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**A qualitative study exploring advanced cancer patients' experiences of symptom  
control clinical trials**

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# **ABSTRACT**

## **Introduction**

It has been suggested that conducting clinical trials in palliative care is unethical and may be burdensome for patients. Despite these suggestions, there is evidence that the opinions of patients with advanced cancer are favourable towards clinical trials. However this evidence is based on hypothetical studies; no studies have been done which explore the opinions or experiences of patients who have actually participated in symptom control trials. This thesis is the first study to examine the experiences of advanced cancer patients who have participated in symptom control trials.

## **Methods**

A qualitative study was conducted using a constructivist grounded theory approach. Patients known to be in the palliative phase of their illness were purposively selected from two double-blind placebo-controlled clinical trials of novel analgesic agents that took place across two clinical centres in Scotland. Semi-structured interviews were conducted until a suitable degree of data saturation was reached. In keeping with a grounded theory approach, analysis of the generated data developed core categories and a central theory that described the studied phenomenon.

## **Results**

Experiences of taking part in a clinical trial were initially divided into three parts: pre-trial experiences, experiences during the trial and patients' reflections on the trial after they had finished. Pre-trial experiences of the patients included the reasons for taking part, their initial contact with the trial staff and their prior knowledge of clinical trials. Experiences during the trial involved the manner in which they went through the trial, the impact on their pain and the interaction with the trial staff. Patients reflected on their overall opinion of the trial that they had taken part in and clinical trials in general.

One of the most significant categories was the impact of the interaction with the research staff. For some patients this relationship was beneficial, independent of the pain response during the trial.

The central theory of the study related to a patient's wellbeing. All the different aspects of participating in a clinical trial made an impact on a patient's sense of wellbeing. Many different components of the trial, such as the relationship with the trial staff, could have a positive impact on a patient's wellbeing. A positive impact on wellbeing could be found even in the presence of something which may have a negative impact on a patient's wellbeing, such as a lack of pain reduction.

### **Conclusions**

This is the first study that explores the experiences of advanced cancer patients in symptom control trials. I have described the factors that motivate patients to take part in clinical trials, their experiences of being in the trials and how they view the experience of the trial after it is finished. The results provide examples of experiences that are very positive from a patient's perspective.

I have developed a concept of wellbeing that the clinical trial impacts upon. While a patient's overall wellbeing is not exclusively linked to the clinical trial, the clinical trial has the potential to have a large impact on the overall wellbeing of the patient. Interventions such as the relationship with the trial staff can have a positive effect on a patient's wellbeing, independent of the outcome of the trial from a pain management point of view. The results of this study contribute to the debate on the ethics and benefits of research in palliative care.

## **DECLARATION**

This thesis is the result of my own work. The material contained in this thesis has not been presented nor is currently being presented, either wholly or in part for any other degree qualification. I was solely responsible for all data collection and analysis.

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## SECTION 1 – INTRODUCTION

# Chapter 1. INTRODUCTION

## 1.1. Rationale

The experiences of patients matter. They matter because as researchers, physicians, health care providers and humans we need to learn from the experiences of one group of patients to better inform the care of future groups of patients. The best way to learn about patients' experiences is to ask them. This thesis studied the experiences of advanced cancer patients with incurable disease who took part in symptom control clinical trials.

The context of this thesis merits some discussion. The majority of symptom control care of advanced cancer patients comes under the responsibility of a palliative care team. The past 20 years have seen a marked increase in research across all aspects of palliative care (Flemming et al., 2008). Despite this, conducting research in the palliative care population is not straightforward. One of the reasons is the existing debate about the palliative care population being a vulnerable one; vulnerable, amongst other things, of taking part in research that is too much of a burden for them.

*'When time is running out on life, can we ask people to give time to research? When such a paucity of information exists on how to help those who are dying, how much individual distress is too much when weighed against the potential future benefit such information will provide to society?'*(Hawryluck, 2004)

There are also ethical concerns of researching patients with life limiting illness.

*'...to research at all into the needs and experiences of this client group could be said to be an affront to the dignity of those people who are terminally ill*

*and an expression of profound disrespect for the emotional and physical state of such patients.* '(de Raeve, 1994)

These views are not shared by all palliative care providers however. Some palliative care providers believe that while *some* patients may be vulnerable, the palliative care population is too diverse in areas such as prognosis, clinical status, and capacity to make decisions to be able to be generalized as a vulnerable population (Berry, 2004). A wide range of viewpoints remain but the unique nature of the palliative care population is beyond doubt. This population has the potential for vulnerability but it also has the potential for poor symptom control and a low evidence base for the treatments available. It would seem that the challenge in palliative care is to undertake the research whilst remaining vigilant, informed and sympathetic to the nuances of the population.

Amongst researchers, the debate may continue regarding research in the palliative care population, but what do the patients themselves think? Opinions are formed by experiences and a question remains as to the opinions and experiences of those palliative care patients who have taken part in research.

## **1.2. Developing a research question**

I developed the following research question that my thesis would address:

*What are the experiences of advanced cancer patients who have taken part in a symptom control clinical trial?*

While the choice of studying only advanced cancer patients is discussed in chapter 1.5, one other point is worth stressing. I did not intend to research patients who were trialling chemotherapy agents. Trials that involve chemotherapy are inextricably linked to the topic of life prolonging treatment. As palliative care aims neither to prolong nor shorten life, I did not want to include chemotherapy trials in my study. I wanted to understand the experiences of patients taking part in clinical trials that did not affect their survival prognosis.

### **1.3. Aims**

In order to address my research question, I developed the following aims:

- To explore the experiences of advanced cancer patients who have taken part in a symptom control clinical trial involving novel analgesic agents
- To find out the impact that this trial had on their lives
- To propose a model of these experiences that can be used to inform current and future practice of clinical trials in advanced cancer patients
- To review critically the study and identify further areas of research that may provide more information on this topic

### **1.4. Layout of thesis**

The thesis is divided into four sections. Section one contains the introduction and a literature review. Section two contains the methodology and methods chapters with explanation and justification for the chosen approaches. Section three contains the results of the study. Section four describes the uniting theory of the study, discusses the findings of the study, appraises the study critically and offers suggestions for future research in the area.

## **1.5. Definition of the population**

For the purpose of this thesis, it is necessary to define a 'palliative care population.' This is recognized to be a difficult challenge (Borgsteede et al., 2006). Although patients with metastatic cancer make up the majority of a palliative case load, chronic conditions such as obstructive airway disease, heart failure and neurological conditions are playing an increasingly large part. To study such a heterogeneous population taking part in clinical trials would pose greater logistical challenges than could be surmounted in one thesis. Therefore the decision was made only to study patients with an advanced cancer diagnosis. Throughout this thesis, any discussion of the palliative population refers to patients with a diagnosis of advanced, metastatic, incurable cancer.

## Chapter 2. LITERATURE REVIEW

### 2.1. Introduction

The purpose of this literature review was to examine previous research into the experiences of advanced cancer patients who have taken part in clinical trials. Before starting this literature review I was aware of two recent systematic reviews that had looked at palliative patients' and their care givers' attitudes towards research (White and Hardy, Todd et al., 2009). The aim of White and Hardy's systematic review was to '*identify the views of palliative care patients and their families towards research, the factors that are important when considering participation and the types of research trial they would support or reject.*' Similarly, the aim of Todd et al was '*to examine the attitudes of patients with advanced cancer towards research and establish common themes.*' The positive themes that emerged from these two systematic reviews were altruism, self benefit and hope.

The primary limitation when drawing conclusions from these systematic reviews, however, was that the majority of papers studied were asking patients to voice their opinion on a topic which they had not experienced. Ross and Cornbleet, for example, asked patients in a specialist palliative care unit about their attitudes towards taking part in theoretical clinical research of increasing invasiveness (Ross and Cornbleet, 2003). In addition, in the systematic reviews, only two papers referred to trials that had taken place (Dobratz, 2003, Ling et al., 2000). In both

instances, the focus was on reasons for patient withdrawal or declining participation in the first case, rather than experiences of the trial itself.

## **2.2. Methods**

Ethical approval was not required for this systematic review. The databases Medline (1988-2010) and Embase (1988-2010) were searched electronically through the Ovid gateway. In addition, the contents of editions of *Journal of Pain and Symptom Management*, *Palliative Medicine*, *European Journal of Palliative Care* and *Supportive Care in Cancer* were searched separately from September 2010 back to the start of 2005. The date of the last literature search was the 23<sup>rd</sup> of September 2010. The reference list of the reviews mentioned above and other significant papers were included.

In an exploratory literature search the terms *'palliative'* and *'advanced cancer'* were used along with *'research'*, *'attitudes'*, *'opinions'* and *'experiences'*. This failed to identify several significant papers in the general field of interest that had been previously cited by both Todd and White. The recent systematic review by White and Hardy used the MeSH terms of *'attitudes'*, *'motivation'*, *'willingness'*, *'preparedness'*, *'clinical trial'* and *'randomized controlled trial'*. The results of this were then manually checked, either in title, abstract or full article form for their relevance to the palliative care population. This method has the advantage of not requiring the variable terminology for palliative patients that features in the literature. Terms for the palliative population can include *'advanced cancer'*, *'limited prognosis'*, *'palliative'*, and *'terminal'*. Checking papers manually for

patients who met the inclusion criteria reduced the chance of missing relevant papers pertinent to this systematic review.

The electronic search was made up of three arms. These arms were '*cancer*' AND '*trial*', '*cancer*' AND '*research*', and '*cancer*' AND '*study*'. Within each arm, the combination of the two search terms was then subsequently searched individually with '*palliative*', '*supportive*', '*opinions*', '*experiences*', and '*attitudes*'. Where possible, for search results of fewer than 6000 papers, any duplicates were removed. Results were assessed firstly by the title. If further information was required, the abstracts and full articles were assessed.

