), PsycINFO (psyf). The search strategy was devised with the input of an experienced medical librarian. Additional references were located by searching the bibliographies of related papers, examining conference proceedings, and using the Google search engine.

Terms were combined to focus on key areas of interest, which resulted in four main areas as shown in Table 4.2. The line number corresponds with the full details of the search strategy in Appendix 4.1.

Table 4.2. Summary of literature search: audiovisual patient information

Combination of Terms	Number of Hits
Line 16 = AV material + clinical trials + patient information	1415
Line 17 = cancer + AV material + clinical trials + patient Information	301
Line 18 = AV material + clinical trials + recruitment	439
Line 19 = cancer + AV material + clinical trials + recruitment	114
Line 20 = line 16 or 17 or 18 or 19	1617
Line 24 = limit to English language, last 20 years, duplicates removed	1049
Line 25 = final total following assessment	325

Although duplicates had been removed across databases, it was anticipated that there would be a substantial number of duplicates across these four lines (Lines 16-19 in Table 4.2). For ease of further searching, results from the four combined terms were then merged together to eliminate duplicates across the sets (Line 20 in Table 4.2). Due to the

large number of potentially relevant articles identified, this was limited to English language and the last 20 years. This resulted in a total number of 1049 hits. These titles and abstracts were then searched manually for relevance which resulted in an overall total of 325 potentially useful articles for consideration. Abstracts that were removed as part of this process were concerned with video-assisted procedures (e.g. endoscopy, surgery), using audiovisual aids to educate health professionals (e.g. communication skills training for junior doctors), paediatrics and neonates, and letters/comments/abstracts from conferences. Full articles were requested for the majority of the final 325 abstracts, and are drawn upon in the following discussion.

4.3 Types of AVPI

4.3.1 Format

Audiovisual patient information is a term used to include a variety of formats for the delivery of patient information. The most popular and the most widely studied is video, although studies have also involved CD-ROM, and more recently DVD, interactive computer programmes and multimedia packages. Other novel approaches include using power point slide shows (Mittal *et al.* 2007, clinical trial information for Alzheimer's disease) or visual illustrations (Brotherstone *et al.* 2006, in relation to flexible sigmoidoscopy). With some formats and newer technologies, there is the opportunity for the approach to be interactive and tailored to individual patients (e.g. De Bourdeaudhuij *et al.* 2007, a nutrition programme for company employees). Interactive computer systems and web based packages have been shown to improve patient information, but have significant practical challenges including cost and restricted access even with broadband internet, as shown by Cumbo *et al.* (2002). In addition, some formats such as videodisk require specialised equipment, which is often set up in a kiosk, with the user having to go to the location of the kiosk (Agre *et al.* 2002).

4.3.2 Comparison of approaches

There has been limited work comparing different types of audiovisual approaches to patient information in relation to knowledge and understanding, behaviour and its effect on decision making. What is available is inconclusive, as is now discussed.

Frosch *et al.* (2003) compared video information with an internet website for Prostate Specific Antigen (PSA) testing. This was a randomised study where 226 patients received either the video information or were allocated the internet information. Patients in the video group were more likely to review the materials and had a significantly greater increase in knowledge about PSA, but were also more likely to decline the PSA test. Patients in the internet group who reviewed the entire presentation showed similar increases in PSA knowledge to the video group (Frosch *et al.* 2003).

Ader *et al.* (1992) compared three different approaches: interactive videodisc, videotape and the surgeon only, in relation to dental extraction and found that patients' receiving the videotape had more knowledge about the procedure. Patients viewing the videodisc were more satisfied with the amount of preparation. However, it must be noted that this was a small scale study (n=60).

Emmett *et al.* (2005) compared a decision analysis tool with the combination of written and video patient information in patients with newly diagnosed hypertension. They found no difference between the groups in relation to blood pressure control, behaviour and compliance with medication. On the other hand, Agre *et al.* (2003) compared four methods of presentation - standard consent, video, computer program and booklet - in relation to knowledge of consent information in 441 participants (comprised of three groups: patients deciding whether to take part in a clinical trial; their family/friends; individuals from the waiting area in a surgical day hospital). Computer and video groups had a better understanding compared with the booklet and standard consent procedures.

Video was superior to the computer format for complex protocols and for minority participants (Agre *et al.* 2003).

Moseley *et al.* (2006) assigned 90 medical students to one of three groups considering informed consent to cataract surgery. All groups received a presentation about the surgery, with one of the groups also receiving diagrams and the other receiving a video. The video group had a better knowledge of facts and risks associated with cataract surgery. The aim of the study was to assess understanding, and it is interesting that this is done via a multiple choice knowledge test and that the terms knowledge and understanding are used interchangeably. This is not uncommon in the literature and has already been discussed in Chapter 3. A limitation of this study is that it does not involve patients and is carried out in a hypothetical context. Gomez *et al.* (1999) also interchange the terms knowledge and understanding in a study of AVPI for end stage renal disease and its effect on treatment selection. They say that they assess knowledge via a questionnaire but conclude that there was a significant improvement in knowledge and understanding. This was a non randomised study which only compared patients to their baseline scores, so it is not possible to tell if the intervention had any effect on treatment selection.

Audiovisual methods are considered to be more expensive than other methods of patient information such as written. French *et al.* (1999) challenge the idea that video in particular, is too time-consuming and expensive to produce. They used computer-based video production to develop and evaluate high quality, low cost patient education videos using digital imagery which improved patient comprehension of radiotherapy. Compared with interactive computer packages, video and CD-ROM are cheaper and more flexible in relation to viewing.

In oncology, video and CD-ROM have both been shown to be acceptable and useful media for information transfer (Thomas *et al.* 2000; Agre *et al.* 2002). In 1999 in a UK oncology study, 89% of patients had access to a video player at home (Thomas *et al.* 1999). With the developments in technology in this area since this study was undertaken, and the advent of DVD, the figure having access to audiovisual playing facilities can be anticipated to be substantially higher now. Patients' particularly appreciate being able to view the information in their own homes (Reid and DePalma 2001; Agre *et al.* 2002; McGregor 2003). In addition to patients valuing being able to view information at home, Deshler *et al.* (2006) reported benefits of home viewing in relation to increased satisfaction with the information and an increase in understanding and awareness of services. They evaluated a patient information programme in a cancer centre in the USA by comparing a video and information booklet mailed home with a video and booklet seen in class or via hospital drop in sessions.

In summary, although there is a lack of research comparing the different types of AVPI, there is substantially more evidence in the literature about the usefulness of video as compared with other formats. Both video and CD-ROM, in addition to DVD, are acceptable and now widely accessible to patients, as well as being relatively low cost compared with other multimedia computer approaches including interactive packages.

4.4 AVPI use in health care

4.4.1 Overview

The majority of the literature evaluating AVPI, evaluates it in combination with standard practice, and compared with standard practice, which is often written information and a medical consultation. Studies that have used AVPI as an alternative to written information and/or interaction (counselling or one-to-one consultation) have usually found that the communication aspect should not be replaced, and advocate administering AVPI in addition to standard practices (Thomas *et al.* 2000; Proctor *et al.* 2006). An exception to

this was in radiology where video was evaluated as an alternative to written information to inform patients about the use of intravenous contrast material (Hopper *et al.* 1994). Knowledge was increased for women receiving the video, but no difference was found in men. This led to the authors recommending that video be used as an alternative to the written consent form in this setting. Another exception was in illiterate populations where audiovisual consent was obtained for a genetic study with Guarani Indians living in Paraguay (Benitez *et al.* 2002) This is now standard practice for clinical research carried out within illiterate populations in the coordinating study centre in France (Benitez *et al.* 2002). A key benefit of audiovisual patient information is in relation to low literacy groups, for whom important information can be simplified using graphical presentations, which can be sensitive to cultural needs. Studies have shown clear benefits of video in terms of understanding and compliance among low literacy and minority groups (Thomas *et al.* 1999, in a large study of patients for pneumococcal vaccination; Tu *et al.* 2006 in screening for faecal occult blood with Chinese Americans).

Often, studies have involved multimedia education packages, which include AVPI with one-to-one counselling, enhanced written patient information, group education sessions and other visual tools; for example, Yeh *et al.* (2005) with printed nursing guides in addition to a CD explaining hip replacement. Patient education packages have also effectively combined practical teaching with AVPI; for example, videotapes, hearing aid fitting and home education as a package for older adults with hearing impairment and their significant others (Kramer *et al.* 2005). When these interventions are shown to be effective, as was the case in the two examples given, it is difficult to know how much the AVPI contributed to the effect, since the design did not isolate the AVPI as a distinct entity.

Audiovisual patient information, particularly video, has been shown to be effective in a variety of areas in health care, most notably in health promotion, screening, surgery and

rehabilitation, as well as cancer care, which will be further discussed in Sections 4.4.2 - 4.4.5. Effects on behaviour, as well as on knowledge and understanding, were noted in a large number of the studies. Less frequently, the effect of AVPI on quality of life and patient symptoms has been investigated, with benefits shown in reducing pain associated with whiplash injuries (Brison *et al.* 2005; Oliveira *et al.* 2006), emotional recovery following coronary artery bypass grafting (Sorlie *et al.* 2007), and an improvement in quality of life and resumption of pre-operative activities in patients undergoing surgical repair of an inguinal hernia (Zieran *et al.* 2007). However improvement is not always maintained in the longer term (Zieran *et al.* 2007).

Video appears to have a role in service redesign. It has been used to reduce consultation times in a family health clinic in Edinburgh, which was struggling to cope with the increasing demand for breast cancer risk counselling (Cull *et al.* 1998). They found that by using video, subjective and objectively assessed patient understanding improved, without an increase in patient distress. When the video was given before the consultation, consultation times were reduced. As a result of this study the authors recommend that video be used as an aid to, but not a substitute for, improved communication about inherited susceptibility to breast cancer (Cull *et al.* 1998). Agre *et al.* (1994) also advocate the use of video information as a time saving tool for doctors. They studied video use in patients prior to colonoscopy, and reported that one of the benefits of the approach is that it permits the doctors to focus on a more personalised discussion (Agre *et al.* 1994).

Patient adherence to treatment is an ongoing challenge in many aspects of health care, and ways of improving it are valuable. Patient education is an important part of the process and different ways of delivering the information to patients, such as video, may have an impact on whether or not the patient adheres to treatment. Jean Wiese *et al.* (2005) used video education about treatment (Continuous Positive Airway Pressure - CPAP) with patients with Obstructive Sleep Apnoea Hypopnoea Syndrome. Adherence to

CPAP is often poor with this patient group. However, in this RCT, comparing the video group with a control group, patients receiving the video had better adherence to treatment. So *et al.* (2003) found a similar improvement in adherence to treatment as a result of video and written information about silicone gel sheeting for burns, which resulted in a better scar outcome for patients.

AVPI has been used as a decision aid in a number of specialist areas including cardiology (Holbrook *et al.* 2007), cancer (McGregor 2003; Brown *et al.* 2004), screening (Hewison *et al.* 2001; Van Roosmalen *et al.* 2004), surgery (Deyo *et al.* 2000) and general practice for hypertension and benign prostatic hypertrophy (Shepperd *et al.* 1995), generating patient perceived benefits as well as improvements in knowledge. Substantial numbers of patients felt that the AVPI as part of a decision aid helped them in making their decision about treatment: 96% in the cardiology study and 71% of patients with hypertension or benign prostatic hypertrophy (Shepherd *et al.* 1995; Holbrook *et al.* 2007). Studies have also shown differences in actual decisions for patients receiving AVPI (Deyo *et al.* 2000 in relation to back surgery; Van Roosmalen *et al.* 2004 in genetic screening for breast cancer).

4.4.2 Health promotion

AVPI has been widely used in health promotion and has been shown to be a useful tool in this setting. Video has been used effectively to increase knowledge and preventative health behaviour in osteoporosis (Kulp *et al.* 2004), to increase breast self-examination in postmenopausal women (Janda *et al.* 2002), and to improve tooth brushing with an electric toothbrush (Addy *et al.* 1999; Renton Harper *et al.* 1999). In prenatal care, pregnant women who were shown a video as part of a health education package had a higher smoking quit rate, reported in the last month of pregnancy, compared with those who did not receive the video, but who otherwise received the same aspects of the education package concerned (Secker-Walker *et al.* 1997). Findings were validated by

exhaled carbon monoxide levels. In a UK study of a health education initiative for malignant melanoma, comparing an interactive video with matched controls, the group receiving the video had a higher knowledge, reported more protective skin behaviours and were more likely to report mole checking (Glazebrook *et al.* 2006).

In Canada, Cook *et al.* (2003) evaluated a video addressing brain and spinal cord injury prevention for ice hockey. Knowledge transfer and behavioural outcomes were evaluated in 11-12 year old hockey players who viewed the video. Concussion knowledge and the incidence of aggressive penalties were assessed before and after viewing the video. Results showed that knowledge was better in the video group, a difference which was maintained at three months. There was no significant change in the total penalties, although specific body-checking related penalties (which are considered a high injury risk) were significantly reduced. This was an interesting study in that behaviour was objectively assessed.

CD-ROM was used to increase fruit and vegetable intake in low income women (Block *et al.* 2004), and an interactive computer programme to increase factory workers' use of hearing protection (Lusk *et al.* 2003). Both these studies were randomised and relatively large scale: 481 participants (Block *et al.* 2004) and 2831 participants (Lusk *et al.* 2003).

A review of video intervention studies in relation to improving knowledge and treatment compliance at sexually transmitted disease (STD) clinics was carried out in the USA (Heaton and Messeri 1993). This showed that the largest effects were those for video on knowledge and attitudes about STDs and condoms. Lower effects were found among interventions targeting treatment compliance outcomes, which is consistent with prior prevention studies that have demonstrated difficulty in achieving behaviour change. However, this review was reported fourteen years ago, and since then there have been

large randomised studies in this area which have shown behaviour change. Of note are the studies by O'Donnell *et al.* (1995 [a and b] and 1998), as discussed below.

A video to promote condom acquisition was tested in a three group RCT of 1653 black and Hispanic patients attending a clinic in New York. Patients were randomised to receive either a control, video viewing or video viewing plus an interactive group session. Both the video groups had an increase in knowledge, attitudes and behaviour with higher rates of condom acquisition. The group receiving the interactive group session in addition to the video had higher levels than the video alone group (O'Donnell *et al.* 1995a). Similar results were shown in another study in New York with 3348 African American and Hispanic patients (O'Donnell *et al.* 1995b).

STD infections were assessed in African American and Hispanic men subsequent to an STD clinic visit where clients were randomised (n=2004) to receive video based education or the control arm (received routine clinic services only). There was a reduction in STD infections in those who received the video. The authors conclude that video to supplement regular STD clinic services and provider interactions can be effective in reducing rates of new STD infections, particularly among those at greatest risk (O'Donnell *et al.* 1998).

Audiovisual methods, mainly video and CD-ROM, have been used, with mixed success, for health education in schools. Studies have addressed promoting a healthy diet and exercise, sexual health, and orthodontic treatment. Casazza and Ciccazzo (2007) randomised pupils to one of three groups: CD-ROM; traditional teaching on nutrition and physical activity; or a control group. They found that although knowledge increased in the two intervention groups, this was accompanied by more positive lifestyle changes only in the CD-ROM group, where there was a self-reported change in eating behaviours and an increase in physical activity. In relation to orthodontic treatment, pupils were randomised to receive a video about the treatment, or to a control group (Anderson and Freer 2005).

Knowledge and attitudes were improved in pupils viewing the video. Although there was a small increase in willingness to have treatment, this was not statistically significant (Anderson and Freer 2005). Similarly, a CD-ROM about sexual health was associated with an increase in knowledge in a study by Yom and Eun (2005); however, there was no difference in attitudes. In all of these studies, any behaviour change was self-reported with no objective assessment being undertaken.

4.4.3 Screening

Another popular area for the development and use of AVPI is screening. The format most commonly used is video, with the majority of studies related to cancer screening, although video has also been used to deliver patient information about screening for Downs Syndrome (Hewison *et al.* 2001). The main outcome measure used in screening studies is uptake of screening, with knowledge the most common secondary outcome measure.

In colorectal cancer, screening uptake was increased when video was part of an educational intervention also involving other methods. Pignone *et al.* (2000) used video as part of a decision aid package, which also included a targeted brochure and a chart maker. This was an RCT testing the intervention video, containing information about colorectal cancer screening, against a control video which addressed automobile safety. Participants receiving the educational package containing the screening video more frequently requested screening tests (self-reported by participants), and had increased completion of screening tests which was determined objectively from review of case-notes. Tu *et al.* (2006) showed an increased uptake of screening as a result of an educational intervention for colorectal cancer screening, compared with usual care. In addition to video, the intervention included a health educator, a motivational pamphlet, an informational pamphlet and faecal occult blood testing (FOBT) instructions and cards. Powe *et al.* (2004) assessed knowledge as well as screening uptake and found that patients with greater knowledge of colorectal cancer were more likely to participate in

FOBT. Again the video was part of a larger educational intervention. Other aspects were posters, brochures and fliers.

Also in colorectal cancer, no effect on the overall screening rate was found in a study by Zapka *et al.* (2004), who compared a video on its own with the usual care. However, it is acknowledged that results may not be generalisable, as the sample was predominantly white middle class and there was already a high baseline screening rate (almost 25%). There was also substantial public media attention to colorectal cancer screening during the timeframe of the study, which is acknowledged by the authors.

In prostate cancer screening, a video increased knowledge when compared with a group not receiving the video, but there was no difference in screening behaviours (Volk *et al.* 2003). Taylor *et al.* (2006) specifically looked at prostate cancer screening in African American men, and randomised patients to three groups: AVPI (video), written information (booklet) and waiting list control. Both the video and the booklet groups had a significant improvement in knowledge, reduced decisional conflict about colorectal cancer screening, and increased self-reported screening rates, which were no different between the two intervention groups.

In mammography screening, Avis *et al.* (2004) compared a pamphlet with an informational video and found a small effect on screening uptake. Van Roosmalen *et al.* (2004) compared video plus written information with a control group among women being tested for gene mutation (breast cancer). The intervention contained information on screening and prophylactic surgery. Results showed that the intervention group had increased knowledge (which was subjectively and objectively assessed), were more satisfied with the information, and more frequently considered prophylactic surgery.

In screening for Downs syndrome, video was used in an RCT involving 2000 patients (Hewison *et al.* 2001). Test uptake, knowledge, and psychological stress were assessed. All women also received written information about screening, and had a discussion with the midwife at their booking visit. The intervention resulted in an increase in knowledge without increasing anxiety, but there was no difference in screening uptake (Hewison *et al.* 2001).

In relation to screening, video appears to have most benefit as part of a wider education package which has been shown to improve cancer screening uptake. However, in some situations, as shown in the study of screening for Downs syndrome, an increase in knowledge does not always result in an increase in screening uptake (Hewison *et al.* 2001).

4.4.4 Surgery and rehabilitation

Benefits have been shown with AVPI in improving knowledge and understanding of a surgical procedure (Mason *et al.* 2003 in female sterilisation; Rossi *et al.* 2004 and 2005 in orthopaedic surgery; Danino *et al.* 2005 prior to aesthetic surgery; Sahai *et al.* 2006 in laparoscopic nephrectomy), without increasing anxiety (Mason *et al.* 2003; Danino *et al.* 2005). As part of describing the surgical intervention, graphic illustrations and video footage of the procedure itself have been included in AVPI, for example in laparoscopy urology (Sahai *et al.* 2006). The main outcome measures, in terms of evaluating AVPI and patient consent to surgery, have been knowledge, understanding, anxiety, and patient satisfaction. Video is the most commonly used format.

A review of RCTs in media-based patient education about anaesthesia was carried out by Lee *et al.* (2003), who assessed the outcomes of knowledge, anxiety and patient satisfaction. They found that video and/or printed materials can increase knowledge and reduce anxiety; however, patient satisfaction was similar in both the intervention and no

intervention groups. The review concludes by supporting the use of video before surgery to inform patients about the process and risks of anaesthesia (Lee *et al.* 2003).

Henrotin *et al.* (2006) studied patient information for low back pain, and found that the majority of information available is in written format and is effective in improving patients' knowledge. With physician-related cues (such as the association of the message with the patient's physician throughout the text, or an educational session with the physician or nurse), this was also effective in increasing adherence to exercise in some cases. They found no evidence that video programmes alone are able to reduce low back pain, disability and health care costs, although it must be noted that only three of the studies included in the review involved video. One study showed no difference with the video, another involved a video as part of an internet intervention involving other multimedia approaches. In the third study involving video, knowledge of treatment options was greater in the group that viewed a video in addition to the standard written information, when compared with the group receiving the written information alone (Phelan *et al.* 2001). In this study, patients had a lower preference for surgery if they had viewed the video, although this was not statistically significant (Phelan *et al.* 2001). However, the review is limited by the fact that despite focussing on randomised trials, the three video studies were all considered to be of low quality, according to the list of criteria for the methodological quality of RCTs, as recommended by the Cochrane Back Review Group and discussed by Henrotin *et al.* (2006).

Similar results were found in a review focussing on RCTs of pre-operative education for hip or knee replacement, to determine whether it improves post-operative outcomes (McDonald *et al.* 2004). Only nine studies met the inclusion criteria, with three of these including video. In light of this, the authors found little evidence to support the use of pre-operative education over and above standard care. The value of AVPI in this setting is therefore unclear due to lack of evidence and the need for further research.

Studies of AVPI in rehabilitation include an RCT of a home-based exercise program (which included video) for ankylosing spondylitis (Sweeney *et al.* 2002); an RCT of customised videotapes in patients with Chronic Obstructive Pulmonary Disease (Petty *et al.* 2006); and an RCT of a diet and exercise video given to patients prior to hospital discharge following coronary artery bypass grafting (Mahler *et al.* 1999). All of these studies showed changes in behaviour although it is acknowledged that, in most cases, this was only via self-report and was not objectively assessed (Mahler *et al.* 1999; Sweeney *et al.* 2002).

4.4.5 Cancer care

AVPI is becoming more commonly used for patient education within cancer care. Video has been used to describe treatments with the aim of improving knowledge and reducing anxiety (Bakker *et al.* 1999; Thomas *et al.* 2000; Dunn *et al.* 2004; Hahn *et al.* 2005; Orringer *et al.* 2005; Walker and Podbilewicz-Schuller 2005), and to assist in decision making about treatment choices (McGregor 2003; Wilkins *et al.* 2006). Within cancer care, video has been shown to increase knowledge (Hahn *et al.* 2005; Orringer *et al.* 2005), increase patient satisfaction with information (Thomas *et al.* 2000; Dunn *et al.* 2004; Hahn *et al.* 2005; Walker *et al.* 2005), reduce anxiety (Thomas *et al.* 2000; Orringer *et al.* 2005) and improve symptoms (Clotfelter 1999). Studies in the cancer setting have predominantly evaluated video on its own rather than as part of a wider educational intervention. In addition to the benefits of AVPI for patient information, several studies also emphasise the importance and value of the clinical encounter/interaction with the health care professional (Bakker *et al.* 1999; Orringer *et al.* 2005; Gysels and Higginson 2007). The potential benefits of tailoring videos to individual diagnoses and patient subgroups is also highlighted (Hahn *et al.* 2005).

A systematic review of randomised controlled trials of effective methods of information-giving to cancer patients and their families was carried out by McPherson *et al.* (2001).

Ten studies were identified which met the inclusion criteria: RCTs that evaluated methods of information giving where the intervention was aimed primarily at educating rather than counselling. Outcomes directly related to the intervention included objective measures of knowledge acquisition, recall and understanding, and the use of educational resources. The greatest improvements were seen in relation to knowledge and understanding. The review was limited in that it focused on studies that included patients with heterogeneous cancer types and excluded studies focussing on just one type of cancer (e.g. breast cancer). Studies of medical procedures such as surgery, chemotherapy and radiotherapy were also excluded. Of the studies included, only one involved video and was of small scale and limited to elderly patients with cancer (Clotfelter 1999). In this study video was used with written information relating to cancer pain. Significantly less pain intensity was reported by the patients receiving the intervention, as compared with patients in the control group; however, the difficulty generalising these results is acknowledged (Clotfelter 1999).

Gysels and Higginson (2007) reviewed the literature specifically in relation to interactive technologies and videotapes for patient education in cancer care. This was carried out as part of a programme of systematic literature reviews on service configurations for supportive and palliative cancer care for the UK National Institute of Clinical Excellence. Gysels and Higginson (2007) looked specifically at the effect of technology on knowledge and satisfaction. They included studies that evaluated interventions providing patient education to improve knowledge, satisfaction, decision making, treatment choice or care management by using videotapes or computer programmes in cancer care. They excluded studies using hypothetical choices, informed consent to take part in a trial, screening for cancer prevention, and paediatrics. Nine RCTs were identified. These were from Canada, America, Australia and the UK and had a total of 1678 patients. Three of these involved video and six involved computer technologies. Of the three video studies, two involved consent to a procedure (Agre *et al.* 1994; Thomas *et al.* 2000), while the

other was designed to promote shared treatment decision making (Brown *et al.* 2004). The review supports the use of video for patient education in cancer care as an aid to (but not a substitute for) communications with health care professionals.

4.5 Content of AVPI

Both tailoring and framing information has been studied in relation to AVPI, with benefits shown in some areas, as discussed below.

4.5.1 Tailoring information

Tailoring information to specific patient groups or interventions appears to be beneficial, although there has been a variety of degrees and approaches to tailoring, making it difficult to compare results. A meta-analysis of 20 studies testing the efficacy of tailored interventions found that, in 50% of the studies, tailored interventions were more effective in promoting health behaviour than standard interventions (Ryan and Lauver 2002). Since this review, Lusk *et al.* (2003) have used a tailored computer intervention to increase factory workers' use of hearing protection in a large study in the USA (n=2831). Pender's (1987) Health Promotion Model and Bandura's (1986) Social Cognitive Theory provided the theoretical foundation, and guided the process for creating the intervention to change workers' behaviour regarding the use of hearing protection. Individuals responded to a survey questionnaire based on the important predictors of the Health Promotion Model, such as perceptions of benefits, barriers, self-efficacy, interpersonal and situational factors (Pender 1987, in Lusk *et al.* 2003), prior to receiving their information via a computer booth in the workplace. The information they received was influenced and hence tailored by their responses to the survey questionnaire. Other factors which contributed to the tailoring were the workers' self-reported existing practices in relation to hearing protection, and their perceived hearing ability.

Travena *et al.* (2006) carried out a systematic review on communicating with patients about evidence. They included 10 systematic reviews of RCTs and 30 additional RCTs and found that communication tools in most formats (for example written, verbal, audiovisual) will increase patients' understanding, but are more likely to do so if structured, tailored and/or interactive. Illustrations also appear to aid understanding (Travena *et al.* 2006). Unfortunately, clinical trial communication about participation was excluded from this review.

Jerant *et al.* (2007) studied the effects of a tailored interactive multimedia computer programme on the determinants of colorectal cancer screening. A personally tailored colorectal cancer screening programme (interactive multimedia via computer) was compared with a non-tailored 'electronic leaflet' (also available as an interactive multimedia programme via computer). This study found no difference in knowledge or perceived benefits to screening between the two groups, with the tailored group showing increased self-efficacy, less perceived barriers, and a greater state of readiness for screening. However, there were substantial limitations to this study, which was small and did not reach its target number (54 v 88). In addition, they did not assess the impact of the intervention on actual screening uptake.

A different approach to tailoring was investigated by Petty *et al.* (2006) in Chronic Obstructive Pulmonary Disease. Physicians selected from a library of 49 exercise segments, and chose from three different intervention times for their patient group (customised video group). These patients were then compared with patients who received a standard video about pulmonary rehabilitation, and a control group who received the usual care from their physicians. Patients in the customised video group showed an improvement in quality of life, reduction in fatigue, and an increase in exercise compliance compared with the other two groups. Patients in the standard video group showed an improvement in exercise compliance compared with the control group.

Within the cancer setting, Hack *et al.* (2007) evaluated the effect of a general audiotape about the trial (breast cancer, radiation) compared with a specific audiotape of the patient's consultation about the same clinical trial. The specific audiotape performed the function of an 'aide-mémoire' to the patient's medical consultation. They found no difference in knowledge or perception about being informed, but patients preferred the individual consultation tapes, as compared with the more general ones (Hack *et al.* 2007).

4.5.2 Framing information

There is mixed evidence in the literature about the effect of framing the information contained in AVPI, although framing and manipulating information was shown to be important in relation to written information in a good qualitative study by Donovan *et al.* (2002). They increased consent rates from 40% to 70% in a difficult-to-recruit prostate cancer trial by altering the way clinical trial information was presented, based on results of in-depth interviews with patients exploring interpretation of study information. This included the avoidance of misinterpreted terms and changes to the order of presenting treatments to encourage emphasis on equivalence. In relation to AVPI (video), Lewis *et al.* (2003) found that framing the information for mammography screening had no effect, but that the video was effective in all groups in correcting misconceptions and improving knowledge. Llewellyn-Thomas *et al.* (1995) also showed no effect of framing in patients' reported preferences for participating in treatment decision making and for trial entry. However, a conflicting finding was reported by Wragg *et al.* (2000), who did show a difference in patients' views as a result of framing in a trial of hormone replacement therapy (HRT). They compared two different videos: (1) information was framed to emphasise the current state of uncertainty about the costs and benefits of HRT (thus justifying the trial); and (2) the same information was framed to offer explicit numerical detail about currently known facts. The second group (focussing on numerical detail and not uncertainty) were more likely to hold stronger views about whether or not they would take HRT, and were more likely to refuse entry to the trial. A substantial limitation of this

study was that patients were asked about an imaginary trial of HRT and were therefore in a hypothetical situation; they may have felt differently when faced with the actual decision.