### **2.2.1. Inclusion criteria**

- Studies where the population was patients with a diagnosis of metastatic cancer
- Studies that examined patients' experiences of taking part in clinical trials for symptom management

### **2.2.2. Exclusion criteria**

- Clinical trials of medication whose primary or secondary aim was to prolong life
- Clinical trials that did not involve medication
- Studies exploring patients' attitudes to research of any nature that they had not explicitly taken part in
- Any studies involving a population less than 18 years old

### **2.3. Results**

The literature search produced a total of 46,735 papers. These were broken down further by search criteria as shown in Table 1.

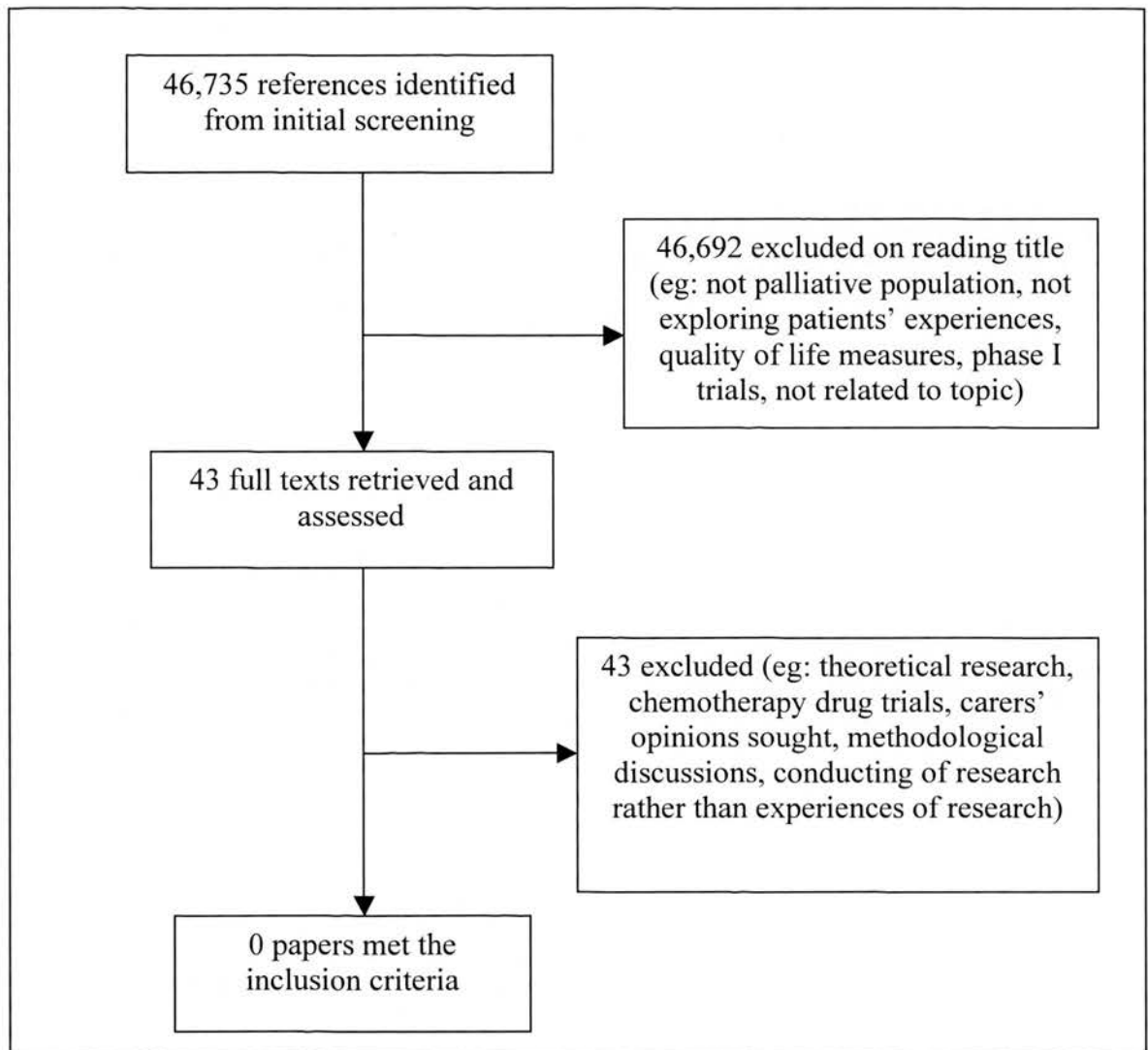
Table 1 - Papers generated from search

	<b>Palliative</b>	<b>Supportive</b>	<b>Opinions</b>	<b>Experiences</b>	<b>Attitudes</b>	Totals
<b>Cancer AND Trial</b>	6742	1837	165	625	720	10089
<b>Cancer AND Research</b>	4651	1725	433	2176	3888	12873
<b>Cancer AND Study</b>	13875	2669	566	2666	3997	23773
Totals	25268	6231	1164	5467	8605	<b>46735</b>

Note: Due to duplicates, some papers featured in more than one search

The results of the searches produced a large number of papers to be reviewed. The search process and assessment process is shown in Figure 1.

**Figure 1 - The search process and exclusion of papers from literature review**



Forty-three full papers were examined to assess for eligibility. No papers met the eligibility criteria for inclusion in this literature review. The most common reasons were either that the drug being trialled was chemotherapeutic or that the study involved theoretical research. An example as described above is Ross's exploration of patients' attitudes to research (Ross and Cornbleet, 2003). This was excluded because the patients were asked about escalating levels of theoretical research rather than experiences of taking part in their own trials. Other papers excluded looked at

caregivers' opinions, discussed methods relating to research or described research that was conducted rather than patients' opinions on the research.

## **2.4. Discussion**

The fact that there were no papers exploring advanced cancer patients' experiences of clinical trials was not altogether surprising. The recent reviews described above have covered individually the area of patients' views on palliative care research systematically in recent years. It was important to search the literature for actual patient experiences of research rather than their opinions on theoretical research, and to make this distinction clear.

Despite the different approach taken by Todd et al and White and Hardy, it is still worthwhile noting the salient findings of their papers. The review by Todd et al, published in 2009, describes the positive and negative aspects of research in palliative care. The three positive themes were that of altruism, self-benefit and hope. The negative themes were of being too unwell to participate, anxiety surrounding the issue of a placebo, concern regarding increased hospital admissions and limited self benefit or deterioration in symptoms. Of the 11 studies included, seven showed altruism as a motivating factor for taking part in clinical trials. Six trials showed that the possible improvement of the patients' own symptoms was a motivating factor. Maintaining individual hope was discussed in three studies examined. These studies were looking at patients with regards to phase I clinical trials.

White and Hardy published another systematic review into patients' and carers' views on research in palliative care (White and Hardy, 2010). The themes of altruism and personal gain were similar to those found by Todd et al. The theme of the importance of patients maintaining their own autonomy was also identified here. Similar concerns regarding randomization, placebo studies and double-blind trial designs were discussed by White and Hardy.

Three papers from the systematic review were of particular relevance to this thesis and therefore merit further discussion.

#### **2.4.1. Hospice patients' views on research in palliative care, (Terry et al., 2006)**

Terry et al interviewed 22 hospice in-patients in Australia. The aim was to find out the opinions of these patients regarding palliative care research. The questions included:

- *'If we were doing research into hospice or palliative care, what do you think we should do?'*
- *'Who would you prefer to ask you about being in research?'*
- *'How much information do you think you would need to be in research?'*

Although patients were not asked specifically about all research designs, they were asked specifically about randomized controlled trials:

*'If we had two treatments and we did not know which was better, would it be OK to give half the patients one and half the other?'*

The results from the interviews were predominantly positive towards research.

- Patients spoke of a continuing utility in their 'unique position' by participating in research and of having a sense of validation
- Although patients spoke in general terms of research towards the ultimate cure of their cancer, when pressed for specific topics to be researched, their answers focused more on symptom control issues

- Patients were clear in their desire that the research should not prolong their life
- Patients were firm in their views that the trial information given to them should focus more on discussion rather than written information
- Patients were opposed to the concept of randomized controlled trials although the authors found that this was in the context of a poor understanding of what a randomized controlled trial entailed

This qualitative piece of work interviewed patients admitted to a hospice. The majority of patients (n=14) died within 48 hours of taking part in the interview. The authors concluded that their study went some way to refute the practical and ethical difficulties cited in palliative care.

## **2.4.2. Participating in a cancer trial**

### **2.4.2.1. Madsen's' work (2007a and b)**

These two papers were published from the same set of interviews conducted on female patients with either breast or ovarian cancers in Denmark. Although the population was not a palliative one, a lot of the issues raised were similar and the grounded theory approach matched that of this thesis. The study explored the experiences of patients who had actually taken part in randomized controlled trials.

Madsen comments on this fact within the papers:

*'The majority of studies investigating attitudes towards clinical research have been based on hypothetical scenarios.... Consequently, it is almost unknown how it actually feels like to be the subject of clinical research.'*(Madsen et al., 2007b)

The difficulty in deciding to take part in the trial was a large part of the results of the study. Thirty patients were interviewed of whom half agreed to take part in the trial

and half declined. Both groups of patients discussed their reasons for their decision. Weighing up the '*pros and cons*' of taking part in the research trial was the central phenomenon of the generated theory. '*The goal was to maximize personal benefits, minimize the risks and at the same time find confidence and trust.*' Interestingly, even those patients who declined to take part in the trial still had a positive attitude towards clinical trials. The theme of participating in research being a moral obligation was both suggested to patients and offered spontaneously.

*'Two thirds of patients stated that trial participation possessed elements of a moral imperative...'* (Madsen et al., 2007a)

The interaction with health staff and the implication for the patients differed between the two trials from which the patients were selected. Breast cancer patients largely felt a lack of personal confidence and trust in their doctors which was put down to the fact that they interacted with a large and variable number of doctors who often gave the impression of incompetence and being rushed for time. Ovarian cancer trial patients only interacted with two doctors and reported a strong feeling of trust and confidence in the '*empathetic and knowledgeable*' team. Being treated '*as whole human beings*' was one of the most important expectations from patients.

The concern regarding the randomization of patients was a strong theme. Patients did not feel confident in the stated clinical equipoise (where clinicians are uncertain of the benefits of one arm of a trial over another, required for a trial to be deemed ethical).

Although the patient group was involved in life prolonging treatment, the fact that patients interviewed had taken part in the research makes the discussion of this paper valid for my thesis.

#### **2.4.2.2. Randomized controlled trials of palliative care (White et al., 2008)**

White et al produced this paper in 2008 before White and Hardy's systematic review paper of 2010. With the use of a questionnaire, the opinions of 101 palliative patients towards research were generated. The specific aim was to enquire about trials that concentrated on symptom control rather than prolonging life, particularly in the context of randomized controlled trials.

Patients were asked about the design of trials, what they would find acceptable in a trial depending on the level of invasiveness and issues regarding potential side effects of trial medication.

Altruism was a strong reason for wanting to take part. As trials became more invasive, fewer patients were willing to participate. The potential for side effects was also a strong consideration for patients prior to deciding to take part in the theoretical trials.

#### **2.4.3. Limitations of literature review**

There are several limitations of this literature review which may have yielded salient papers. Not every database available online was searched. Major authors in this field, such as Janet Hardy, were not contacted directly to highlight any papers that

they were aware of that had not been considered. The abstracts of conferences such as the *European Association of Palliative Care* were not studied as this was felt to be too time consuming for the yield that it may produce. Although several key journals were hand searched, not every journal which may have published a significant paper, such as the '*Journal of Clinical Oncology*' or '*Journal of Palliative Medicine*', was hand searched. Despite the limitations identified, I am confident that no key papers have been missed.

## **2.5. Conclusion**

To our knowledge there has yet to be a study that explores the experiences of palliative patients who have taken part in a clinical trial for symptom control. There are two good quality systematic review articles regarding the area of palliative patients' views towards research which have been discussed above (White and Hardy, Todd et al., 2009).

The individual studies by Terry and White give a useful insight into the views of palliative patients towards research; however, the theoretical opinion of patients has limited value. It is only through the lived experience of patients that firm data can be generated.

Several of the papers discussed by both Todd et al and White and Hardy in their systematic reviews used questionnaires to interview patients. An argument against the use of questionnaires is that the questions being asked are related to the pre-existing knowledge and opinions of the research team (*a priori*) rather than allowing the patients to take the project in a direction that may not have been expected or

predicted. In contrast, by using the broader tool of grounded theory, Madsen et al's research into patients' experiences of phase I oncology trials offers an interesting insight into a similar phenomena to the one that is explored in this thesis (Madsen et al., 2007a and b). The one significant difference is the use of potentially life prolonging treatment. Madsen et al's work can be viewed with interest as a close relative rather than for direct comparison, due to the fundamental difference that the issue of life prolonging treatment provides.

With no studies to compare with directly, this thesis was the first to explore the experiences of palliative care patients who take part in clinical trials for symptomatic benefit.

## **SECTION 2 - METHODOLOGY AND METHODS**

## **Chapter 3. METHODOLOGY:**

*'Not everything that matters can be counted. Not everything that can be counted matters.'* Albert Einstein

### **3.1. Introduction**

Every individual's experiences are unique. In the same situation, another person would have a different experience and would subsequently describe the experience differently.

It is the personal, unique experience of each individual's participation in a symptom control trial that forms the basis of this thesis. The patients have a common condition - advanced cancer, and a common exposure to a trial - a double-blind randomized controlled trial (RCT) of symptom control analgesics, but they have hugely diverse experiences. This diversity is driven both by the variable nature of conditions in a RCT (e.g. the possibility of receiving a placebo) and by inter-person differences in the perception of experiences.

The challenge of this thesis was to capture the diversity of these experiences in as vivid detail as possible. This chapter outlines and justifies the methodology of the thesis which allowed me to capture the diversity of these experiences.

### **3.2. Qualitative vs. quantitative research**

Before starting this thesis I thought that the main distinction in research was between qualitative and quantitative research. However, I am now aware that there are significant differences underpinning these contrasting approaches. These differences

are both in the abstract principles guiding the very paradigm (belief system) of that research, and in the emphasis and expected outcomes of the research.

*'These principles combine beliefs about ontology (What is the nature of reality?), epistemology (What is the relationship between the inquirer and the known?), and methodology (How do we know the world, or gain knowledge of it?). These beliefs shape how the qualitative researcher sees the world and acts in it.'* (Denzin and Lincoln, 1994)

Complex issues indeed but ones that required careful consideration if I was to fully understand the studied phenomenon and my reasons for studying it in the way that I chose.

Broadly speaking, quantitative research adopts a positivist paradigm of research. This belief system is based on one truth that is 'out there' awaiting discovery, independent of the consciousness or awareness of this truth. Although qualitative research can adopt many paradigmatic styles, including positivism, a constructivist paradigm is a more common approach. This constructivist paradigm is a belief in multiple truths, cognizant of the mind that is creating the meaning; in other words, an interaction between the subject and the object to 'construct' an interpretation of reality.

Crotty illustrates the difference through the example of the existence of a tree. A positivist view of the tree is that it is a tree regardless of an awareness of its presence. Its '*treeness*' is waiting to be discovered. (Crotty, 1998). The positivist stance deals in absolute fact. In a constructivist paradigm, '*there is no meaning without a mind. Meaning is not discovered, but constructed...different people may construct meaning in different ways, even in relation to the same phenomenon.*'(Crotty, 1998). In

relation to the tree, although the tree may exist without a conscious mind, the tree-like properties that we ascribe to it would not. In relation to a clinical trial, different people may construct different meanings to the same phenomenon.

When different meanings are being constructed from the same phenomenon, how might a researcher approach this situation?

*'Qualitative researchers stress the socially constructed nature of reality, the intimate relationship between the researcher and what is studied, and the situational constraints that shape inquiry. Such researchers emphasize the value-laden nature of inquiry. They seek answers to questions that stress how social experience is created and given meaning. In contrast, quantitative studies emphasize the measurement and analysis of causal relationships between variables, not processes. Proponents of such studies claim that their work is done from within a value-free framework.'* (Denzin and Lincoln, 1994)

While not always as clear cut as Denzin and Lincoln describe, the '*value-laden nature of inquiry*' involved in qualitative research was an important consideration for this thesis. As a widely held belief, '*The goal of qualitative research is enriching the understanding of an experience.*' (Polkinghorne, 2005). I wanted to take in the various constructions of reality along with my own interpretation of them to enrich the understanding of advanced cancer patients' experiences of clinical trials. I chose the qualitative approach as the best way of exploring this phenomenon.

### **3.3. Framework for principles of quality in research**

*'Quality is elusive, hard to pre-specify, but we often feel we know it when we see it. In this respect research is like art rather than science.'* (Seale, 2002)

All research has the aim of reaching a wider readership than those who were involved in the research. However, the reader has to decide whether the presented material is of sufficiently high quality to contribute to previous knowledge; whether

they can trust what has been presented. But how is the quality to be measured and how can a reader trust what they are reading?

In the methodological literature, there is debate regarding the measurement tools of quality in qualitative research. Lincoln and Guba lay out their criteria of principles to apply to a piece of research in order to provide evidence of the trustworthiness of that research. These principles are credibility, transferability, dependability, confirmability and latterly authenticity (Lincoln and Guba, 1985, Guba and Lincoln, 1989). However this approach is potentially flawed:

*'But it became evident....that their criteria depended on a contradictory philosophical position since their belief in 'multiple constructed realities' (Lincoln and Guba, 1985: 294) rather than a 'single tangible reality' (Lincoln and Guba, 1985: 295), which lies at the heart of the constructivist paradigm, is not consistent with the idea that criteria for judging the trustworthiness of an account are possible.'* (Seale, 2002)

To be truly relativist, and in so doing accept the belief of multiple realities, would be to reject all form of validation, citing that each piece of research is individual and valid in its own form. This creates a difficulty in relating the relevance of any work to another situation. Alternatively, a traditional realist quantitative researcher presents work with a definitive answer. Within this process they look to eliminate all researcher bias from a study. By doing this, they are suggesting that there is a true reality that the researchers' perspectives, something key to a constructivist approach, are hindering them from seeing (Kuper et al., 2008). Mays and Pope adopt the stance of a subtle realist (Mays and Pope, 2000). Although rejecting the notion of one definitive 'truth' they accept that there is an underlying reality which can be studied. This allows general criteria of quality such as validity and relevance to be applied (Mays and Pope, 2000).

Within qualitative research, practices exist to show evidence of rigor. The criteria outlined by Lincoln and Guba above are examples. Rather than adhere to a fixed checklist of rigor and the difficulties that this come with (Barbour, 2001), in the methods chapter, I will describe the processes used to adhere to the principles of validity and relevance. These processes, described in more detail in chapter 4.3, were theoretical sampling, member checking, negative case analysis, use of thick description of the methods used, reflexivity, peer debriefing and audit of analysis process. (Guba and Lincoln, 1989, Lincoln and Guba, 1985, Seale, 2002, Barbour, 2001, Mays and Pope, 2000, Kuper et al., 2008). Mays and Pope also outline a list of questions that can be asked of a study by reader and researcher that can assist in the assessment of quality (Table 2).

**Table 2 - Assessing qualitative research**

- *Worth or relevance—Was this piece of work worth doing at all? Has it contributed usefully to knowledge?*
- *Clarity of research question—If not at the outset of the study, by the end of the research process was the research question clear? Was the researcher able to set aside his or her research preconceptions?*
- *Appropriateness of the design to the question—Would a different method have been more appropriate? For example, if a causal hypothesis was being tested, was a qualitative approach really appropriate?*
- *Context—Is the context or setting adequately described so that the reader could relate the findings to other settings?*
- *Sampling—Did the sample include the full range of possible cases or settings so that conceptual rather than statistical generalisations could be made (that is, more than convenience sampling)? If appropriate, were efforts made to obtain data that might contradict or modify the analysis by extending the sample (for example, to a different type of area)?*
- *Data collection and analysis—Were the data collection and analysis procedures systematic? Was an “audit trail” provided such that someone else could repeat each stage, including the analysis? How well did the analysis succeed in incorporating all the observations? To what extent did the analysis develop concepts and categories capable of explaining key processes or respondents' accounts or observations? Was it possible to follow the iteration between data and the explanations for the data (theory)? Did the researcher search for disconfirming cases?*
- *Reflexivity of the account—Did the researcher self consciously assess the likely impact of the methods used on the data obtained? Were sufficient data included in the reports of the study to provide sufficient evidence for readers to assess whether analytical criteria had been met?*

I tried throughout this thesis to be mindful of these questions and apply them to my work.