4.5.3 Tailoring and framing AVPI

Tailoring information has been shown to be a useful approach in terms of understanding, and also in changing behaviour. However, the usefulness of framing in AVPI is unclear from the literature and further research is warranted

4.6 Clinical trials

4.6.1 Clinical trials in health care generally

There is less research about AVPI as a tool to improve consent in clinical trials in health care, as compared with the literature concerned with AVPI and health education/consent outwith the clinical trial setting. AVPI has been used indirectly as a tool for decision making in many of the areas already discussed through its function of information provision. It has been used directly as a decision aid (or part of a decision aid) in screening, and prior to consent to anaesthesia and surgery, as previously discussed.

It has been suggested that the use of informational videos may enhance the informed consent process for clinical research, and that the understanding of difficult concepts such as randomisation may be improved by using visual examples (Jimison *et al.* 1998; McLaughlin *et al.* 2002). Jimison *et al.* (1998) developed a prototype multimedia tool based on focus groups and interviews with health care professionals, and three groups of patients with depression, breast cancer and schizophrenia. Patients could access the interactive programme to obtain both generic and specific trial information. The content of the specific modules was based on a drug trial that had already taken place. The approach was well accepted by patients, but was unfortunately not tested prospectively in a specific trial situation.

McLaughlin *et al.* (2002) identified the potential benefits of AVPI and registered a Cochrane protocol to undertake a review to examine the effects of providing an information video, alone or in conjunction with standard forms of information provision, to potential clinical research participants, compared with the provision of standard forms of information alone. They planned to assess understanding, satisfaction, recall of study information, level of anxiety and participant discussion. It is unclear if this work was undertaken as nothing appears to have been reported in the literature since the protocol was posted, and attempts to contact the author were unsuccessful.

In Flory and Emmanuel's (2004) systematic review of interventions to improve research participants' understanding in informed consent for research (from 1966 to 2004), 12 of the trials they reported on involved multimedia interventions. Five of these showed benefits in understanding, including two studies which showed delayed improvement in retention of knowledge several weeks after the consent procedure, but not immediately after disclosure (Fureman *et al.* 1997; Weston *et al.* 1997). The authors suggest that multimedia is useful outwith the clinical trial setting, but not within it, and offer reasons as to why this may be the case. They suggest that it could be because the informed consent process is already formalised through regulatory requirements, including the need for a written consent form, and that multimedia interventions may not add much to this already thorough disclosure process (Flory and Emmanuel 2004). However, it must be noted that, as previously highlighted, they were limited by the terms used in their search strategy, as they did not include the term 'knowledge', and as a result may have missed relevant papers.

Since this review, there have been several studies showing a benefit of AVPI in the clinical trial setting which will now be discussed, although it is acknowledged that further research in this area is necessary. Only randomised studies were included in the Flory

and Emmanuel (2004) review, and so other relevant non-randomised studies will also be discussed below.

In schizophrenia trials, a video was made to enhance the consent process, and knowledge was measured before and after viewing via an 80-item quiz (Wirshing *et al.* 2005). A highly structured educational video about the consent process was compared with a control video, which was about research generally and contained nothing about the consent process. The study sample included three groups: (a) patients with schizophrenia (n=83) who were being recruited for ongoing clinical trials (taken from 10 RCTs); (b) medical patients without self-reported psychiatric comorbidity; and (c) university undergraduates. Wirshing *et al.* (2005) found that knowledge was increased by the highly structured video, and that video was an effective teaching tool across all populations.

Joseph *et al.* (2006) evaluated a two-step education approach for patients potentially eligible for an HIV trial in Haiti. Firstly, patients were shown a video based on the consent form. The second session involved a one-to-one discussion with the social worker. Two hundred and fifty volunteers received the education. Comprehension was assessed with 16 true/false and 4 open-ended questions. Volunteers who failed the evaluation received a repeat one-to-one education session. Ninety percent of the sample (225/250) passed either the first or second evaluation, and were then considered eligible to enrol in the study. This was an interesting study in that patients were not allowed to enrol in the study unless they met a certain standard in relation to understanding. It is difficult, however, to generalise the results as the sample was specific to HIV and came from a developing country where illiteracy is common. It did not employ a randomised design, so it is not possible to gauge how effective the intervention was compared with other methods. In addition, they used a new tool to assess understanding which would require further validation work.

Knowledge and adherence to trial requirements were assessed in a complex and demanding long-term trial for diabetes following the introduction of an education package consisting of written and audiovisual patient information as well as behavioural practice (Diabetes Control and Complications Trial Research Group 1989). Results showed excellent knowledge scores following the intervention, and these were retained twelve months later. There was also good adherence to the trial. Limitations include the fact that the study was not randomised and therefore could not compare approaches or consent/compliance rates.

Another non-randomised study of note is the large-scale disease prevention study, the Women's Health Initiative in the USA (McTiernan *et al.* 1995). McTiernan *et al.* (1995) effectively used a multi-component informed consent process, similar to that in the diabetes study described above, as an ongoing informed consent process, updated as new information becomes available. The aim is for 160,000 women to be recruited over a period of 8-12 years at 40 clinical centres. No details are currently available on the results of this study.

Norris and Philips (1990) assessed patient understanding scores in relation to informed consent to clinical trials in two groups of patients in a duodenal ulcer study: those who received a video and those who did not. Both groups received the standard written information. Patient understanding was assessed via a 10 question multiple-choice quiz, with the video group having substantially better understanding than the control group. As a result of this, the authors strongly recommend using video as part of the informed consent process to clinical trials, as do Agre *et al.* (2003), who found that computer and video improved comprehension over written information alone for later phase clinical trials.

4.6.2 Cancer clinical trials

Cancer education materials, including clinical trial consent forms, have been shown consistently to have readability levels exceeding patients' abilities (Grossman *et al.* 1994; Cooley *et al.* 1995). Their value in preparing patients for clinical trials must therefore be questioned. A potential solution to this is 'easy-to-read' written material, which would not have the same level of detail as one written at a higher level. It may not therefore resolve a knowledge gap (Chelf *et al.* 2001). It has been suggested by Chelf *et al.* (2001), following a review of the literature on cancer patient education, that because spoken vocabulary is at a much higher level than written vocabulary, audiovisual approaches may be a better solution. Cancer patients often overestimate their prognosis with standard therapy and this may inhibit accrual to randomised controlled trials where standard therapies are the alternative, should they choose not to participate in the trial (Sheldon *et al.* 1993). Sheldon *et al.* (1993) suggest that trial-specific AVPI, with general background information, could be given prior to the consultation to enable the doctor to focus on more sensitive subjects such as prognosis with standard therapy.

AVPI has not been widely used to improve consent in the cancer setting, although it has potential value, as has been discussed in relation to the general clinical trial literature and within other areas of health care. Three recent studies have shown benefits in the cancer trial setting in relation to the consent process itself (Curbow *et al.* 2004; Hitchcock-Bryan *et al.* 2007; Strevel *et al.* 2007).

In phase I cancer trials, an educational DVD was compared with a placebo DVD (Strevel *et al.* 2007). The educational DVD increased patient knowledge and satisfaction regarding participation. The knowledge test was carried out with patients, but physicians also gave their perceptions of patient knowledge. Although knowledge was increased as a result of the DVD, there was no difference in consent rates. Fifty-five percent of patients felt that the DVD helped them to decide about participation. This was a small scale study

(n=49) and limited to a very specific group of patients, for whom the main aim of the trial is to determine the toxicity rather than the efficacy of the drug/treatment. Hence, these are patients with a poor prognosis, and with limited (if any) options for standard treatments.

Curbow *et al.* (2004) investigated the effect of video vignettes on clinical trial knowledge and beliefs using a pre-test post-test design. As discussed in Chapter 2 (Section 2.6.1.1), they distinguish beliefs from the concept of attitudes, as being cognitive statements rather than affective or evaluative statements about clinical trials. Knowledge is defined as 'correct factual information', and beliefs as an 'attribute linked with an object' where the object is clinical trials (Curbow *et al.* 2004). Curbow *et al.* (2004) involved 161 patients with breast cancer and 101 controls, and found that video vignettes were a powerful tool for increasing clinical trial knowledge, but not for improving clinical trial beliefs. In their summary, they suggest that a more concerted attempt to change beliefs rather than just by increasing knowledge is important. They suggest that this could be done by providing patients with direct experience of someone who has taken part in a trial, or by focussing on patients' positive emotional responses to being in a trial (Curbow *et al.* 2004).

Hitchcock-Bryan *et al.* (2007) developed a video about clinical trials, and tested it in a randomised trial in relation to informed consent of patients in a cancer centre in the USA. They found no difference in objective and subjective assessment of understanding of those in the intervention group, as compared with the control group. However, it was reported at the American Society of Clinical Oncology conference (ASCO 2007) that the lack of difference may be due to the fact that the clinical trials clinicians at the cancer centre already put a substantial emphasis on the oral part of the consent process, and spend significant time with patients as part of this process. A limitation of the study was that pre and post testing was not carried out, and it is not known if the groups were comparable in terms of understanding at baseline prior to the intervention. It must also be acknowledged that this was a small scale study (n=77). Despite this, patients found the

video useful in terms of information and decision making, both to themselves and to their family and friends. In view of this, the video is now used routinely as part of the informed consent process in the cancer centre that undertook the study.

Llewellyn-Thomas *et al.* (1995) randomised 100 patients undergoing radiotherapy to receive information about a hypothetical trial, either by audiotape or interactive computer programme. They found no difference in understanding or satisfaction between the groups, but found that the computer programme group reported a more positive attitude to trial entry.

4.7 AVPI and recruitment to clinical trials

4.7.1 Introduction

Although video has been used to some extent during the informed consent process for clinical trials, the research is limited, particularly in relation to its effect on patient decisions about whether or not to take part. Interventions to increase patient recruitment are of particular interest in the current health care climate. There is high political interest in increasing recruitment to cancer trials, and also reviews advocating further research in this area, particularly in relation to AVPI (McLaughlin *et al.* 2002; McDaid *et al.* 2006).

4.7.2 Evaluation of studies aimed at increasing recruitment to clinical trials

There have been a small number of studies specifically focussing on AVPI as a tool to increase clinical trial recruitment, both in the general health care setting and specifically in cancer trials.

4.7.2.1 *Generally*

In health care generally, two studies of interest were found. In Canada, Weston *et al.* (1997) investigated the effect of a patient information video in a perinatal trial in which 90 women were randomised to written information versus written information plus video.

They were asked to complete a questionnaire immediately after entry and 2-4 weeks later. Knowledge, feelings about how worthwhile they thought the study was, and willingness to participate in the trial (should they become eligible) were assessed. When initially asked, more women who watched the video thought they would consent to the study. There was no difference initially in knowledge, but the video group retained more knowledge 2-4 weeks later. Weston *et al.* (1997) concluded that a patient information video combined with an information sheet may result in greater participation in a research trial. However, the study showed 'interest in participation', but not how that translated into actual recruitment rates. The authors acknowledge that it was not possible for them to determine whether it translated into improved recruitment for this trial. In addition, the participants in the study were all highly educated.

In HIV vaccine trials, Fureman *et al.* (1997) investigated the benefits of video used as a supplement to written information for 186 injection drug users, and assessed 'willingness to participate' in the trial. Results suggest that written information should be combined with oral or visual materials to help people retain information. They found that willingness to participate was not associated with knowledge but was associated with 'trust in the government' in relation to safety of the vaccines. Limitations to the study were that the participants were in a hypothetical decision situation and were already enrolled in a study.

4.7.2.2 Cancer setting

Generally, there is no strong evidence for interventions that increase cancer patients' recruitment to trials (McDaid *et al.* 2006), and it is an area where further research is much needed. There is even less research specific to audiovisual interventions as a tool to increase recruitment in the cancer trial setting. These studies will now be discussed.

Du *et al.* (2008) conducted a randomised trial to investigate the effect of an educational video on clinical trials enrolment for patients with lung cancer. Patients (n=145) were

randomised to receive either the National Cancer Institute video, 'Cancer Clinical Trials: An Introduction for Patients and Their Families' (viewed before their first clinic appointment), or standard care (the clinic appointment). The primary endpoint was patients' self-assessed likelihood to enroll in a clinical trial, which was measured on a scale of 1-5. Actual enrolment rates were also recorded. Patients were surveyed via a one-page questionnaire which claimed to assess knowledge and attitudes towards trial participation. This was completed at baseline (prior to the intervention) and follow up (two weeks later). In addition to the one question assessing likelihood of enrolment, the questionnaire contained a total of 15 questions in 3 subscales which assessed 1) patients' altruism, 2) perceived personal benefits and 3) perceived negative aspects related to participation in clinical trials. The sample included patients who were potentially eligible for one of a wide range of clinical trials running at the centre, which included therapeutic and non therapeutic clinical trials, such as, educational, behavioural, chemoprevention and tissue collection trials. More than a quarter of the sample was African American (Du *et al.* 2008). Results showed that for patients assigned to the video intervention, enrolment rates were higher for therapeutic trials (17.5% v 11.1%) and for all trials combined (25.4% v 15.9%). However, this was not statistically significant. The intervention had a statistically significant impact on patients' attitudes towards clinical trial participation and the likelihood to enrol score was significantly associated with actual trial enrolment. For all three subscales on the knowledge/attitudes questionnaire, there were no differences between study arms at baseline or follow up and no difference in the change scores for the subscales by study arm.

There were several important limitations of this study, most of which have been noted by the authors. The small sample size meant that there was insufficient statistical power to detect a difference of less than 20% (Du *et al.* 2008). Analysis comparing enrolment to therapeutic trials between the study arms was not restricted to eligible patients, since data concerning eligibility status was not collected at this time point. This means that ineligible

patients were also included, which does not give an accurate picture of enrolment. The three knowledge/attitude subscales correlated poorly with patients' trial enrolment. From the information reported in the paper it is not clear to what extent the questionnaire measured knowledge and attitudes, since subject areas only are given and not the questions within each section. Attempts to contact the author, to clarify, were unsuccessful. It would appear from the subject areas that the focus was on attitudes rather than knowledge. In order to assess the effect of the intervention on knowledge, the tool would need to be more specific to the content of the video, in order to be sensitive to changes as a result of the intervention.

Work presented at the American Society of Clinical Oncology conference (ASCO 2003) showed an increase in consent rates by using audiovisual patient information in early phase drug trials. Daugherty *et al.* (2003) studied the effect of a CD-ROM educational intervention for advanced cancer patients enrolling in phase I-II trials. They developed an interactive CD-ROM with touch screen monitor, which contained phase I-II trial information and videos of patients and oncologists talking about early phase trials. Potentially eligible patients (n=199) were randomised to either view the CD-ROM or receive a written information leaflet. After consulting with their clinician, patients were interviewed about their understanding. CD-ROM users reported that it changed the way they made a decision to enter a trial (28%, compared with 12% of patients receiving the written information), and in some cases changed the decision itself (20% v's 5%). Daugherty *et al.* (2003) did a subset analysis and found that 71% of those who completed the CD-ROM subsequently enrolled in a trial compared with 58% who received the written information. Although this was a very specific patient population – advanced cancer, and a unique trial setting (phase I-II), the same issues of vulnerable cancer patients and complex trial information exist for patients in randomised cancer clinical trials.