### **3.4. The use of grounded theory**

There are many qualitative methodological approaches available to researchers. These include phenomenology, ethnography, case studies, content analysis and grounded theory. I will briefly discuss the approaches that I considered for this study before describing in detail the reason for choosing a grounded theory approach.

A phenomenological approach seeks to understand the phenomenon of a lived experience. However, phenomenology is concerned with the study of experience from the perspective of the individual, seeking to describe rather than explain (Punch, 1998). An example is a study that used a phenomenological approach to examine and describe the barriers experienced by health care providers to timely palliative care referral (Melvin, 2009). As I was interested in interpreting the patients' experiences, I rejected the use of a phenomenological approach.

The basic premise of ethnography is to explore the culture of a group of people. Ethnographic methods rely '*substantially or partly on 'participant observation'*' (Denzin and Lincoln, 1994). To a variable degree, the researcher involves themselves with the activities that the studied population take part in. I had two concerns regarding an ethnographic approach to this study. Firstly, I felt that although patients had much in common with each other, they had almost no interaction with each other. Subsequently, there was very little scope for them to

influence or be influenced by each other and develop a culture amongst themselves. Secondly, being a participant in the clinical trials in any form was not an option for me. It was for these reasons that I rejected ethnography as an unsuitable approach.

Case study analyses have been used in palliative care research. The value of case study analysis lies in the examination of complex cases where context is important and a deep understanding of each case, from multiple perspectives, can be achieved (Walshe et al., 2004). Williams et al used a case study analysis to track the evolution of hospice palliative care Canada (Williams et al.). Although a deep understanding is important in this thesis, the lack of previous knowledge on the topic, and so the lack of information on the best cases to select led me to reject case study analysis as the most beneficial methodological approach.

Qualitative content analysis has been defined as a *'research method for the subjective interpretation of the content of text data through the systematic classification process of coding and identifying themes or patterns.'* (Hsieh and Shannon, 2005). One of the strengths of the approach is the ability to work through a large volume of data collating similar or related pieces. However, the approach is suitable when testing prior hypotheses rather than exploring a new area of which little is known (Miles, 1994). For this reason, content analysis was rejected.

While there were aspects of each methodological approach described above there made them unsuitable, other aspects were appealing. For example, a description of patient experience was relevant to this study, as used in the phenomenological

approach, but it was important also to interpret these findings. Similarly a case study approach was appealing but it unclear which cases to study. I felt that a grounded theory approach would draw on the strengths of several of the methodological approaches described above. The detailed reasons for this decision are discussed below:

### ***Summary of grounded theory***

The methodology of grounded theory is known in qualitative research to be appropriate when there is a '*lack of knowledge or theory of a topic.*' (Bluff, 2005). Theory is generated from the collected data rather than testing a pre-existing theory. The literature search described in chapter two revealed the lack of research into the experiences of advanced cancer patients who had taken part in symptom control trials. With this lack of research, and no pre-existing theory to test, I chose grounded theory as an appropriate methodology to develop further knowledge of this topic.

A 'grounded theory' comes from a large collection of data and will have taken its influences only from that collection of data. The theory is grounded within the data. Other work that may have taken place before should only be considered towards the end of the process. The data studied are usually a collection of information gathered from the studied population, typically in the form of transcribed interviews. These data are studied carefully for similarities, differences, patterns and comparisons between different contributing participants. Throughout the process, the data are broken down, analysed and refigured to direct the course of the research. By the end of the research, as the last pieces of data are being collected, the overall grounded

theory will have emerged from the data as a way of explaining succinctly the studied phenomenon and will be able to link all other aspects of the phenomenon to it.

This short summary of grounded theory does not cover all of its subtleties. These subtleties and the important points that make up the process of using a grounded theory approach are described and discussed throughout chapter 3.4. I have found grounded theory a difficult concept to understand fully. It is for this reason that I go into grounded theory in detail to put across what I understand to be the important factors of this methodological approach.

### **3.4.1. The history of grounded theory**

The creation of grounded theory was a defining moment for social science research. However its use as a research tool has evolved in the four decades since its inception. These two facts merit some discussion of the background to grounded theory.

*The Discovery of Grounded Theory* was written and published by sociologists Barney Glaser and Anselm Strauss (Glaser and Strauss, 1967). This seminal work was published as a description of their methodology while studying dying patients in hospitals. At the time of publication, qualitative research was not viewed as scientifically credible by the research community. The aim of Glaser and Strauss was to redress this opinion.

Before grounded theory, qualitative theory development of a phenomenon was conceived from *a priori*, or previously known, knowledge. The novel difference in grounded theory was that this was '*the discovery of theory from data*' (Glaser and

Strauss, 1967). As Kelle describes, *'One of the main purposes of Glaser and Strauss' "Discovery book" was to challenge the hypothetico-deductive approach which demands the development of precise and clear cut theories or hypotheses before the data collection takes place.'* (Kelle, 2005)

Fundamental to grounded theory is the belief that knowledge may be increased by generating new theories rather than analysing data with existing ones (Heath and Cowley, 2004). Generating new theories is an inductive process, contrasting with the deductive approach of testing theories or hypotheses to be true or false.

According to Strauss and Corbin, grounded theory must include four essential principles: fit, understanding, generality and control (Strauss and Corbin, 1990).

- Fit entails that the theory fits the substantive data
- Understanding entails that the theory be comprehensible to all involved in the area of study
- Generality entails that the theory is applicable in a variety of contexts. It may be that this aspect of the theory is undertaken in further studies in another setting
- Control implies that the theory should provide control with regard to action toward the phenomenon. The researcher should control the conditions of the study positively toward the theory generated

The completed theory *'...provides the best comprehensive, coherent and simplest model for linking diverse and unrelated facts in a useful and pragmatic way. Theorizing is the process of constructing alternative explanations until a "best fit" that explains the data simply is obtained.'* (Morse, 1994)

### **3.4.2. Differences in grounded theory**

After the original work on grounded theory, Glaser and Strauss' views altered towards the theoretical paradigm underpinning their work. Glaser remained true to the original concept while Strauss, with his subsequent research partner Juliet Corbin, published work which challenged and modified the original concept. Glaser felt that these deviations were not in keeping with the original concept of grounded theory (Glaser, 1992).

The commentary on the differences in their work is prolific with several theoretical issues still unresolved. Annells claims that the methodological differences between Glaser's and Strauss & Corbin's work are created by an ontological and epistemological divergence. (Annells, 1996). Heath and Cowley describe a shared ontology with epistemological differences (Heath and Cowley, 2004).

The main differences between Glaser and Strauss & Corbin's work lie in previous knowledge of the studied phenomenon, subsequent data analysis and verification of the generated theory.

#### **3.4.2.1. Previous knowledge of the studied phenomenon**

Emergence is one of the key components of grounded theory. It is the phenomenon of allowing the theory to develop from within the data. Glaser maintains that this is done most effectively when all preconceptions on the studied topic are put to one side. With respect to the topic, the researcher's mind is a *tabula rasa*, or blank slate, so that generated data are not contaminated by preconceptions. He or she has to put aside all preconceived notions so that they can "*remain sensitive to the data by being*

*able to record events and detect happenings without first having them filtered through and squared with pre-existing hypotheses and biases” (Glaser, 1978).* Strauss and Corbin felt that what was more important was to be aware of your previous knowledge so that you were able to discern what was relevant in the data and what was not. Dey comments that *‘there is a difference between an open mind and an empty head.’ (Dey, 1999).*

#### **3.4.2.2. Data analysis**

Data are generated by interaction with participants, usually in the form of an interview. Coding is the term that is used for the process of organising sections of data from different interviews into comparable collections. The complex differences between the coding approaches of Glaser and Strauss have been well described (Kelle, 2005). Strauss and Corbin, through the use of *axial coding*, offered a much more directive approach to the elaboration of categories. This was particularly aimed at novice researchers. Glaser offers theoretical codes that can be adapted to categories to aid their elaboration. His criticism of Strauss and Corbin was that axial coding *‘forces’* the data into a preconceived framework that it may not have naturally developed into, thus being a consequence of the researcher’s previous influences, rather than *‘emerging’* from the data (Glaser, 1992). Once the process of axial coding has taken place, Strauss and Corbin outline the process of *‘selective coding’*. This is the process of selecting the core category and systematically relating other categories to this. The core category is the central phenomenon around which all other categories are based. A more detailed description of the coding process is found in chapter 3.4.5.

### **3.4.2.3. Verification of the generated theory**

The ontological and epistemological incongruence that developed between Glaser and Strauss created a further difference on the issue of verification. Glaser thought that if the findings of the grounded theory were felt to be significant, “*a verificational study (an experiment or survey) can be made to verify its true import*”(Glaser, 1992). Strauss and Corbin would maintain that the findings would be verified “*throughout the course of the research project,*” by the multiple realities being offered and assimilated (Strauss and Corbin, 1994).

### **3.4.3. Constructivist Grounded Theory**

The original grounded theory has been described as positivist or at least post-positivist in its theoretical stance (Kelle, 2005) (Annells, 1996). Strauss and Corbin’s later work is more complex.

*‘Undoubtedly however, their work demonstrates a mixture of language that vacillates between post-positivism and constructivism, with a reliance on terms such as recognising bias and maintaining objectivity when describing the position the researcher should assume in relation to the participants and the data. Nevertheless, they mix these ideas with observations such as “we emphasize that it is not possible to be completely free of bias.” This has led some researchers to remark that ‘people can find support in it for any ontology that they wish (Macdonald & Schreiber, 2001)’ (Mills et al., 2006c).*

An emerging form of grounded theory, with sociologist Kathy Charmaz being largely credited as its pioneer, is that of a constructivist approach. She lays out her manifesto towards constructivist grounded theory thus:

*‘In the classic grounded theory works, Glaser and Strauss talk about discovering theory as emerging from data separate from the scientific observer. Unlike their position, I assume that neither data nor theories are discovered. Rather, we are part of the world we study and the data we collect. We construct our grounded theories through our past and present*

*involvements and interactions with people, perspectives, and research practices.*' (Charmaz, 2006)

Rather than the theory waiting to be discovered, Charmaz argues that the generated theory is an interpretation of the studied phenomenon with the influence of participant and researcher being central to the construction. My belief system puts this interaction between participant and observer at the centre of the grounded theory. I therefore adopted a constructivist approach to this study.