In another small cancer phase I trial, already referred to in Section 4.6.2, an educational DVD was compared with a placebo DVD (Strevel *et al.* 2007). No difference was found in consent rates to the trial, despite the finding that 55% reported that the DVD influenced their decision making about participation.

In an attempt to improve accrual to a difficult clinical trial comparing very different treatment arms (radical prostatectomy with brachytherapy), a multidisciplinary patient information session (MDS) was established (Wallace *et al.* 2006). The MDS involved a talk by a cancer patient who took part in an RCT, an information video, and discussion with a urologist and oncologist about the trial and both proposed treatments. Recruitment was increased from 0 out of 27 patients to 34 out of 263 patients. Patient understanding was also increased following introduction of the MDS. This led to the conclusion that men who understand their treatment options and trial rationale, as presented jointly by specialists from competing treatment modalities, may be better equipped to make an informed decision, and are more likely to consent to random assignment (Wallace *et al.* 2006). The value of this approach appears to be in the combination of methods in the MDS rather than just the video itself.

4.7.3 Why AVPI might be of value in increasing cancer clinical trial recruitment rates

The *potential* value of video in increasing clinical trial recruitment rates is not a new finding, despite the fact that the *actual* value is at present unknown. The use of video, among other things, was identified as potentially helpful in explaining clinical trials to patients when investigating ways to improve enrolment to cancer clinical trials in 1991. Fisher *et al.* (1991) identified the major obstacles to patient enrolment by community oncologists, and identified potential aids to overcome them. Primary obstacles were (1) time demands on oncologists and staff, and (2) explaining clinical trials to patients. They planned to implement the potential aids identified, which included video, and to study their

impact on patient accrual. Although this was reported in 1991, there does not appear to have been any follow-up work from the authors since then.

AVPI, particularly video, has been shown to increase uptake of cancer screening, although it is acknowledged that the majority of studies included video as part of a wider education intervention. Within the health promotion literature, an effect on decision making in terms of an increase in compliance and also behaviour change was shown in randomised clinical trials where patients receive an informational video or CD-ROM.

As argued in Chapter 3, patient understanding appears to be the key component of informed consent, in terms of understanding *that* you are being asked to take part in a trial and understanding *what*, as the content of the information disclosure about the trial. It is known that misconceptions and poor understanding about clinical trials are common and that this is a contributor to patient refusal to clinical trials, and hence low clinical trial recruitment rates. Although there is not the evidence, it has been suggested that patients who have a better understanding of clinical trials have more favourable attitudes towards randomised trials, and are more willing to consider participation in a clinical trial (Ellis *et al.* 2001). It would therefore appear that by improving understanding, patients would be more likely to consent to a clinical trial.

Within the cancer trial setting, AVPI has been shown to improve informed consent by increasing patient knowledge and understanding, although it is acknowledged that there is a lack of research in this area. This is despite AVPI being an established way of delivering patient information in other areas of health care, with clear benefits in relation to knowledge and understanding (without increasing anxiety), improving compliance, uptake of screening, and also in assisting patients with decision making. Since it is known that AVPI can improve patient understanding of information, and in some cases influence

decisions, it would appear that it has the potential to increase clinical trial recruitment rates.

4.8 Limitations of previous work

There are two substantial limitations with previous work testing AVPI. Video is often used as part of a wider educational intervention involving other methods, such as written information, one-to-one discussion, counselling, charts and checklists. It is therefore difficult to say how much of an effect was due to the video itself and how much was due to the other aspects on the intervention. This was an issue in a substantial number of studies. In addition, as already discussed, knowledge or understanding was the main outcome measure for determining effectiveness of AVPI in much of the research. There were substantial challenges in assessing this, since a variety of different tools were used, at a variety of different time points relative to the intervention, and with a lack of clarity of the terms knowledge, understanding and comprehension.

4.9 Summary of Part III - AVPI

Within the health care setting, AVPI has been shown to be an effective tool for increasing knowledge and understanding (without increasing anxiety), and patient satisfaction in relation to information received. It appears to influence behaviour in health promotion, screening, management of side-effects and adherence to treatments. In the cancer setting, AVPI is widely accepted as a useful patient education tool, but limited work has been done in relation to its effect on the informed consent process in cancer clinical trials. Even less evidence is available in terms of its effect on consent rates themselves, although this is an area of increasing interest from researchers. There is a paucity of research examining the association between knowledge/understanding of the research, anxiety, and willingness to participate in a randomised clinical trial (Ellis 2000), although the potential benefits of AVPI on consent rates have been highlighted.

Video and CD-ROM, as methods of delivering patient information, have been shown to be effective, feasible and acceptable to patients. With DVD technology also now widely available for patients, DVD provides another means of delivering the same information. For reasons of effectiveness, flexibility of viewing, patient acceptability and cost, video, DVD and CD-ROM were chosen as the intervention for this study.

Major conclusions from the literature

Conclusion 1

AVPI has been shown to be an effective and useful tool for patient education in a variety of health care settings including health promotion, screening, surgery, rehabilitation and cancer care. It has been shown to increase knowledge and understanding, improve compliance, increase uptake of screening and to assist patients with decision making.

Study implications

- AVPI (video/DVD/CD-ROM) was chosen as the intervention for this study due to its effectiveness in increasing knowledge and understanding and because it appears to be a widely available and acceptable medium for patients.

Conclusion 2

AVPI has been shown to be an effective tool for increasing knowledge and understanding without increasing anxiety, and in some cases reducing anxiety.

Study implications

- Patient anxiety as well as knowledge/understanding was assessed at baseline and post intervention.

Conclusion 3

Further research is needed to evaluate AVPI in terms of improving the consent *process* in clinical trials and also in terms of its effect on consent *rates*. The few studies that have been done in this area suggest that by increasing understanding, AVPI can improve the process and also increase recruitment rates.

Study implications

- The aim of the AVPI was to increase understanding as a means to increasing recruitment rates via a reduction in patient refusal.
- The literature was used to determine optimal ways to develop the AVPI to achieve this aim (e.g. patient involvement, summaries on screen, medical consultants involved in the production).

Conclusion 4

Tailored AVPI appears to be more effective than generic AVPI

Study implications

- Some degree of tailoring was incorporated into the AVPI which was developed specific to tumour type and localised geographically.

4.10 Summary of the literature review: Parts I-III (Chapters 2-4)

The need to increase recruitment to cancer clinical trials has been highlighted, along with the need to do this in an ethical manner when supporting patients to make an informed choice about whether or not to participate in a trial. Patients are asked to consider complex terminology at a very difficult, anxious time in their lives, soon after being given a diagnosis of cancer or news about recurrence. The evidence from the three parts of the literature review, suggests that audiovisual patient information to improve patient understanding is a potential way of both increasing recruitment and improving the informed consent process. AVPI has been shown to be an effective and acceptable medium for information giving in the cancer care setting. It was decided to focus on randomised trials because these trials involve the largest number of patients in cancer clinical trials, and also because of the problems associated with patients' understanding of the term 'randomisation', and the substantial misconceptions discussed in the literature (e.g. Sutherland *et al.* 1990; Corbett *et al.* 1996; Featherstone and Donovan 2002). There is much potential for improvement in patient understanding in this area, which could lead to a more informed decision and higher numbers of patients being recruited to clinical trials. Key points from the full literature review are summarised briefly in Table 4.3.

Table 4.3. Key points from the literature review

Key Points
<p>1. Further research is much needed to determine effective interventions to increase recruitment to cancer clinical trials. Research involving interventions targeted at the informed consent process to increase clinical trial participation should not be considered independently of the quality of the informed consent process, due to the dangers of coercion.</p>
<p>2. Patient refusal is the most common reason for potentially eligible patients not participating in cancer trials, with issues around patient understanding (especially of randomisation) and informed consent widely identified as factors negatively affecting recruitment and contributing to patient refusal rates. It would appear, therefore, that by increasing patient understanding about the research, refusal rates can be reduced.</p>
<p>3. Informed consent can be viewed as an autonomous choice, and as a consequence requires patient understanding as the key component, along with voluntariness and competence.</p>
<p>4. AVPI (particularly video) has been shown to increase knowledge/understanding without increasing anxiety. It has also been shown to assist patients with decision making. AVPI therefore has the potential to reduce clinical trial refusal rates (and so increase recruitment) in an ethical manner, by improving patient understanding of the information they are being asked to consider, prior to decision making about clinical trial participation.</p>

4.11 Aims of the study

The aims of the study were:

- 1) to determine the effect of an audiovisual patient information intervention on
 - a) refusal rates to randomised cancer trials
 - b) knowledge and anxiety
- 2) to investigate patients' perceptions of the AVPI
- 3) to investigate reasons for accepting and declining clinical trial participation.

4.12 Hypotheses

4.12.1 Hypothesis

The addition of a patient information video/DVD/CD-ROM, to supplement written information in the informed consent process for patients considering participation in cancer clinical trials, will increase knowledge/understanding and reduce rates of patient refusal without increasing anxiety.

4.12.2 Null hypotheses

- 1) There will be no difference in knowledge/understanding between the two groups - a) patients receiving the audiovisual information in addition to written information and b) those that receive written information only.
- 2) There will be no difference in clinical trial refusal rates between the two groups.
- 3) There will be no difference in anxiety between the two groups.

CHAPTER FIVE: METHODS

5.1 Introduction

This chapter will describe and discuss the methodology employed to meet the aims of the study, taking into account the clinical context and information from the literature. Study design and coordination will be discussed first, followed by sampling, recruitment and randomisation. The measures and process for data collection will then be addressed, and finally ethical considerations, timescales and funding.

5.2 Study design

5.2.1 Design

The study design was experimental in the form of a randomised controlled trial (RCT) (Robson 2002, p116). This two group RCT aimed to compare patients who received the video/DVD/CD-ROM (intervention) with patients who did not (control).

An RCT was considered the design of choice for this study because it provided an experimental setting to determine if the intervention (AVPI) is effective, with the best chance of controlling for confounding variables. Randomisation is designed to maximise the likelihood that if a variable is likely to affect the outcome (known and unknown), it will be equally distributed between the groups – in this case, in both (a) the written information group and (b) the AVPI + written information group.

The standard reasons discussed by Shadish *et al.* (2002) where random assignment is not feasible or desirable were considered in relation to this study: if information is needed rapidly; when much high quality prior information already exists; where the independent variable cannot be manipulated (e.g. age); and ethical reasons (e.g. cannot assign a patient to an event that can cause harm, e.g. cigarette smoking). None of these reasons were applicable in this study.

Further justification for the study design came from the comprehensive guidance developed by the Federal Judicial Centre (1981) (in Shadish *et al.* 2002, p277). They stated that prior to conducting an RCT, it is important to justify that:

“.. the present conditions need improvement, that the proposed improvement is of unclear value, that only an experiment could provide the necessary data to clarify the question, that the results of the experiment would be used to change the practice or policy, and that the rights of individuals would be protected in the experiment”.

All of these points were applicable to the AVPI study where clinical trial recruitment rates and the informed consent process needed to be improved. Although the AVPI intervention was considered to be potentially useful in this situation, the effect was unclear, due to lack of research evidence.

The practical challenges of an RCT as discussed by Shadish *et al.* (2002) and Robson (2002), which included recruiting large numbers of suitable and willing patients, attrition, and compliance with the intervention, were not anticipated to be a problem in this study.

5.2.2 Threats to validity

“ A validity typology can greatly aid design....” (Shadish *et al.* 2002, pp38-39). Validity was an important consideration in this study and it is acknowledged that “validity is not the property of a method, but is a characteristic of knowledge claims, ...in this case claims about causal knowledge” (Shadish *et al.* 2002, p54). Random assignment of patients to study arms was carried out to reduce the threat to internal validity by eliminating selection bias (Shadish *et al.* 2002, p56). In an attempt to prevent reactivity to the experimental situation, the hypotheses were not discussed with participants. However, to meet ethical requirements, patients were informed that the study was looking at ways of improving information and making it easier for patients to decide whether or not to take part in research trials. They were told that the aim of the study was to see if information in video/CD-ROM/DVD format improves peoples' knowledge about clinical trials, and if it

makes any difference to their decision about whether or not to take part in a clinical trial. Due to the nature of the intervention, blinding was not possible (Shadish *et al.* 2002, p78). However, the randomisation process was handled by administrative staff in the Clinical Trials Unit. Clinical staff involved in recruiting patients to the study, were therefore not involved in the randomisation process and had no way of knowing which patient the intervention would be assigned to.

5.2.3 Context of study

The study can be viewed as a 'sub study' of the cancer clinical trial as it is nested inside the cancer trial. To avoid confusion with the clinical trial being considered by the patient, throughout the thesis, and as already noted in Chapter 1, this study is referred to as the 'audiovisual patient information study' (AVPI study) or 'study'.

5.2.4 Intervention

For ease of reading, the control arm is described first since the intervention arm involves standard practice as described in the control arm, in addition to the intervention itself.

5.2.4.1 *Control arm*

The control arm of the study (also referred to as the no-intervention arm) involved current standard practice in The Beatson West of Scotland Cancer Centre for discussing clinical trials with patients. Patients see either a registrar or consultant from the tumour site team, who discusses the trial and administers a trial-specific information sheet and consent form (visit 1). An appointment is then made for them to return to the clinic the following week. At this visit (visit 2), they see a clinician from the same team to decide on treatment and whether or not this will be part of a clinical trial.

5.2.4.2 *Intervention arm*

The intervention consisted of an audiovisual patient information tool (AVPI) which addressed both generic and cancer site-specific clinical trial information, with a particular focus on randomisation. It aimed to complement the written information sheet received by the patient about a specific trial, and was administered in addition to standard practice, as described above.

The AVPI was developed by clinical and technical staff within the acute division of NHS Greater Glasgow and Clyde, via a multi-professional team. Three different versions were made (lung, breast and colorectal cancer) with the same core content. Patients were given the AVPI to watch at home: there were three different formats (video, CD-ROM, DVD) to allow for patient preference and availability of equipment at home. The process of developing the AVPI is described in detail in Chapter 6.

5.2.5 Primary endpoint

The primary study endpoint was the percentage of patients who declined participation in the clinical trial that was offered to them. Based on the literature, as discussed in Chapter 2, it was assumed that 40% of patients refuse participation in cancer clinical trials. Given that assumption, the power calculation indicated that, and in order to have an 80% chance of detecting a 20% difference at the 5% significance level (two-sided), a total of 164 patients were required (Machin *et al.* 1997, p45-table 3.1). This number would then detect a reduction in refusal rate from 40%-20%. This sample size also provides approximately 80% power to detect a moderate standardised difference of 0.45 between continuous variables such as knowledge and anxiety scores.

5.3 Co-ordination of the study

The study was planned, initiated and led by the Cancer Consultant Nurse (CCN) for NHS Greater Glasgow and Clyde as Principle Investigator, with the support of a Research

Practitioner (RP) for patient recruitment and data collection. During periods of absence of the RP, the CCN exercised the responsibility for recruitment and data collection. A multi-professional steering group (also known as the study team: Appendix 5.1) was set up to oversee and steer the project throughout its duration, and was chaired by the CCN. The steering group consisted of the Professor of Medical Oncology, Research Practitioner, two patients who had previously participated in a randomised clinical trial, and the lead medical consultants and nurses for breast, lung and colorectal cancer at The Beatson West of Scotland Cancer Centre. The lead for clinical psychology was involved – mainly by email, owing to staff shortages within clinical psychology.