The differences between Glaser and Strauss and now Charmaz in their approach to grounded theory is complex and at times more philosophical than practical. A lot of criticism of grounded theory has been aimed at the initial work rather than at the later and modified approaches. Glaser and Strauss maintained at the time of their first publication that this was an evolving process and so it has proved. Mills puts the differences of Glaser, Strauss and Charmaz most eloquently:

*'...all variations of grounded theory exist on a methodological spiral and reflect their epistemological underpinnings. The form of grounded theory followed depends on a clarification of the nature of the relationship between researcher and participant,'* (Mills et al., 2006b)

#### **3.4.4. Summary of the constructivist grounded theory approach adopted**

A grounded theory approach has several key stages to be followed: data collection, data analysis, patient sampling and data saturation. This section will describe these elements in theoretical terms before discussing them in relation to this study, in chapter four (Methods) and appendix A (Data Analysis).

### 3.4.4.1. Data collection

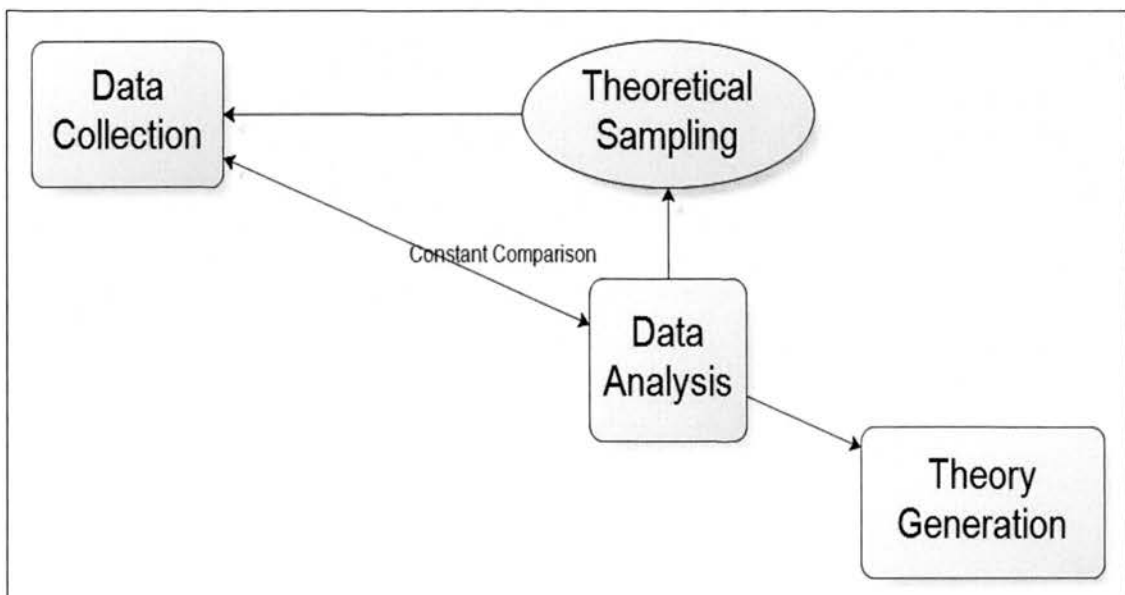
Glaser stated that '*all is data*' (Glaser, 2002). Data can be in the form of observation studies, written documents, interviews or focus groups. The form of data collection that will generate the richest data to be analysed should be chosen. Focus groups or semi-structured interviews are commonly chosen as the primary means of data collection. The strength of a grounded theory depends on the quality and depth of the data generated. Superficial data will only provide a superficial insight into a phenomenon.

As an example of generating rich data, Kvale describes the art of the second question; following up a patient response with another pertinent question (Kvale, 2009). It is the second answer that may shed more light on a topic than has been already offered. The intention of the second question is to start the data analysis during the data collection phase, or at least to make the data analysis easier.

### 3.4.4.2. Data analysis

The components of grounded theory analysis are shown in Figure 2.

**Figure 2 - The components of grounded theory data analysis**



The move from transcribed interviews to a generated theory is one that seems to be the hardest conceptual leap to make. Kvale asks the question '*How shall I find a method to analyse the 1,000 pages of interview transcription I have collected?*' (Kvale, 2009). The answer lies in avoiding getting to the stage where this question may be asked. Data analysis occurs concurrently with data collection. The ongoing analysis shapes the data collection and the direction in which it proceeds.

The next two sections look at the two main components of data analysis: coding and memo-writing. Coding is further divided into initial coding, focused coding and theoretical coding.

### **3.4.5. Coding**

As previously mentioned in chapter 3.4.2.2, the process of coding organizes data into comparable collections. The first process, initial coding, aims to break down the transcriptions into small sections of data such as a sentence or phrase from an interview. During focused coding, these smaller sections can be built up again, not around the person who generated the data but around collected concepts and categories into which the section of data fits. As the process develops into theoretical coding, the codes and categories become increasingly abstract from the original source and move towards the final theory. Each of these three processes, initial, focused and theoretical coding and their ramifications are now discussed separately.

The description of the data analysis for this thesis is in appendix A – Data Analysis.

### **3.4.5.1. Initial coding**

Charmaz outlines the aim of initial coding as one which '*sticks closely to the data*' while '*remaining open to exploring whatever theoretical possibilities we can discern in the data*' (Charmaz, 2006). Every line of a transcript, potentially every word, is studied and described. She suggests the use of words that describe actions rather than topics. The use of gerunds (words ending with *-ing*, e.g. avoiding, feeling, anticipating) helps with this process (Charmaz, 2006, Glaser, 1978).

*'This method of coding curbs our tendencies to make conceptual leaps and to adopt extant theories before we have done the necessary analytic work.'*  
(Charmaz, 2006)

Codes are flexible and one should expect to have to re-organize codes as they emerge from data. Codes should be modified to accommodate new data rather than forcing data into codes that do not fit. Codes should be precise and descriptive to offer a flavour of what they are describing.

Most codes are developed constructs of the researcher. Some codes, *in vivo* codes, are a direct quote from a patient. *In vivo* codes can have specific and descriptive meaning beyond the scope of the words used and create a strong connection with the generated data; more so than the substantive codes developed by the researcher.

### **3.4.5.2. Focused Coding**

Focused coding is the next stage after the initial coding. Focused coding uses the most significant and/or frequent earlier codes to sift through large amounts of data.

*'Focused coding requires decisions about which initial codes make the most analytic sense to categorize your data incisively and completely'* (Charmaz, 2006). The aim is to develop the initial coding to give a clearer structure of preliminary directions of

interest. It is a dynamic process whereby you return to the data to explore a new concept or clarify or modify an existing one. The researcher looks for new concepts to emerge. *'You act upon your data rather than passively read them.'* (Charmaz, 2006) As the interviews progress, they do not have to be analyzed in as much detail as the initial interviews. Coding a similar response to an already well outlined topic generates data that will add to complexity without adding further descriptive weight. Although initial coding may be more common at the start of data analysis and focused coding more common as analysis progresses, data are continually coded in both ways throughout the process as ideas and categories vary in their development through the study.

The type of coding that may be best known in relation to grounded theory is *axial coding*. This was developed by Strauss and Corbin in an attempt to give specific instructions into the process of coding for novice researchers. Axial coding puts the codes back together around an 'axis'. Categories and sub-categories are linked and described. Axial coding has its critics as well as its champions (Charmaz, 2006, Kelle, 2005, Strauss and Corbin, 1990, Strauss and Corbin, 1998). Charmaz does not feel that it is an essential step in the process:

*'Axial coding provides a frame for researchers to apply. The frame may extend or limit your vision, depending on your subject matter and ability to tolerate ambiguity....Those who prefer simple flexible guidelines...do not need to do axial coding. They can follow the leads that they define in their empirical models.....At best axial coding helps to clarify and to extend the analytic power of your emerging ideas. At worst, it casts a technological overlay on the data – and perhaps on your final analysis.'*(Charmaz, 2006)

I chose to not to adopt axial coding in the data analysis.

### **3.4.5.3. Theoretical coding**

Once the data are organized into more manageable sections, these sections, or categories can be analysed between themselves. Relationships between categories can be explored and described. In this manner the analysis moves away from the direct data towards a more theoretical level. Glaser has developed over 18 theoretical codes that can *'hone your work with a sharp analytic edge'*(Charmaz, 2006). However Charmaz also warns that they have to earn the right to be in the final grounded theory. Otherwise the researcher runs the risk of forcing context and a framework onto a situation which is not present within the data. In relation to previous concepts of grounded theory, theoretical coding is similar to selective coding. Within this stage of coding, the central category is sought for comparison with all other categories.

Constant comparison is a key aspect of data analysis. This is the process of comparing actively data to the category to which they are assigned. Constant comparison allows the growth of the theory by finding areas in categories that need to be expanded and going back to the data to address these gaps.

### **3.4.6. Memo writing**

Memo writing is the corner-stone of conceptual writing in grounded theory. It is the process where the organized codes and concepts move into a narrative description of the theory.

Early memo writing can be colloquial and informal. Getting ideas, observations and thoughts onto paper about initial codes and extracts from the data begins to collect

and refine the study of the data as a whole. Memos allow you to explore categories to see conceptual gaps or weaknesses. The data can then be re-examined or more data can be collected to fill these gaps.

As the analysis continues, the memos become increasingly abstract to move towards the completed theory. Memos are collected into similar topics and are compared with other groups of memos. Further memos are written on these comparisons.