5.4 Sample

Sampling was carried out at The Beatson West of Scotland Cancer Centre during January 2005 until August 2006.

Patients were eligible for the study if they:

- had a diagnosis of colorectal, breast or lung cancer;
- were clinically eligible for entry into a cancer treatment trial randomised against control/standard treatment, or best supportive care, running at the cancer centre;
- had access to a video recorder, CD-ROM or DVD playing facilities;
- could understand English.

It is recognised that optimal practice would require the development of information in appropriate languages, in addition to English. However, due to issues of cost and feasibility, it was decided in this study to use English only. It was anticipated that, if the intervention proved to be a useful resource, translation would be considered for any future work.

All clinical trials for breast, lung and colorectal cancer which involved randomisation against control/standard treatment, or best supportive care, running at the cancer centre during the recruitment period, were identified for inclusion in the study (Appendix 5.2).

5.5 Raising awareness

Following identification of the clinical trials to be included, there was discussion with the tumour site-specific teams involved in the recruitment process for those trials. These discussions involved registrars and consultants, clinical nurse specialists (CNSs) and data managers; they were carried out on a one-to-one basis for those directly involved in the consent process, and also as a group at team meetings. Nurses in the relevant wards were given both written and verbal information about the study at their regular ward meetings. The aim of discussions was to ensure high awareness of the project and also to enlist support in the recruitment process. Information about the study was made available through the intranet on The Beaston West of Scotland Cancer Centre website (which included the option to view the AVPI), and via the internet where study information could be viewed externally on the website.

5.6 Patient recruitment

5.6.1 Timeframe and targets

The timescale for recruitment was estimated at 12-18 months based on numbers of patients entering randomised clinical trials in the six months prior to the commencement of the AVPI study. It was recognised that recruitment would be dependent on the numbers of randomised trials open at the cancer centre, and that this would fluctuate due to the nature of multicentre clinical trials, with some trials inevitably opening or closing earlier or later than initially anticipated. A graph of recruitment targets based on an 18 month timeframe was produced, with a target of 9.1 patients per month to meet the overall target of 164 patients by June 2006. Every month, recruitment rates were mapped against the

target. Cumulative monthly recruitment targets for the duration of the study are shown in Figure 5.1 along with the actual numbers of patients recruited.

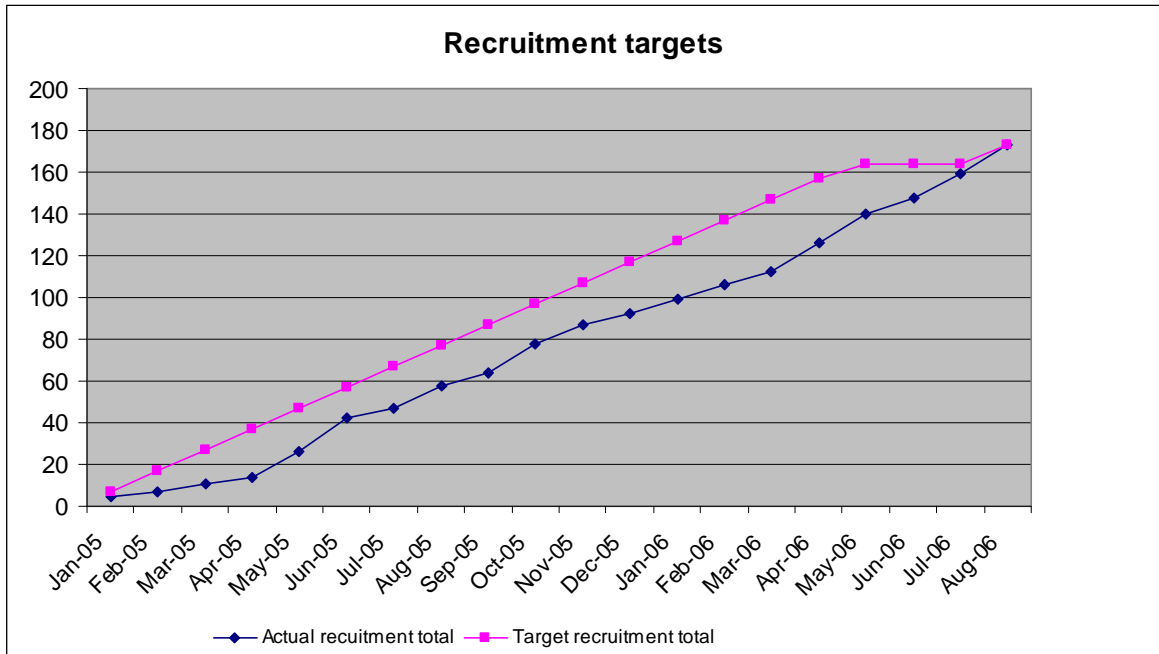


Figure 5.1. Monthly recruitment targets

The overall target of 164 patients was reached by June 2006 but as the graph shows, recruitment continued until August 2006 to take into account the 9 patients that were replaced, as discussed in Section 5.6.4.

There were a number of patients who had been entered into randomised clinical trials but had not been considered for the AVPI study because the RP was unaware of them. These patients were referred to as 'missed' patients. In addition, to mapping the number of patients recruited to the study against the target figure, the data manager collated a monthly list of these missed patients. Every month, the RP and the CCN reviewed recruitment figures, and the list of missed patients, to determine ways of preventing similar patients being missed in the future. The majority of patients considering participation in a cancer clinical trial are routinely seen in the out-patient clinic, although some patients do

take part in this discussion in the ward. In this study, it was anticipated that patients would come from both areas. The recruitment review process showed that, overall, approximately 75% of potential patients were identified for the AVPI study (337/450), with the majority of those missed, receiving care in ward areas. Action that was taken as a result of identifying missed patients was additional education to ward areas, and with clinicians, to increase awareness of the study and of the process for referral of potential patients.

Clinically eligible patients who were missed for the AVPI study, and who were not entered into a clinical trial (usually because of patient refusal), would be difficult to identify. It is recognised that the process adopted for reviewing missed patients would not identify this group of patients, which was anticipated to be relatively small in number because of the active recruitment strategies employed in this study. Taking into account the reported clinical trial refusal rates from the literature, numbers of patients consenting to a clinical trial that were being missed in the AVPI study, and also the fact that monthly recruitment rates to the AVPI study were acceptable, no further action was taken to try and identify this group.

5.6.2 Recruitment process

Potential participants for the AVPI study were identified by the researcher from weekly clinic lists, discussion with clinicians, and by attending clinics and reviewing patient case-notes. Clinicians, CNSs and data managers were given contact details for the RP/CCN and encouraged to phone if they had a potential AVPI study patient. Weekly contact with clinicians was made to maintain the intensity and profile of the study and to optimise awareness of potential new patients.

Patients were approached for the study by their clinician, at the same consultation visit to discuss the clinical trial. Patients were not approached if subsequent clinic appointments

(including the visit to discuss their decision about entry into the clinical trial) were expected to be arranged outwith the cancer centre. This was mainly for practical reasons since, due to the commitments of the study at the cancer centre, it would not have been possible for the RP or the CCN to attend outlying clinics. It was considered important to limit the number of people involved in administering the questionnaires, in order to reduce variation and maintain consistency in approach. For this reason, nurses in the outlying hospitals were not approached or asked to see patients for the purposes of this study.

If the patient was willing to have further discussion about the AVPI study, the clinician or RP/CCN checked that they had access to video, DVD or CD-ROM playing facilities, and a follow up discussion was undertaken by the RP/CCN. An information sheet (Appendix 5.3), and consent form (Appendix 5.4) for the AVPI study, which were developed according to requirements of the West Research Ethics Committee in relation to format and content, were given as a separate pack from the clinical trial information sheet and consent form.

5.6.3 Screening

In order to achieve the target number of patients for the study, 450 patients were potentially eligible from case-notes and clinical trial entry sheets: of these, 113 were identified retrospectively as having been missed/not referred for the AVPI study; 98 were not approached (85 because they were known to be receiving care outwith the cancer centre, and 13 mainly because they were considered too upset to be approached - see Section 5.6.3.2); 56 patients refused the AVPI study; and 3 patients were excluded as a result of the eligibility criteria (see Section 5.6.3.1). It was not possible to approach 7 patients who had consented to their cancer clinical trial at the same medical consultation that they received information about the trial. This was an unexpected situation since standard ethical practice for the consent process in clinical trials, which is supported by

the cancer centre, is to allow at least 24-48 hours after patients receive the information before they make the decision about whether or not to participate in the clinical trial.

As already mentioned in the previous section, a large number of the missed patients were inpatients. Despite the additional education and awareness-raising sessions for ward staff, the majority of potentially eligible ward patients were still not identified and referred for the AVPI study. It is difficult to know why this is the case but it could have been because the ward staff were busy with higher priorities related to patient care. It is recognised that the presence of the RP or CCN in the ward may have helped to identify potential patients. This was not undertaken because larger volumes of potential study patients were attending the clinics and it was considered that time was better spent focussing on recruitment from these areas.

5.6.3.1 Exclusions

Three patients were excluded from the study: two because they did not have access to video, DVD or CR-Rom playing facilities, and so they did not meet the eligibility criteria; and the other because she was deaf and unable to lip-read.

5.6.3.2 Patients not approached for the AVPI study:

In addition to the patients that were seen outwith the cancer centre (n=85), there were a small number of patients (n=13) who were not approached for the study for other reasons. This decision was made by the clinician, specialist nurse or the RP/CCN, primarily because of the patient's degree of distress as a result of being given bad news, or uncontrolled symptoms from their disease as shown in Table 5.1.

Table 5.1. Patients not approached for the AVPI study

Reasons that clinically eligible patients were not approached for the AVPI study	Number of patients
Receiving care/treatment discussions outwith cancer centre	85
Considered by the clinician, CNS or RP/CCN to be too distraught to be approached.	9
Known to RP	1
Cross for having to wait so long to be seen (breast clinic) so left before AVPI discussion	1
Needed immediate symptom control (pain)	1
Needed an urgent investigation	1
Total	98

5.6.4 Consent

Written and verbal information about the study was given as previously described in Section 5.6.2. The decision was taken not to enforce the usual minimum period of 48 hours between receiving information about a study and consenting, as it was considered important for the time to treatment not to be delayed. If this time period (or longer) was introduced, taking into account practical implications, either the patient would be asked to attend for an additional visit to discuss the AVPI study, or the discussion with the clinician about their clinical trial would be delayed by at least one week. Both these outcomes were considered by the steering group to be ethically unacceptable for patients with cancer waiting for treatment, and this was supported by the Ethics Committee.

There was no pressure or expectation that the patient would consent to the study at the initial visit; however, the option was available should they wish to make the decision that day. It was anticipated that some patients would choose this option to potentially give them more time to view the AVPI.

If the patient decided that day to take part in the AVPI study, he/she was randomised while at the clinic. If the intervention arm was drawn, a choice of video, DVD or CD-ROM was offered, and it was received that day to take home. If patients wished more time to consider whether or not to take part in the AVPI study, they were given the information sheet to take home with them, and a time was arranged for the RP/CCN to phone, to further discuss the study. If the patient then decided to participate, the RP/CCN checked the randomisation status, phoned the patient back with the result, and if they drew the intervention arm, posted out the video, DVD or CD-ROM as chosen by the patient. All patients received the standard written information about the clinical trial in which they were considering participation. Patients who did not draw the intervention arm were reassured that their information needs would continue to be met by their clinical team. The clinical psychologist agreed to be available for staff and patient support should any issues arise, but this proved not to be necessary and was not accessed by either group. If patients chose not to take part in the AVPI study, whether or not this was accompanied by the decision to accept or refuse the clinical trial, they were not approached again for this study.

The initial target of 164 patients was reached within the anticipated timeframe; however, a further 9 patients were recruited to replace those who were identified at their second study visit as having become ineligible for the clinical trial, thus making their decision about trial entry hypothetical. Hypothetical situations are not always representative of the real life experience and previous research has shown that patients can act differently when making personal decisions (Cassileth *et al.* 1982; Trauth *et al.* 2000)

5.6.5 Refusal to the AVPI study

Of the patients approached for the AVPI study (n=232), 56 refused to take part (24%). A large proportion of those who refused the AVPI study did not go on to enter the clinical trial (73%). Therefore, of those who refused the AVPI study, 27% (n=15) did go on to take

part in the clinical trial offered to them. In general, a 24% refusal rate is fairly low, however one has to acknowledge that there may be a recruitment bias because the majority of refusers (73%) also refused the clinical trial. If patients gave a reason for their decision not to take part in the AVPI study, this is shown in Table 5.2.

Table 5.2. Reasons for AVPI study refusal

Reason given by patient for refusing AVPI study	Number of patients
I have too much to think about/take in	13
I don't want any further information	8
I have already made my decision	7
I don't want the control arm	3
I'm too upset	3
I don't want the extra hassle	2
I don't like questionnaires	1
I feel squeamish at the thought	1
I can't decide whether to have treatment at all	1
No reason given	17
Total	56

5.6.6 Recruitment challenges

There were a number of challenges recruiting to this study. One of the main issues was that recruitment depended on the type of trials that were open at the cancer centre. Important factors included the nature of the treatments within the trial compared to 'off study' treatment options, where patients had treatment preferences. This was particularly difficult when study arms were very different, for example, a standard chemotherapy regime being compared against a new type of drug treatment. Another factor was the eligibility criteria for the clinical trial, which was particularly challenging if this was very restrictive, for example, excluding patients with co-existing medical conditions or symptoms that would be potentially exacerbated by the treatments in the trial. In addition, there was only one opportunity to approach the patient, which was immediately after their

consultation with the clinician about treatment options, so the RP/CCN had to be present for this time. This was potentially: (a) the patient's first visit to the cancer centre; (b) when they were told the extent/nature of their disease for the first time; and (c) when they were told about disease progression. As a result of this, patients were often very anxious and upset and not always receptive to further information.

There were also substantial practical challenges recruiting patients from 15 medical consultants and their teams, with clinics often running concurrently, as well as the challenges associated with discussing the study in a busy out-patient setting.

5.6.7 Recruitment summary

Despite the challenges, a total of 173 patients, (target number plus those replaced), were recruited to the study over a period of 20 months, from January 2005 to August 2006. A summary of recruitment is shown in Figure 5.2.