*'As in Glaser's approach, the sorting of memos keeps the researcher in contact with the data while descriptive concepts are gradually replaced by abstract categories as the analysis progresses.'* (Heath and Cowley, 2004)

The abstraction is vital to avoid the result of a '*grounded description more than theory*', a criticism of some attempts at grounded theory (Charmaz, 2006). Despite the move away from direct handling of the data, Charmaz advocates continuing to use quotes from the data so that the theory remains grounded in the data and participants' voices still resonate through the text.

### **3.4.7. Patient sampling**

Qualitative research in general and grounded theory in particular does not look for a representative sample of a population. Instead, sampling of a population is performed to give the fullest description of the population being studied.

*'The selections are based on the likelihood that they will confirm or elaborate on the emerging descriptions or provide opportunities for disconfirmation of the emerging pattern.'* (Polkinghorne, 2005)

Authors have described many different types of sampling (Strauss and Corbin, 1990, Sandelowski, 1995, Coyne, 1997). At the start of the project, patients may be selected where the phenomenon is known to exist. This can be termed selective sampling or purposive sampling. Once the initial data have been examined and

tentative topics are identified, subsequent patients are selected on the basis of these topics. This step is known as theoretical sampling.

In keeping with the principles of grounded theory, theoretical sampling is emergent. *‘Initial sampling in grounded theory is where you start, whereas theoretical sampling directs you where to go’* (Charmaz, 2006). Theoretical sampling is central to the inductive-deductive components of constant comparison in grounded theory. Data are generated and studied. From these data, preliminary concepts may be considered cautiously. Specific patients are selected theoretically to test or elaborate on these concepts. Depending on their responses, further theoretical sampling takes place for further data generation and analysis. At the same time, the interview schedule changes to address issues that are emergent and to remove issues that are less prevalent. It is in this manner that sampling, coding and analysis take place concurrently and are all influenced by each other (see Figure 2: The components of grounded theory data analysis).

#### **3.4.8. Data saturation**

The number of cases studied in qualitative research tends to be smaller than in quantitative research. In quantitative research, a larger number of recruited patients allows a greater chance of being able to claim statistically significant findings, one of the key aims of quantitative research.

As outlined already, the aim of data collection in qualitative research is to explore all dimensions of a topic, rather than interview a representative sample. But when do you stop interviewing? When have all aspects of a phenomenon been fully explored?

The term used in qualitative research is “data saturation”.

*'Categories are 'saturated' when gathering fresh data no longer sparks new theoretical insights, nor reveals new properties of your core theoretical categories.'* (Charmaz, 2006)

However, there is a risk of claiming saturation too early. Charmaz describes the incorrect perception of saturation when researchers *'keep finding the same patterns.'* The real goal should be to achieve *'theoretical saturation'* (Charmaz, 2006). On this point she is happy to agree with Glaser:

*'Saturation is not seeing the same pattern over and over again. It is the conceptualization of comparisons of these incidents which yield different properties of the pattern, until no new properties of the pattern emerge. This yields the conceptual density that when integrated into hypotheses make up the body of the generated grounded theory with theoretical completeness.'* (Glaser, 2001)

By probing a topic superficially, conceptually thin categories which are quickly saturated may emerge. Charmaz offers the following questions when considering saturation:

- *Which comparisons do you make between data within and between categories?*
- *What sense do you make of these comparisons?*
- *Where do they lead you?*
- *How do your comparisons illuminate your theoretical categories*
- *In what other directions if any do they take you?*
- *What new conceptual relationships, if any, might you see?*

(Charmaz, 2006)

When considering saturation of certain categories, I tried to apply these questions to that area.

Strauss and Corbin maintain that saturation is a *'matter of degree'* (Strauss and Corbin, 1998). While there will always be the potential for the *'new to emerge'*, beyond this point, the data generated do not add to the overall theory or framework.

### **3.5. Conclusion**

This chapter has outlined the theoretical discussions and justifications for the approach that I chose for this study. The next chapter will discuss the specific methods used during the study.

## **Chapter 4. METHODS**

This chapter describes the methods used to explore the phenomenon of advanced cancer patients' experiences of taking part in symptom control clinical trials. It details ethical approval for the study, patient selection, the interview process and an assessment of quality of the research process that took place.

### **4.1. Ethical Approval Process**

It is appropriate that ethics committees want to be reassured that the use of patients in research is done in the correct manner. This is particularly true in patients with advanced cancer. When their life expectancy is limited, it is critically imperative that the central tenants of ethics i.e. that patients' time is used considerately and with their best interests in mind, is upheld. To this end, ethical approval was sought and gained for this study (See Appendix H for ethical approval letter).

At the time of submission to the ethics committee, there was the possibility that a third trial would be used for patient recruitment. This was the Menthol in Neuropathic Type Pain trial (MiNT-P). The ethics application included this trial as one from which patients would be recruited. However, this trial did not begin at the time that was expected and patients were not recruited from it.

It was also intended that part of the data collection would be in the form of focus groups. This was included in the ethics application. However, as the trial progressed, the decision was made not to recruit patients into focus groups. During

recruitment, some patients had indicated a reluctance to take part in a focus group. In addition to this, the relatively small number of patients who were eligible to take part in this study posed problems. The intention of focus groups is to compare groups rather than individual opinion within each group (Barbour, 2005). Patients with similar characteristics who might be recruited into one focus group could be either separated by 50 miles in distance or several months in time. It was felt that if a suitable number and quality of focus groups could not be arranged, it would be better not to use them at all.

### ***Recommendations of the Ethics Committee***

The ethics committee felt that the study was a meaningful piece of research that was worth doing. However they had some concerns that were highlighted. They were very keen that patients did not feel that they were put under undue pressure to take part in the study. Therefore they stressed that patients should only be contacted once by telephone after they had been given the information leaflet. If they did not verbally consent they were not to be contacted again. As discussed in chapter 10.4.2.1 this posed difficulties if patients did not answer their telephone or there was an answer machine. In these instances I exercised tact and judgement whether to contact a patient again. With this comment taken into consideration, the ethics committee approved the study.

## **4.2. Patient selection**

At the time of this study, the Edinburgh Palliative and Supportive Care Group (EPaS) were conducting two randomized controlled trials. These were the Ketamine Pain Study (KPS) and the Pregabalin Bone Trial (PBT). The trials were double

blind, randomized controlled trials studying the use of ketamine and pregabalin as novel analgesics against a placebo control. These trials were being conducted in multiple centres in the United Kingdom. Patients taking part from the Edinburgh and Glasgow centres provided a suitable patient cohort for this thesis. Descriptions of these trials can be found in Appendices B and C.

Although I was a member of the EPaS group, I had no involvement in any aspects of the PBT or KPS and had no contact with patients in these trials prior to contacting them for this study.

A set of inclusion and exclusion criteria was devised for patients in this study.

#### **4.2.1. Inclusion criteria:**

- A cancer diagnosis of an incurable nature i.e. metastatic spread
- Age  $\geq$  18 years
- Ability to complete the necessary interview
- Participation in either the PBT or the KPS (patients who had completed the study and those who withdrew before completing the study were both eligible for inclusion)
- Written informed consent
- Undergoing or had completed palliative treatment (this can include tumoricidal therapy or supportive care) for cancer

#### **4.2.2. Exclusion Criteria:**

- Age  $<$  18 years
- A cancer diagnosis with a potential curable outcome
- Patients in the dying phase of their illness

'The dying phase of their illness' is deliberately ambiguous. Rather than require a rigid guide for such an intangible state, it was felt better to allow this decision to be made in conjunction with those health care professionals who were looking after the patient. Such a decision is potentially controversial. One of the key arguments against palliative care research that I hope to consider is the supposition that palliative care patients are too unwell to take part in clinical research. However it was felt that it would not be appropriate to approach patients who were actively dying for this study.

#### **4.2.3. Suitability of patients**

The KPS included patients with terminal and curative cancer. As this thesis was looking at patients with a diagnosis of a terminal nature, this was the first distinction to be made when reviewing patients for suitability. All patients in the PBT were being treated for metastatic bone disease with radiotherapy, making them all eligible for inclusion.

The trial nurses in Edinburgh and Glasgow referred patients who were eligible to take part. The initial patients recruited were purposively sampled to cover both trial centres. Patients were contacted either by myself or by a member of the trial staff and informed of this study. If interested in the study, patients were given the information sheet and allowed at least 24 hours before being contacted again. This time delay was in adherence of the ethics committee guidelines on patient recruitment. Patients were given the opportunity to raise any questions they might have. If patients were happy to take part in the study, a date and venue were arranged at the patient's choosing. Most often patients were happy to be interviewed

at home but occasionally patients were interviewed on hospital grounds. This was either because the patient was visiting the hospital already or they preferred to be seen in the hospital. Also in compliance with the ethics committee's guidance, patients were only contacted once after they had been given the information sheet unless they gave consent to be contacted again. An example of this might be if they were not feeling well at the time of the telephone call but were happy to speak at a later date.

The details of all patients who had taken part in both the KPS and PBT were collected to keep record of who had and had not been recruited to the study. Of those who were not recruited, the reasons for this were documented. Common reasons might be that they were not eligible for the study, they declined to participate, they were deemed too similar to previous patients interviewed or I was interviewing other patients at the time that they had finished the trial. I made an effort to try and recruit patients who had recently completed the trial so that their memories could be fresher in their mind. On occasion, I interviewed patients some months after being on the trial. Some patients struggled to recall details of the trial which may have been clearer in their mind the interview taken place sooner after the completion of their trial.

#### **4.2.4. Theoretical sampling of patients**

The principles behind theoretical sampling have been discussed in chapter 3.4.7. As the study progressed, patients were chosen more selectively. Initially, I intended to interview similar patients from Edinburgh and Glasgow. Once the initial data were analyzed, a group of patients with similar experiences were those who felt their pain

had reduced during the trial. These patients were very positive towards the trial and found few flaws in it. Because patients with a perceived pain reduction were positive about the trial, I became interested in the responses of those patients who had not had a reduction in pain from the trial. I began to look at the pain scores of the patients before and after the trial. The scoring systems used were the Brief Pain Inventory (BPI) for the PBT and the McGill Pain Questionnaire (MPQ) for the KPS. By looking for a pain reduction of >30% in the BPI or a drop of 5 points in the MPQ, patients were deemed to have a significant pain reduction. I began to contact patients who had not had a significant pain reduction. I also interviewed patients who had withdrawn from the trials for any reason. It was felt by the trial staff that some patients had not been happy with them when they withdrew from the trial. I wanted to try and find out why this was and tried to target these patients specifically. However these patients were reluctant to be recruited to the study and I did not manage to recruit any. Finally, I became interested in those patients who had contacted trial staff members after the trial had finished. I was interested in patients who might have felt a great significance in the relationship they had developed with the trial staff. I wanted to find out how they felt after the trial had stopped and the impact this had on their relationship with the researchers.

### **4.3. Interviewing**

#### **4.3.1. Interviewing Theory**

Patients were interviewed using a semi-structured format.

*'Semi-structured interviews are conducted on the basis of a loose structure consisting of open ended questions that define the area to be explored, at least initially, and from which the interviewer or interviewee may diverge in order to pursue an idea in more detail.'*(Britten, 1995).

This fits well with the principles of grounded theory and semi-structured interviews are the most commonly adopted format for data collection. Interviews are also thought to be appropriate in the palliative care setting (Gysels et al., 2008). When this study was submitted to the ethics committee, it was also with the intention of conducting several focus groups. The primary aim of focus groups is to stimulate discussion and to compare groups (Barbour, 2005). As the study progressed however, it was felt that patients' opinions would be better heard individually rather than in a group.

In preparation for the interviews, I studied several texts, in particular *InterViews: Learning the Craft of Qualitative Research Interviewing* (Kvale, 2009). In line with the constructivist approach that I have taken in this thesis, I was aware of the shared construction of the data; the data being 'co-authored' (Kvale, 2009). In the same manner, the power dynamic should be as equal as possible, rather than the traditional objectivist, hierarchal structure with the participant being subordinate to the researcher (Mills et al., 2006c, Fontana and Frey, 1994). Seymour writes of two dimensions of the power differential: '*that between 'well' person and 'unwell' person; and that between 'professional' and 'patient'.*' Rather than resolving these tensions completely, the imbalance can only be '*more or less*' equal. (Seymour and Clark, 1998). I was guided by Mills regarding the power imbalance:

*'In order to move the researcher and participant to a more equal position of power within the relationship, the researcher needs to assume a more reflexive stance and proactively plan for the time they and the participants spend together.'* (Mills et al., 2006c)

During the study my age was 30-32 years. I was a doctor specializing in palliative care with concurrent clinical commitments in a Scottish hospice. I am a white,

middle class, unmarried male with an English non-regional accent; a 'posh' accent for want of a better word. I think that my accent is pertinent as a lot of the patients I interviewed were from a low socio-economic background which might put my immediate persona at odds to theirs. I felt that I might appear as a stereotypical doctor and wanted to attempt to reduce any barrier that this may represent from patients' previous experiences. Rather than try to alter any of the facts of my background, I acknowledged these and their impact on the power dynamic as part of the construction of data that would be generated.

Prior to the interviews, patients were made aware in the information sheet that my background was a doctor in palliative care. If I was posed a question regarding their medication for example, I answered this as I was able to do rather than shy away from my position and the knowledge that I held.

I used several questions to consider the power relationship and the bearing that it had on the constructed data:

*'How is this [person] like me?*

*How [are they] not like me?*

*How are these similarities and differences being played out in our interaction?*

*How is that interaction affecting the course of the research?*

*How is it illuminating or obscuring the research problem' (Seibold, 1992)*

I actively undertook several measures to try and reduce any power imbalance:

- Invited patients to call me Tom

- Arranged interview at time and date (where possible) and venue of patient's choice
- Accepted any offer of food or drink
- Established rapport at beginning and end of interview with social discussion
- Offered my opinion at times and gave my professional experience in appropriate context of the discussion
- Assured patients of the confidential nature of the study and that anything they said would be anonymized
- Sent copies of the transcript back to patients to read and comment on if desired

The impact of my personal and professional background is explored in the discussion in chapter 10.

#### **4.3.2. The process of the interview**

##### ***Before recording started***

At the start of the interview, I would discuss with the patient what was planned. I would also check that they did not have any questions that had arisen since we had arranged the interview. I accepted any offer of food or drink in order to develop an early rapport. After this introduction, I would invite patients to read and sign the consent form. Some patients had difficulty holding a pen or filling in their full names and I would assist as possible. I was happy to accept a patient's initials rather than their full signature in order to keep the process as undemanding for patients as possible.

During this initial period before recording started, I would also assess a patient's capacity to take part in the study. As has been discussed in the literature, as the study

posed minimal risks to the patient, this was conducted '*with an informal assessment of understanding*' (Casarett, 2003). The assessment of capacity was also for my own benefit to assess whether I felt that the patients would be sufficiently lucid and eloquent to put across their recollections of the trial.

### ***The presence of a partner during the interview***

Often I would be met at the door by a partner or they would be present during the introduction. My intention had always been to interview patients alone. I felt that this would make interpretations of the data more straightforward as it was only the views of patients that the study was investigating rather than the views of relatives and care-givers as well. Sometimes partners were present during interviews. I felt that this had a negative impact on the quality of data generated. Depending on the relationship, patients might defer to their partner for their opinion rather than have to explain their own mind. Also, when I tried to employ a pause in an interview, to allow a patient to consider the topic or elaborate further, this silence was filled on occasion by the partner. As the interviews progressed, I requested that I saw patients on their own. Clearly, if patients and partners felt strongly about them being present, despite only the gentlest request that the partner was not present, I relented to this, albeit reluctantly. I was subsequently to discover other reflections on this topic; it was reassuring to read a shared experience on the matter (Gysels et al., 2008).

### ***During the interview***

When all the preliminary work had been done, I would start the recording. At the start, I would explain to patients the format of the interview. I also explained that

although I worked with the research staff, I did not work on the trials that they had taken part in. I stressed that what they said would be anonymized and would not have any impact on their care. I wanted patients to feel that they were able to discuss positive and negative features of the trial without reservation or concern of repercussion.

An interview schedule was designed initially to explore four main topics. These were:

- How the patients found out about the trial
- Patients' thoughts before entering the trial and their previous experiences or knowledge of clinical trials
- Patients' experiences of being on the trial
- How the patients would improve or change the trial

As the interviews progressed, this interview schedule altered as topics emerged, grew or receded in importance. Copies of the first and final interview schedules can be found at appendix F and G.

At the start of an interview these topics were covered with open questions to allow patients to raise areas that were important to them. I explored these areas with patients, using a range of initially open and latterly closed questions during each interview to fully understand their opinion or experience. I tried to allow patients to put across their views as much as possible while keeping them on the topic of interest. I was mindful of the art of the second question, as discussed by Kvale, and

tried to consider future data analysis during the course of an interview (Kvale, 2009). As I was unlikely to be able to contact patients again after the interview, it was important to consider and ask any further questions that I might have during the interview rather than be left speculating about a topic at a later date.

Interviews ranged in time from 20 minutes to over an hour. Once I had completed my questions, patients were given the opportunity to mention anything else that had not been covered. Patients usually did not have anything else to add at this point and the recording would be stopped.

#### *After the interview*

After I stopped the recording I conducted a debriefing session with the patient. This involved asking the patient how they had found the interview and what we had discussed. I was aware through previous reading that patients may have wanted to say something after the recording had finished (Kvale, 2009). My aim was to give them this opportunity. However patients did not feel the need to say anything ‘off the record’ which they had been unwilling to say during the interview. Again I accepted any offer of food or drink before leaving. Once in my car, I recorded my own views on how the interview had gone and on the surroundings of the house and the condition of the patient. This helped in future analysis to remind myself of the patient interviewed and as part of the reflective process. I described areas of the interview that were new or had prompted new thoughts in my mind.

### **4.3.3. Transcription**

Patients were allocated a patient number in sequential order. For the transcription, their initials were used, however for any published material and throughout this thesis their sequential patient numbers are used. Similarly any mention of any professional staff members by name has been anonymized. Every new statement by the patient was numbered for ease of reference during data analysis.

The transcription of your own interviews allows a researcher to gain great depth of intimacy with the data. However, it is also time consuming with every hour of recording taking approximately eight hours of transcribing. As this project was conducted two days a week over a two year period, I did not feel that the full transcription of every interview was a justifiable use of my time. Some of the interviews were transcribed by a medical secretary. However, I transcribed over half of the interviews. Of the interviews that were not transcribed by me, I went over the transcripts with the recording to check for the validity of the transcript. I often found that I was able to fill in gaps in the transcription that the transcriber had not been able to decipher as I could remember the conversation as it had happened.

Once the interview was transcribed, patients were given the opportunity to be sent a copy. They were invited to read over the transcript and contact me if there was anything that they were not happy with or that they wished to discuss further.

### **4.3.4. After the interview**

Once a patient had taken part in an interview, I entered their anonymous details onto a database. This included their demographic details, cancer diagnosis and in which

trial they had taken part. A list of the participants can be found at appendix H. I informed their GP that they had taken part in the study with a letter.

As previously mentioned, a copy of the transcript was sent to patients. However, I found that no patients contacted me to discuss their interview. I did see one patient some time later at the hospice during my clinical work. Although he had not contacted me at the time, he told me that he and his wife had enjoyed reading the transcript and remembered the interview very well. I was pleased to receive this information as although patients may not have contacted me, I felt that they or indeed relatives after a patient had died may have taken some pleasure in having a document of their views and nuances in speaking to look over in the future. This could be along similar lines to Prof Harvey Chochinov's work into dignity therapy (Chochinov, 2009).

#### **4.4. Assessment of quality**

In the methodology chapter, I outlined the steps taken to ensure the quality of research. These are now discussed in more detail.

##### **4.4.1. The interview process, the accuracy of interview data and member checking**

Throughout the interviews, I remained flexible with the interview schedule and allowed patients to discuss issues that were important to them. The intention was to allow patients to feel that their views were important and also to increase the potential of patients bringing a new insight into a particular topic. As the interviews progressed and the schedule changed, I altered the direction of interviews into areas

that I felt were underdeveloped rather than going over similar points to previous patients.