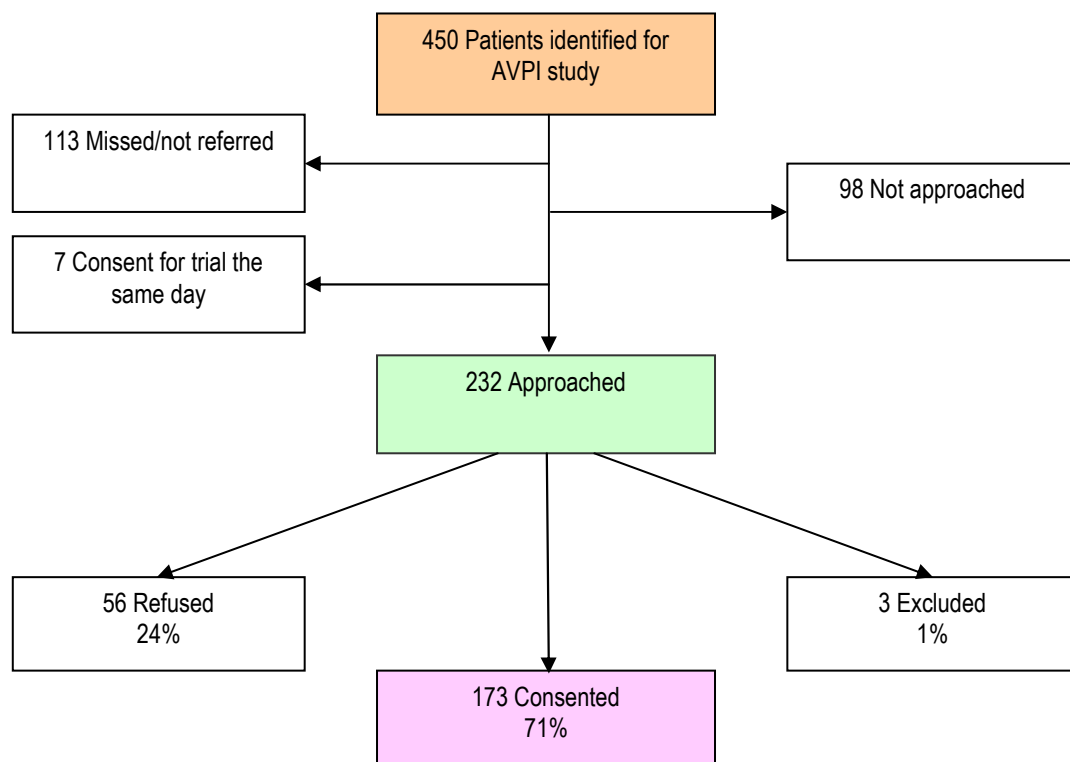


Figure 5.2. Recruitment summary

5.7 Patient randomisation

Attention will now be focussed on the 173 patients who consented to take part in the AVPI study. Following consent, patients were randomised to intervention or no intervention (1:1) by the data manager in the Cancer Research UK Clinical Trials Unit (CTU), from the information completed by the RP/CCN on the Registration Form (Appendix 5.5). Figure 5.3 shows the patient pathway through randomisation.

Stratification was used to increase the statistical power of the study and to promote statistical conclusion validity (Shadish *et al.* 2002, pp45-46). 'Minimisation' is a method of adaptive stratified randomisation which is used in clinical trials, as described by Pocock and Simon (1975). Connolly and Low (2000) advise that socio-demographic and socioeconomic factors are considered in the planning stages of a trial, however, due to the inconsistencies in the literature across studies as discussed in Chapter 2, it is acknowledged that this needs to be on an individual trial basis taking into account the clinical context. In light of this, the age and sex of the patient, in addition to the tumour type and trial were agreed as factors for stratification. The study was stratified for individual trial, tumour type, age and sex using the minimisation method, which was implemented in the CTU's Oracle database.

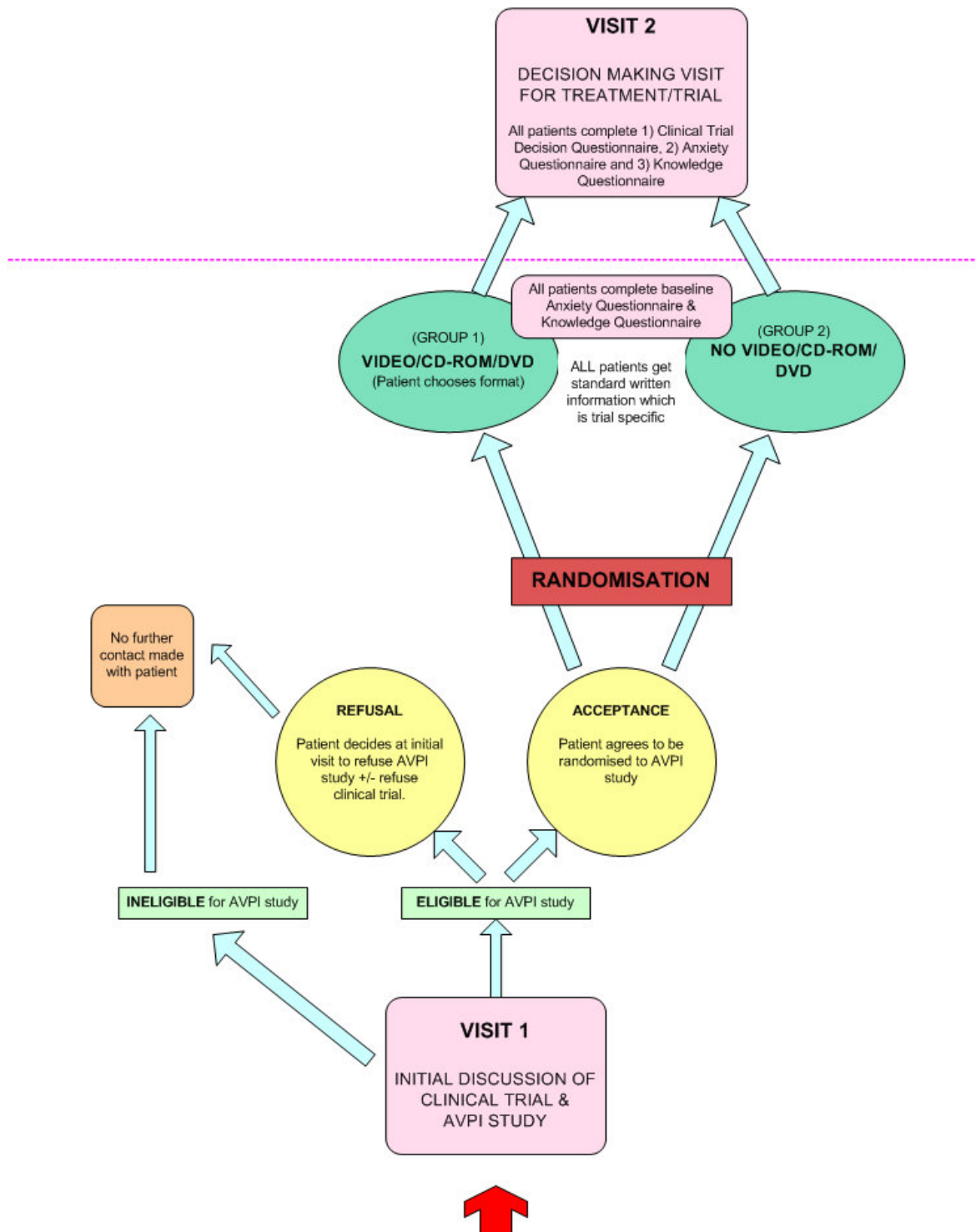


Figure 5.3. Patient pathway through randomisation

5.8 Data collection

Patients were seen on two occasions for the purposes of this study. These visits were part of patients' general medical care, as they were attending the hospital anyway on these days. These are known as 'Visit 1' (explanation of the clinical trial) and 'Visit 2' (return visit, usually 1 week later, to discuss decision). Data was collected at both time points via structured questionnaires.

A quantitative approach to data collection was employed in this study for two main reasons.

(a) The primary endpoint was concerned with determining a causal relationship (between patient understanding and clinical trial refusal rates). This could not be addressed using qualitative data.

(b) For the other study objectives, there is already substantial evidence in the literature, particularly in relation to knowledge and anxiety. It was considered that by using questionnaires to determine knowledge, anxiety, and factors affecting the clinical trial decision, this would enhance the evidence already available within the specific context of this study. Knowledge would not be easily assessed in a qualitative setting and there are already well established tools available for assessing anxiety and for assessing factors affecting the clinical trial decision, which were used in this study.

5.8.1 Measures/instruments

In addition to the log sheet which contained mainly demographic data, three different questionnaires were used, as per Table 5.3, to measure understanding (referred to as the knowledge questionnaire), anxiety and factors affecting decision making. These tools will now be described.

5.8.1.1 Log sheet

Demographic data on all patients who were approached for the AVPI study was collected by the RP/CCN and entered into a log sheet (Appendix 5.6). Data collected was: code for potential clinical trial; patient name; diagnosis; stage of cancer; date of birth; referring consultant; clinician describing trial to patient at visit 1 and at visit 2; and whether or not the patient was then entered into the clinical trial. Information about the patient's gender was collected on the Registration Form (Appendix 5.5). Deprivation status was determined according to deprivation categories measured by the Carstairs scores for Scottish postcode sectors (Carstairs and Morris 1991) using data from the 2001 census (McLoone 2004). Patients' post code details were available from the knowledge questionnaire.

5.8.1.2 Knowledge questionnaire (Questionnaire: Patient Understanding of Research)

This is a new questionnaire developed for the purposes of this study to assess patient understanding of research, with a particular focus on randomisation, as there is currently no appropriate validated tool available. The questionnaire was developed from the literature, and with patient and professional consultation. It was then tested with patients and nurses, and as a consequence small changes were made prior to usage in the main study. The final questionnaire that patients completed at baseline (visit 1) and at visit 2 is shown in Appendix 5.8. The development and testing of the questionnaire is described and discussed in detail in Chapter 7.

5.8.1.3 Assessment of anxiety (STAI-S)

There are several well established tools available to assess patient anxiety. In order to select an appropriate measure for this study, the literature was reviewed to determine which instruments were most commonly used within the clinical trial setting. Sesti and Arbor (2000) reviewed the Medline and Health and Psychosocial Instruments databases from 1966 and 1985 respectively, and found that the measures most commonly used in

medication clinical trials were the Hamilton Anxiety Rating Scale (HAM-A), the Covi Anxiety Scale, the Hospital Anxiety and Depression Scale (HADS) and the State-Trait Anxiety Inventory (STAI). The first two are clinician-rated, and were therefore excluded as potential instruments for this study, as it was considered important to assess anxiety from a patient perspective.

The HADS is a 14 item self-report questionnaire which contains 7 items measuring depression and 7 measuring anxiety. It has been used as part of quality of life assessments in clinical trials, and is popular in the cancer setting in randomised trials of two or more treatments, where a wider psychological assessment than just anxiety is warranted. The HADS is often used with physical symptom questionnaires, such as the Rotterdam Symptom Checklist, or quality of life questionnaires, such as the EORTC QLQ-30.

The Spielberger State-Trait Anxiety Inventory (STAI) is a self-report measure, which is concerned fully with anxiety and distinguishes between state anxiety (how one feels at the moment) and trait anxiety (how one generally feels). The vast majority of studies on informed consent, and also clinical trial recruitment interventions which investigate anxiety, have used the STAI, allowing comparisons to be made across studies. In addition to being used in many clinical trial settings, the STAI has been used in studies aimed at increasing knowledge, including those using video (e.g. Agre *et al.* 1994; Luck *et al.* 1999).

The STAI is composed of two scales: 20 items measuring situational or state anxiety (STAI-S) and 20 items for trait anxiety (STAI-T). 'State' anxiety refers to situational feelings such as apprehension, tension, nervousness and worry, whereas 'trait' refers to general feelings of anxiety-proneness (Sesti and Arbour 2000). State anxiety refers to a palpable reaction or process taking place at a given time and level of intensity

(Spielberger 1983). The STAI-S has been widely used to assess the level of state anxiety induced by stressful experimental procedures and also real life stressors such as surgery, job interviews and exams (Spielberger 1983).

The STAI was the measure chosen to assess anxiety in this study, because the tool is well established and validated within the clinical trial setting, it has been widely used in informed consent and clinical trial recruitment studies, and also because it focuses solely on anxiety, with the particular advantage of being able to focus on state anxiety.

The use of the STAI-S scale without STAI-T can be justified in this study, as the trait anxiety levels of the two study groups would be expected to be similar since the study is randomised. In addition, all patients with cancer will experience anxiety to some degree but the study is assessing the difference (if any) in anxiety as a result of the intervention +/- its effect on understanding. Anxiety was therefore assessed at the same time as understanding (at baseline and at visit 2) and decision making (visit 2), to investigate whether the AVPI had any effect on anxiety levels.

The STAI-S consists of 20 items that evaluate how respondents feel 'right now, at this moment'. Individuals respond to each item on a 4 point Likert scale, indicating the frequency with which each strategy is used. The average time to complete it is minimal at 6-10 minutes. Sample questions from the scale are shown in Appendix 5.9. Permission was obtained from the publishers (Mind Garden), and questionnaires were purchased for use in this study.

Scoring was carried out according to guidance in the manual (Spielberger 1983). Each STAI item is given a weighted score of 1-4. A rating of 4 indicates the *presence* of a high level of anxiety for 10 of the STAI-S items and the *absence* of anxiety for the other 10

items. Scores are then added together for all 20 items with overall scores varying from a minimum of 20 to a maximum of 80.

5.8.1.4 Clinical Trial Decision Questionnaire

The Clinical Trial Decision Questionnaire (CTDQ) is a two-page self-report form to assess patients' reasons for accepting or refusing participation in the trial, perceptions of the consent process, and value of the AVPI (Appendix 5.10). Patients completed this at visit 2 only, after making their decision about whether or not to take part in the clinical trial that was offered to them. Reasons for accepting or declining the trial were the main focus of this questionnaire.

The CTDQ was designed specifically for this study, but includes the questionnaire used by Jenkins and Fallowfield (2000) to assess reasons for accepting and declining a trial (with kind permission from Dr V Jenkins). Jenkins and Fallowfield (2000) report in their paper, that the questionnaire was a similar design to that used by Penman *et al.* (1984). Jenkins and Fallowfield's questionnaire was piloted on fifty patients with cancer who had agreed to take part in clinical trials, prior to the revised version being used in their study (Jenkins and Fallowfield 2000). In the CTDQ, questions about the consent process and usefulness of the AVPI were derived from the literature and consultation with a panel of experts – clinicians and clinical trials nurses – to ensure content validity.

5.8.2 Process

An overview of the process involving the two patient visits and administration of data collection tools, is shown in the schedule of events table: Table 5.3.

Table 5.3. Schedule of events

VISIT 1 – Hospital visit for initial discussion of clinical trial		
Discussion with potential participants for the AVPI study to determine eligibility. Information given about the study.		
Patients asked to consider the study and if desired, given further verbal information by the RP/CCN.		
1) Patient said ‘no’ Those who chose not to take part in the AVPI study +/- the clinical trial were not approached again.	2) Patient unsure Those who wished more time to consider whether or not to take part in the AVPI study were given the information sheet home and a time arranged for the RP/CCN to phone them. If they then decided to participate, the RP/CCN checked the randomisation allocation, and phoned back the patient with the result. Action was then as for ‘patient said yes’.	3) Patient said ‘yes’ a) Patients randomised to receive the intervention were asked whether they would prefer the video, DVD, or CD-ROM format. Where possible, they received it prior to leaving the hospital. b) Patients randomised to ‘control’ were reassured that their information needs would continue to be met by the clinical team.
Demographic details entered into log (Appendix 5.6).		
Letter sent to GP (Appendix 5.7).		
Patients given questionnaires to complete: <ul style="list-style-type: none"> • Knowledge questionnaire (Questionnaire: Patient Understanding of Research) (Appendix 5.8) • STAI-S questionnaire (Appendix 5.9) 		
VISIT 2 – Decision making visit for treatment/clinical trial		
All patients were given questionnaires to be to be completed after their medical consultation and posted back to the RP/CCN: <ul style="list-style-type: none"> • Knowledge questionnaire • STAI-S questionnaire • Clinical Trial Decision Questionnaire (Appendix 5.10) 		
Patient recruitment status (to clinical trial) was entered into a log.		
Record of returned questionnaires was kept (Appendix 5.11).		
Following questionnaire return, sheet of ‘correct answers’ to the knowledge questionnaire was given/sent to patients (Appendix 5.12).		

Data was collected from patient case-notes and from questionnaires. Questionnaires were considered less intrusive than interviews when asking about sensitive areas such as reasons for acceptance and refusal. Although not assessed in this study, it is

acknowledged that there would be variation in the approaches of individual clinicians during the patient consultation in relation to factors such as the quality of the interaction and presentation of verbal information about the trial (Albrecht *et al.* 2003). However, the written information provided routinely, would be consistent.

It was also acknowledged that there could be variation across patients for factors such as previous education, age, preference for method of information (e.g. AVPI v's written). In anticipation of this, the randomised study design was chosen to minimise effects of any unanticipated confounding variables. Other variables included were patient demographic details, previous education and research experience.

Patients agreeing to take part in the AVPI study were allocated a study identification (ID) number which was then used in all subsequent trial documentation.

5.8.3 Data entry

Data from the registration form, log sheets and the patient questionnaires were entered into the Oracle database and SPSS (version 15, running on Windows XP). The data was entered by an experienced data manager and then checked by a clerical officer via comparison with the original data collection forms, as per the standard procedure within the clinical trials department. All data fields were numbered according to a predetermined coding system. Once the details from the registration form were entered, the patient's unique study number and randomisation result were allocated, and a set of data entry forms for the patient was automatically generated, along with a diary highlighting forthcoming patient visits and data collection time points. Security checks were built into the system, such as each page having a number of patient identifiers including the patient's unique study number, treatment allocation, and their initials, as well as password protection for the users. Features to enhance accuracy, in addition to the data checking, were drop-down menus giving options rather than free text (e.g. for the parent study that

the patient was considering), and the RP/CCN had to check and sign-off patient study forms, prior to the second data check, if this had not already been done prior to data entry.

5.9 Analysis

Analysis was carried out on the entered data as described below.

5.9.1 Primary endpoint: clinical trial refusal rates

The main comparison between the study arms, in terms of the primary endpoint, was performed using logistic regression using all randomised patients. An attempt was made to incorporate minimisation factors used at the time of randomisation into the logistic regression, but the high degree of confounding between gender, tumour type and study meant that, of these, only age and gender could be used. The odds ratio was derived from the logistic regression and the p-value for the comparison derived by the likelihood ratio method. The association between baseline patient characteristics and study entry was also assessed in the context of a logistic regression model.

5.9.2 Knowledge/understanding

The change in knowledge score from baseline was compared between the two groups using the Mann-Whitney U test (the knowledge score is the number of correctly answered questions expressed as a percentage mark). The statistical significance of within-patient changes in knowledge score in each group was assessed using the Wilcoxon signed-rank sum test. An assessment of the prognostic value of various baseline characteristics for change in knowledge score was assessed in the context of a linear model incorporating the study arm; the dependence of the prognostic value on the study arm was assessed by incorporating the appropriate interaction term. Multiple imputation (Rubin 1987) was applied to assess the robustness of the results of these analyses to missing data. Bootstrap methods were used to estimate the difference in median changes and associated 95% confidence intervals.

The association between baseline characteristics and baseline knowledge levels was assessed using the Mann-Whitney U test (2 categories), Kruskal-Wallis test (>2 categories) or, for age, Spearman's rank correlation.

5.9.3 Anxiety

A parallel analysis to that described for the knowledge score was conducted for the anxiety score.

5.9.4 Reasons for accepting and declining clinical trial participation

Reasons for accepting and declining clinical trial participation were tabulated, and the Chi-square test used to compare the frequency of each reason in the two groups. Patients' perceptions of the consent process were tabulated and the Chi-square test used to compare the frequency of each reason in the two groups.

5.9.5 Patients' perceptions of usefulness of the AVPI

Descriptive statistics were employed, using frequencies to determine patients' perceptions of usefulness of the AVPI.

5.10 Ethical considerations

5.10.1 Protocol approval

Prior to initiation of the study, the protocol was submitted to the West Research Ethics Committee, the Research and Development Department within NHS Greater Glasgow and Clyde, and the Department of Nursing and Midwifery Research Ethics Committee at the University of Stirling. Following review by the West Research Ethics Committee, the patient information sheet required small amendments to the wording, in addition to changes to the knowledge questionnaire, to simplify the wording. When this was undertaken, the protocol received full ethics approval. Minor changes were required as a result of review by the University ethics committee: they included clarification of the

recruitment process and simplification of the flow diagram showing the randomisation process.

The protocol was also submitted to, and approved by, in-house (The Beatson West of Scotland Cancer Centre) research committees – specifically, the Internal Trials Advisory Board (ITAB) and the Clinical Trials Executive Committee (CTEC).

The study was conducted within the Research Governance Framework of NHS Greater Glasgow and Clyde, and was run according to internationally agreed Good Clinical Practice Guidelines (ICH 1996). The Declaration of Helsinki was followed where relevant (World Medical Association 1964, 2004).

5.10.2 Patient information and support

Patients considering cancer clinical trials are potentially very vulnerable, and there was the possibility that, as a result of completing a questionnaire on decision making about the trial, more questions would arise, and patients would need additional support. Provision of additional support was made available from their own medical clinician, and also from the Clinical Psychologist. The AVPI study information sheet advised patients to contact their own clinician, should they have any issues. In addition, the potential for issues was highlighted to clinicians and CNSs who were vigilant in assessing the need for additional support, although in reality this proved not to be required. The patient's GP was also informed about the study (See Appendix 5.7).

The AVPI written information sheet and consent form contained the essential elements for informed consent, as required by the ICH Good Clinical Practice (GCP) guidelines (ICH, 1996). Contact numbers were given for the Cancer Consultant Nurse and the Research Practitioner, and the patient was advised that their GP would be informed.

5.10.3 Questionnaires

Patients were given each questionnaire only once at each time point. Questionnaires were kept short and user-friendly to minimise the burden on the patient. Although the patient was given three questionnaires at the same time point, it was anticipated that they should take no longer than 15-20 minutes, in total, to complete. After completing the knowledge questionnaire at visit 2, all patients received a copy of the 'correct' answers in an attempt to correct any misconceptions that still existed.

5.10.4 Confidentiality

Confidentiality was respected at all times throughout the study, with adherence to the Data Protection Act (Department of Health 1998) and compliance with the NHS Scotland Code of Practice on Protecting Patient Confidentiality (Scottish Executive 2003).

The only information that contained patients' names was the demographic log sheet. This was considered necessary to ensure that the correct patients were followed up at visit 2. This log was kept in a locked drawer in the CCN's office. All other study information, including returned questionnaires, was kept in a separate locked cupboard. Patients were informed in the written information sheet that demographic details would be collected. The information sheet also included reassurances about anonymity and confidentiality.

Patients were allocated a Study Identification (ID) number. This was used on all questionnaires, and made it possible to link them to the demographic data, which was entered into the computer without the patient's name or hospital number. Electronic information was password-protected. The computer in the CCN's office, to which no-one else has access, was used, in addition to a computer in the RP's office and in the Clinical Trials Unit. These offices were locked when vacant. Following completion of the study, the data was stored and destroyed in accordance with Standard Operating Procedures in the Clinical Trials Unit, specifically No 002, Filing and Archiving of Clinical Documentation.

5.11 Timescales

A work plan with approximate timescales was drawn up as shown in Table 5.4 as a guide for the steering group and this was adhered to throughout the duration of the study

Table 5.4. Study work plan

Extended literature review	3 months
Development of questionnaires	2 months
Ethics submission	4 months
Develop and test video	4 months
Pilot study of knowledge questionnaire	6 months
Training for Research Practitioner	2 weeks
Informing staff about study	1 month
Data collection	12 -18 months
Analysis	4 - 6 months

5.12 Costs and funding

5.12.1 Costs

Approximate costs were calculated for the project and these are shown in Table 5.5. The majority of costs were associated with developing, filming and producing the intervention.

Table 5.5. Costs

Item	Cost (£)
Consumable costs such as paper, envelopes and ink	met by department
Time required by Research Practitioner for data collection, and Clinical Trials Unit input in relation to randomisation	met by department
(a) Returning of consent forms (prepaid envelope - estimated as necessary for half of study population, n=82) 82 x £0.28	22.96
(b) Sending out video/DVD/CD-ROMs (estimated as necessary for a quarter of study population, n=41) 41 x £0.69 (packaging) + 41 x £1.15 (postage)	75.44
(c) Returning questionnaires (all patients) 164 x £0.28	45.92
Videos/DVD's/CD-ROMs. Filming and production costs (includes Medical Illustration, actor and music license)	5,400.00
Data management	499.72
Permission rights for STAI	200.00
Total Costs	£6,244.04

5.12.2 Funding

Full funding for the study was secured, with £6,044 from the Chief Scientist Office as a Cancer Programme Support Grant, and £200 from The Beatson West of Scotland Cancer Centre Fund to cover permission rights for the STAI questionnaire.

CHAPTER SIX: DEVELOPING THE INTERVENTION

6.1 Introduction

The aim of this chapter is to discuss the development of the study intervention, which was audiovisual patient information (AVPI), in the form of a video, DVD and CD-ROM. The purpose of the AVPI was to inform patients about randomised controlled trials, as a supplement to their trial-specific written information sheet.

6.2 Background

Audiovisual patient information is known to be an effective way of informing patients about treatment, as discussed in Chapter 4. Nurses are key providers of patient information in many areas of clinical care, and are becoming more and more involved in developing it (Strachan 2004). They have a crucial role in ensuring that the information is accurate, appropriate to the patient and useful. However, most nurses have never been taught how to develop patient education materials, and there is limited research evidence in the literature, which focuses on the materials-development process. What *is* available tends to focus on speciality-specific written information and on assessing readability (Griffen *et al.* 2003). Less attention, however, has been given to developing other formats such as the audiovisual route.

In relation to AVPI, most articles briefly discuss the development of the video as part of an intervention study designed to assess the effectiveness of the AVPI, often in terms of increasing knowledge. Minimal attention is given to the process of development itself, and to the quality of the resultant production. An exception to this is the work by Carey *et al.* (2007), who adopted a systematic approach to the development of audiovisual materials for oncology patients. They examined literature relating to the preparation of patients for potentially threatening medical procedures, psychological theory, the theory of innovation diffusion, and patient information. From this, they identified four key principles as being

important: stakeholder consultation; provision of information to prepare patients for the procedure; evidence-based content, and promotion of patient confidence. They then used this to develop an audiovisual resource to prepare patients for chemotherapy treatment.

Steinke (2002) also describe the development process, in this case for a videotape intervention for sexual counselling after myocardial infarction. This paper provides useful practical guidance, and highlights the importance of patient involvement throughout the process. Production challenges are described in another publication, and include issues such as copyright, intellectual property and establishing content validity of the video-script (Steinke 2001).

In cancer education, Meade (1996) reviewed the literature and describes a systematic process for producing videotapes for cancer education and research. This work highlights practical aspects such as budget considerations, script development, narration and location, as well as the importance of involving members of the target audience throughout the development process, which in the AVPI study would be patients eligible for randomised cancer clinical trials.

Several authors/organisations have produced generic guidance for developing patient information, mainly focussing on written approaches: for example, the Scottish Executive Guidelines for writing patient information (2001c), local hospital policies, and the step-by-step guide for producing patient information literature written by North *et al.* (1996), all of which provide useful practical advice. The Macmillan Information Materials Guide (Macmillan Cancer Relief 2003), although focussing predominantly on written materials, does offer some support for nurses in developing other formats, advising on issues such as structuring the production and copyright.

Developing audiovisual patient information is still a relatively new role for nurses and, although the literature was used where relevant in this study, a lot of the process which will now be discussed was dependent on clinical and technical expertise of the staff involved.

6.3 Development of the AVPI

Development of the AVPI involved staff and patients working together to achieve the overall aim of ensuring that the end-product was user-friendly and fit for purpose – to inform patients about randomised controlled trials, as a supplement to their trial-specific written information sheet. There were many components of the development process which will be discussed under the headings of: content; logistics and organisational issues; patient involvement; ethics; finance; script; filming; editing and copyright.

6.3.1 Content of the AVPI

Although it was considered important to deal generally with the concept of clinical trials in the AVPI, and focussing particularly on randomisation, in order to meet the aims of the study, it was also considered important for patients to identify personally with the content. Three separate AVPI productions for the three cancer types involved in the study – lung, breast and colorectal – were produced. Most of the core content was identical, but each version was also tailored to the individual cancer type. In view of increasing availability of DVD and computer technologies to the general public, the production was made available in both DVD and CD-ROM format, in addition to video, to allow patient choice depending on preference and availability of technology at home. Although AVPI could potentially also be made available to patients as web-based information via the internet, this approach was not pursued, in light of the common complaints reported with this technology, such as the inability to open video clips and the length of time needed to load each page (Cumbo *et al.* 2002). In addition, many patients do not have access to Broadband technology which would be a necessary requirement.

6.3.2 Logistics and organisational issues

The steering group set up for the purpose of the study (as described in Chapter 5, Section 5.3) was responsible for overseeing the development of the AVPI. The steering group provided the stakeholder consultation aspect discussed by Carey *et al.* (2007). Expertise was also sought, where appropriate, from the lung, breast and colorectal cancer lead medical consultants and specialist nurses, a radiographer-counsellor, and clinical trials unit personnel. Ethical advice was sought from the Professor of Clinical Oncology, who previously chaired the Local Research Ethics Committee. In addition, guidance was directly sought from two patients who had previously participated in a randomised cancer trial; they commented on various drafts of the scripts, as did members of the steering group. As well as participating in the work of the steering group, the patients also contributed through separate meetings with the CCN and RP as described in Section 6.3.3. The steering group guided all aspects of developing the AVPI: for example, the decision to include a visual description of 'randomisation' by using images of flip charts showing medications, and also the decision to involve clinicians speaking in the production, in addition to the actress-presenter.

There was also a dedicated operational project team with the specific task of developing the intervention. This team dealt with logistics and numerous other related issues such as: ethics; finance; scriptwriting; filming; editing and intellectual property rights which will be discussed later in the chapter. The operational project team consisted of three nurses undertaking the functions of (1) project lead, (2) script writer, (3) director and (4) co-ordinator (Table 6.1), all of them working in conjunction with a professional actress and the hospital's Medical Illustration Department.

Table 6.1. Roles of nurses directly involved in developing the intervention

Role in Project	Person / Nursing role
Project lead	Cancer Consultant Nurse
Script writer	Cancer Consultant Nurse and University Lecturer/Researcher
Director	University Lecturer/Researcher
Coordinator	Research Practitioner

The director, who co-wrote the script with the project lead, was a colleague of the CCN who had extensive previous expertise and experience in both directing and script writing, within and outwith nursing. The coordinator role was crucial for ensuring planning and organisation of operational issues pertaining to the project.

As part of the general study timetable (Chapter 5, Table 5.4), four months was allocated to video development. This consisted of two months for script development and two months for filming, editing and production.

6.3.3 Patient involvement

There are some good examples of work where patient involvement has greatly contributed to high quality patient information materials (Steinke 2002 (video); Chavez *et al.* 2004 (video); Paul *et al.* 2004 (information booklet)). From the beginning of this project there was a real commitment to have patients meaningfully involved in the planning and development of the AVPI. It is acknowledged that selecting the most appropriate service users or patients is crucial to meaningful user involvement. There is, however, no definitive guidance currently available on the best way to do this (Symon and Clegg 2005). In the absence of such guidance, Clinical Nurse Specialists were asked to purposively select patient representatives according to the following criteria:

- diagnosis of lung, breast or colorectal cancer – one patient from each of the cancer sites being addressed in the AVPI;
- experience of taking part in a randomised cancer trial;

- willing to attend meetings to discuss the script and the AVPI production itself, also to comment on draft work outwith the meetings.

The advice sheet 'Top tips for effectively involving and recruiting patients and carers' developed by the Picker Institute Europe and the NHS Modernisation Agency Clinical Governance Support Team was used as a guide for patient involvement (Picker Institute 2008). Patients were asked to represent their cancer group in addition to personal interests, and effectively to act as key informants and expert advisors to the project. It would have been preferable to have involved more than one patient from each cancer group, but this was not possible, as logistics and timescales necessitated a quick turnaround of script development and production.

A preliminary meeting was arranged outwith the hospital setting, so that the project lead and coordinator could meet with the patients to discuss the project and elicit their thoughts on a very early draft of the script. Two of the three patients identified by the specialist nurses participated. The identified patient with breast cancer was keen to be involved, but in the event was unable to participate due to personal circumstances.

Both of the patients involved had previously taken part in a randomised cancer trial, one for lung cancer, the other for colorectal cancer. One was currently receiving treatment as part of a clinical trial. One of the patients was involved in professional film production (this was initially unknown to the specialist nurse and the project team), and he had a wealth of experience which he was keen to share, in addition to what he could contribute from a patient perspective. Over time, several drafts were discussed with the patients, which led to very useful changes in visual images and wording. An example of this was the cutting of scenes showing treatments being prepared under sterile conditions in pharmacy labs, where staff wore gowns, masks and gloves. These images were considered 'scary' and unnecessary by the patients.

6.3.4 Ethics

6.3.4.1 *Ethics review*

Since the AVPI was part of a research study, a full ethics submission had to be completed, as discussed in Chapter 5, Section 5.10. This included an outline of the subject areas to be covered in the AVPI, developed from the literature, Good Clinical Practice Guidelines for clinical trial information-giving, and expert opinion. The study protocol made provision for a previous chairman of the ethics committee to review the draft script prior to filming, and to ensure that the content was objectively balanced. This review resulted in minor changes to some of the wording to the final script prior to filming. The Ethics Committee were happy with the outline presented to them and did not ask to review the full script or the final AVPI prior to it being used in the study.

6.3.4.2 *Consent*

Written consent for filming was obtained from all patients and staff participating in the production, whether they had speaking parts, or whether they were filmed as part of the foreground or background. No staff refused to take part. One patient and her family were reluctant to be filmed as part of a background scene, and subsequently were not consented, nor filmed.

6.3.4.3 *Protection of images*

The Medical Illustration Department were requested to return all images (both used and unused takes) to the project lead for safe, locked storage, and provided a written agreement that images had not, and would not, be used by them for any other purpose. This was primarily to ensure the protection of the images due to ethical requirements regarding consent, confidentiality and storage. It was also considered important to be able to certify that the images developed, obtained and co-ordinated for the purposes of the AVPI remained unique and were not then utilised by others in subsequent AVPIs or other health care materials.

6.3.5 Finance

As discussed in Chapter 5 (Section 5.12), funding for the study was secured from the Chief Scientist Office as part of a Programme Support Grant. The majority of funding was budgeted to cover the costs of developing the AVPI, including medical illustration costs, actress, props, and the music licence for the soundtrack.

6.3.6 Script

6.3.6.1 Content and writing

The main function of the AVPI was to give people information to help them understand more about randomised cancer trials. Patients would be receiving the AVPI at the same time as they received written information about the specific randomised trial that they were considering taking part in.

The broad outline for the structure and content of the AVPI, as well as the detail for the full script, was developed from the following sources:

- International Conference on Harmonisation (ICH) Good Clinical Practice Guidelines (ICH 1996);
- Scottish Executive Guidelines for Patient Information (Scottish Executive 2001c);
- patients/users;
- existing written patient information about clinical trials;
- the literature;
- discussion with expert clinical trials nurses and clinicians.

Areas covered in the AVPI include: how drugs/treatments are developed; importance of clinical trials; what randomised trials are and when they are carried out; criteria for taking part; benefits/disadvantages of taking part in a randomised trial; funding issues; voluntariness of decision and freedom to withdraw at any time.

Additional creative writing was used to demonstrate the difficult concept of randomisation, which is described by the actress-presenter using flip charts with pictures of bags of chemotherapy as a visual aid. Within the production, to try to assist with understanding of the randomisation concept, several examples are given of types of randomised trials, including a trial where one of the arms is 'best supportive care'. There are pictures of patients receiving treatment and a voiceover describing the main principles such as that of uncertainty about which treatment is best (equipoise) and also emphasising that the doctor does not decide which treatment the patient will get.

At the end of the AVPI the presenter encourages patients to consider their decision carefully about whether or not to take part, reassuring them that whatever they decide, it will be fully supported by their clinical team. She then refers them to their trial-specific information sheet for further information.

Content validity of the final script was established by the steering group, project team and the lung, breast and colorectal cancer teams, who reviewed several drafts before the final version – draft 6 – was ready for use. The final script used in filming is shown in Appendix 6.1.

The Macmillan Information Materials Guide for developing new patient information served as a production guide for the video, including basic principles of signposting to alert the patient to what will be covered, on-screen graphics to make it possible for patients to read while they listen, and summaries of important points (Macmillan Cancer Relief 2003).

6.3.6.2 Presentation and delivery

A personable and professional local actress, someone patients would identify with, was considered desirable to present the AVPI on behalf of the cancer centre. The preference was for someone who would be slightly familiar and recognisable, but not be so well

known as to detract from the content. To minimise the potential effects of mismatch of race and gender (Lenert *et al.* 2000), a female white presenter was considered desirable. The majority of the study sample was anticipated to be white Caucasian and a large number would be female patients with breast cancer. Age was also considered, in order to select a presenter who patients could relate to (Steinke 2002). Because the majority of patients were expected to be between 40 and 60 years of age, an actress of this age was chosen. An actress colleague was initially contacted, who was interested but unable to commit to fixed filming sessions owing to other work commitments. Numerous agencies were then contacted with a brief, and various actresses were offered as potentially appropriate. The actress who was contracted to present the AVPI was known to the director, and had previously worked with her on a separate project. This further confirmed suitability.

During early discussions, it was determined that using autocue would speed up the filming by reducing rehearsal time and, more importantly, facilitate accuracy of the content, which was essential given the nature of the project. The Medical Illustration Department was able to arrange and operate this function. In addition, the actress was given the script one week in advance of filming in order to familiarise herself with the terminology and general ambience of the piece.

6.3.7 Filming

6.3.7.1 *Clinical setting*

Filming requirements were both internal and external, with the majority of internal filming carried out in the clinical setting. Internal filming took two days, and external filming half a day, as originally planned, although schedules were very tight. The clinical setting was chosen in preference to the studio, and filming was undertaken during working hours to ensure that the AVPI reflected the 'real' clinical environment, and to avoid a 'staged'

effect. However, this did pose substantial organisational challenges, and required detailed preparation.

Participating clinical departments were areas that the patients would be familiar with, and included the out-patient department and day case clinic area, clinical research department (out-patient and day care), patient reception area, radiotherapy department and pharmacy. The clinical research department was used for the majority of the formal presentation in the AVPI. All of the areas are continually busy with patients, and filming was scheduled in advance to work around quieter times wherever possible. Early involvement of clinical departments in the planning stages facilitated access to the areas required for filming, and also encouraged staff themselves to participate in the production.

6.3.7.2 Localising the production

In keeping with the need to ensure relevance for the three patient groups, the AVPI was localised by utilising clinical areas for the internal filming and involving an actress with a local accent. External filming reflected city landmarks leading to the cancer centre, which were used at the start of the production. These were all places that the patients would already be familiar with, hopefully making identification more likely. Visual images were supported by the title music, which also reflected the local culture and would be familiar to the target audience. The lung, breast and colorectal cancer medical clinicians presented a short section at the beginning and end of the relevant versions of the AVPI, to provide a spotlight on the individual cancer type, to help maintain a clinical focus, and to make it instantly identifiable. Medical involvement at the beginning and end of the AVPI was used because patients view medical consultants as experts and authority figures, and the intent was to draw viewers to the credibility and importance of the content (Steinke 2002).

Separate photographs were taken of the lung, breast and colorectal cancer clinical teams, which were used on the back cover of the AVPI packaging. This was included to help patients identify with the production, as they would recognise staff involved in their care. Getting the teams together for these photographs proved challenging, since clinicians were often at clinics outwith the department. Consequently, it took four weeks to get the team photographs, and it was not possible to get the group together for one sitting. As a result, it was necessary to take between two and six individual/group photographs for each team, and to merge them together on the back cover. The cancer treatment centre and a nurse/patient information-giving scene set in the day ward of the cancer centre, were shown on the front cover.

6.3.8 Editing

Following discussion with the Medical Illustration Department, three days were planned for editing: one day for Medical Illustration to sort and number the final takes of clips from the 26 scenes, and to digitise them; two days for the nurses directing and producing to work with Medical Illustration to edit the production. As advised by Steinke (2002) it was essential that the nurses were involved in the editing process with Medical Illustration. In practice, editing took one full day longer than the anticipated three days. This time was needed to improve continuity and visual effects, and was a crucial part of the process.

A draft copy of the production was reviewed by the project team on two occasions. Small changes were made, and then a formal viewing session arranged with the steering group. This resulted in minor changes to visual effects and timing of sequences.

6.3.9 Copyright/intellectual property rights

The issue of copyright was particularly challenging owing to the number of stakeholders/experts involved, and also because the work was being undertaken as part

of a university course. The AVPI was copyrighted to the CCN as project lead, and the hospital's Research and Development Office were also involved, according to the NHS Greater Glasgow and Clyde Policy on Intellectual Property Rights. This included a meeting with Scottish Health Innovations Limited (SHIL) and the preparation of preliminary documentation that could be progressed, pending the results of the study and future plans for the AVPI.

As stated previously, a local cover version of a well-known song was chosen as the title track for the video. Since it was a cover version of a song that was written and originally recorded by a different artist, permission rights had to be sought from the two record companies involved. The company and artists responsible for the cover version recording were very supportive of the use of the track for the purpose intended, and were keen to see all royalties waived. However, the company representing the original writer in the USA would not support this and, following negotiations, an agreement was reached which included the payment of royalties and use of the track for 5 years, which was limited to the UK.

6.4 Discussion

The study intervention was successfully developed, but there were substantial challenges and opportunities during the process which will now be discussed.

6.4.1 Challenges

The main challenges were centred around the financial and technical constraints, scope of the project, and involving a new team with varying expertise to deliver to tight schedules. The financial constraints led to the decision to involve the hospital's Medical Illustration Department; this then led to technical constraints, specifically around sound editing and restricted types of filming. Whilst Medical Illustration did have experience in audiovisual

information production, this was mainly focussed on developing teaching videos with traditional formal scripting and presenting. These projects were usually undertaken entirely by the Medical Illustration Department and were developed with minimal input from nursing and medical staff. This project was on a relatively large scale and required a developmental approach to incorporate expertise from a variety of areas (patients, nursing, medical, scripting and filming).

Filming was difficult in some clinical areas, mainly owing to busy patient environments, but also as a result of small spaces with restricted access, where it was sometimes difficult to find appropriate camera angles. Scenes were filmed according to location rather than script order, which led to some compromises in editing to address issues of continuity. However, this did not affect the quality of the final production.

A particular challenge in relation to expertise was in trying to harness the skills and talents of the nurses involved, and supporting the development of non-traditional nursing roles such as script-writing and film direction, whilst at the same time collaborating with, and valuing, the contribution of other members of the production team. The majority of the team did not know each other prior to working on the project, and had to develop very quickly as a team so that they could work together closely during the filming, in a fairly intense environment where good leadership was essential.

The scope of the project, developing three different AVPIs with the same core content, resulted in substantial additional time being required by various members of the production and clinical teams in filming, and also in the editing phase. This proved to be more onerous than initially anticipated. Other challenges, which have already been discussed, were associated with ethics and issues of copyright.

6.4.2 Opportunities

Although there were substantial challenges associated with the project, there were also important opportunities. Effective team-working across multi-professional clinical teams and technical staff led to mutual respect and a better understanding of individual roles. The ability to use the team expertise effectively was invaluable. Collaborating with colleagues with diverse expertise was a positive finding of the process that was also reported by Meade (1996) in her work in developing AVPI. There was significant goodwill generated from both patients and staff, all of whom were enthusiastic and motivated about the work and keen to help in any way they could. The process itself was fun and exciting, and provided important learning opportunities, leading to much discussion about various areas of patient care, such as informed consent and ethical issues. As found by other AVPI projects (Meade 1996; Steinke 2001), organisation and preparation was key to the success of the project. The process allowed expert clinical nurses to extend their roles and develop additional skills, which will ultimately be used for patient benefit.

One of the most important opportunities was the contribution of patients. This experience led the team to a fuller appreciation of the patient's contribution. The experience also enabled a better understanding of how to involve patients meaningfully in future work. It must be acknowledged, however, that patient numbers were small, and that it would have been useful to consider factors such as age, gender and cultural background as these variables may influence patient responses to the format and wording used in the production. In addition, it would have been useful to have spent more time on identifying, recruiting and engaging appropriate patient representation.

6.5 Conclusion

As a result of the commitment and enthusiasm of the project team, the AVPI was developed as planned, within the allocated timescales, and was considered user-friendly

and fit for the purpose intended. Much was learned from the process of developing the intervention, which has implications for practice as discussed.