The interviews were transcribed verbatim either by me or by the medical secretary. I reviewed all transcripts while listening again to the interviews to aim for the most accurate transcript possible. Some comments were inaudible despite best efforts and these were annotated on the transcripts. The transcripts were also sent to the patients to give them the opportunity to read the transcripts to either correct a statement or expand on a topic. No patient took up this opportunity to contact me.

#### **4.4.2. Peer debriefing**

The interviews were read by one of my supervisors, Dr Laird. We would discuss my questioning and the data that were being generated. This also happened on two occasions with an independent person, Prof Mari Lloyd-Williams over May and June 2010.

#### **4.4.3. Presentation of data**

A poster of the main findings was presented at the *European Association of Palliative Care Annual Meeting* in Lisbon in 2011. I also gave an oral presentation of the study in St Andrews Hospice, Airdrie to a group of multidisciplinary professionals.

#### **4.4.4. Theoretical sampling and negative case analysis**

The sampling of patients had the intention of examining the widest range of experiences of advanced cancer patients taking part in clinical trials. Attempts were made to conduct a negative case analysis of patients who it was felt had not had a

good experience of the trial. However, it was not possible to recruit these patients to take part in the study.

#### **4.4.5. Audit of analysis process**

Appendix A gives an in-depth description of the data analysis process from initial coding up to the generation of the central theory. The intention is that the reader is able to see the steps that were taken to build up the concepts of the generated theory.

#### **4.4.6. Use of thick description**

Thick description is considered appropriate for demonstrating the potential for the transferability of a study (Seale, 1999). My findings have been presented with thick description of the responses of patients, both in summary and direct quotes. I have also described the methods used in detail.

### **4.5. Conclusion**

This chapter has outlined the processes that took place during the running of the study. I have described how patients were selected to be approached, the process of patient recruitment and the interview situation. I have also described the processes that attempted to ensure the study was conducted to a high level of quality.

Data analysis has been discussed in a theoretical manner in the methodology chapter. Appendix A outlines the process of the data analysis in this study with examples used to illustrate the description. The next section looks at the results of data that were generated during the interviews.

## SECTION 3 – RESULTS

The results section is made up of chapters five to nine. The results are divided along a linear time frame. Chapter five looks at patient experiences before starting the trial. Chapters six, seven and eight look at patient experiences during the trial. Chapter nine looks at patient reflections of being on a trial.

I have chosen to present the data in this way as a reflection of the initial interview schedule. The interviews naturally flowed along a linear manner which I think myself and the patients intuitively expected. As the interviews developed, I did not adhere to this pattern in the interviews but still kept this in my mind for the analysis. Before I developed the overriding theory of the study, I conceptualized the study over a linear time frame to aid the data analysis.

The majority of the data related to the time when patients were taking part in the trial. This may have been expected at the start of the study. Rather than collect these findings into one large chapter, I have divided the findings into three chapters. Chapter six, *Experiences of being on a trial*, relates largely to the practical aspects of patients' experiences of being on a trial. Within the experiences when patients were on the trial, there were two categories of particular significance. These were *Pain* and *The interaction with the trial staff*. These have been given their own consideration in chapters seven and eight.

The conclusions and overriding theory of the study are examined in Section four, Discussion.

### **Sampled Patients**

Figure 3 is a CONSORT diagram detailing the patients who were eligible to take part in this study.

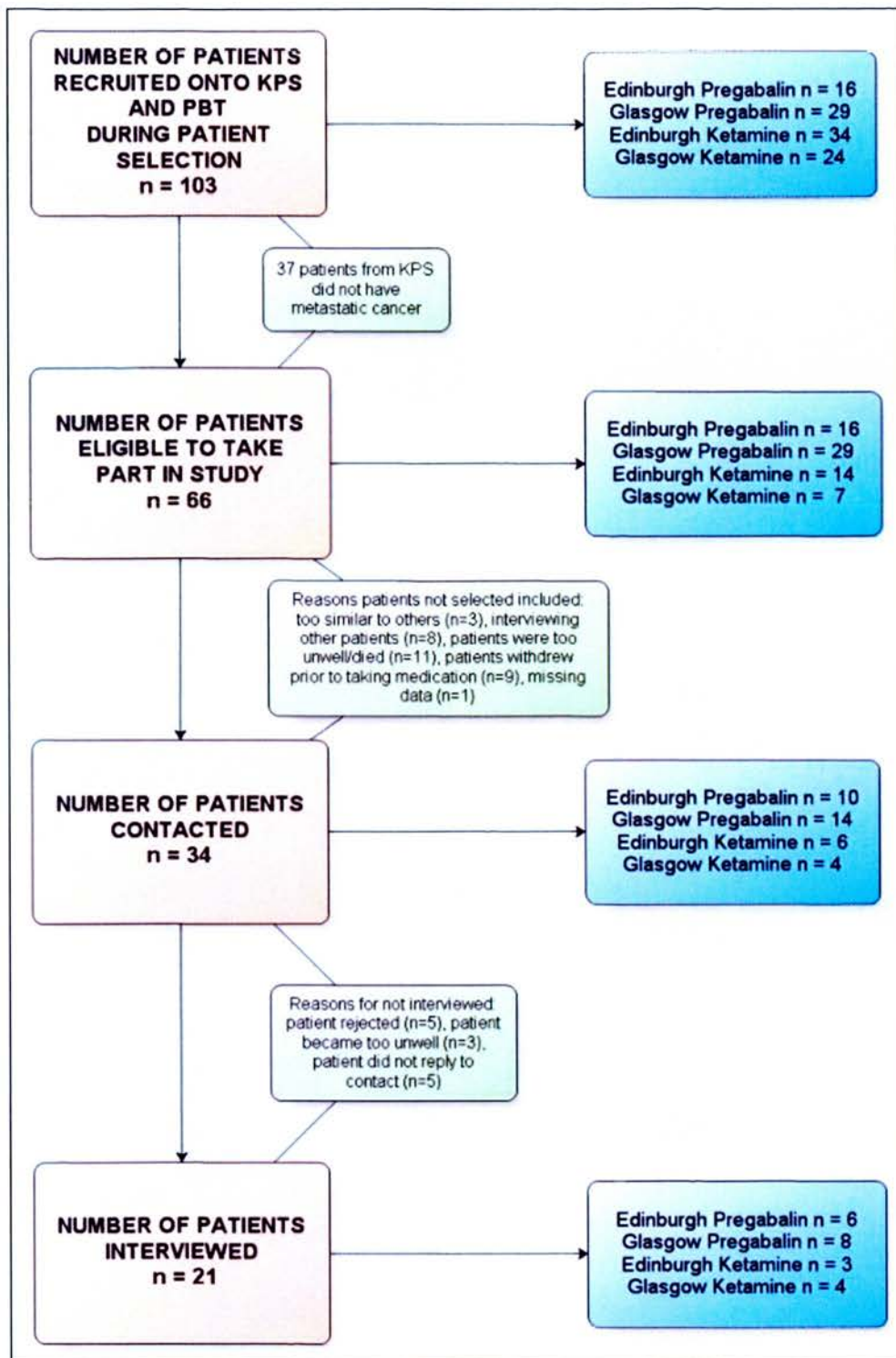


Figure 3 – CONSORT diagram of patient recruitment

## Patient Demographics

Table 3 shows the demographics of the patients who took part in this study.

**Table 3 – Patient Demographics.**

Patient	Sex	Age	Primary Cancer	Trial Centre	Trial	ECOG	Days Between Interview and Death
1	M	61	Lung	Edinburgh	KPS	1	Still alive
2	M	49	Chronic Myeloid Leukaemia	Edinburgh	KPS	2	Still alive
3	M	74	Prostate	Edinburgh	PBT	3	221
4	F	58	Breast	Edinburgh	KPS	3	Still alive
5	M	57	Lung	Glasgow	PBT	2	43
6	M	48	Pancreas	Glasgow	KPS	1	390
7	M	55	Head and Neck	Glasgow	KPS	0	Still alive
8	M	77	Gastric	Glasgow	PBT	2	116
9	M	57	Prostate	Edinburgh	PBT	1	82
10	F	48	Breast	Edinburgh	PBT	1	Still alive
11	M	63	Prostate	Glasgow	PBT	1	Still alive
12	M	72	Prostate	Glasgow	PBT	1	Still alive
13	M	72	Prostate	Glasgow	PBT	2	Still alive
14	M	69	Prostate	Edinburgh	KPS	1	62
15	F	60	Breast	Glasgow	PBT	2	30
16	M	66	Pancreas	Edinburgh	PBT	3	95
17	M	68	Renal	Glasgow	PBT	3	223
18	M	63	Prostate	Glasgow	PBT	2	Still alive
19	F	64	Breast	Edinburgh	PBT	1	Still alive
20	F	59	Breast	Glasgow	KPS	2	Still alive
21	F	63	Breast	Glasgow	KPS	2	Still alive

(patients still alive at 13/10/11)

Table 4 shows a comparison of those patients who were recruited into the study with those who were eligible to take part in the study but were not recruited.

**Table 4 – Comparison of recruited and eligible patients’ demographics**

	<b>Interviewed Patients</b> n=21	<b>Eligible Patients</b> n=66
<b>Gender</b>		
Male	15 (71%)	38 (58%)
Female	6 (29%)	28 (42%)
<b>Age</b>	mean = 62.1 years (range 48-24)	mean = 62.1 years (range 32-84)
<b>Diagnosis</b>		
Breast	6 (29%)	20 (30%)
Colorectal	0 (0%)	4 (6%)
Haematological	1 (5%)	6 (9%)
Lung	2 (10%)	9 (14%)
Prostate	7 (32%)	15 (23%)
Other	5 (24%)	12 (18%)
<b>Trial</b>		
KPS	7 (33%)	21 (32%)
PBT	14 (67%)	45 (68%)
<b>Trial Site</b>		
Edinburgh	9 (43%)	30 (45%)
Glasgow	12 (57%)	36 (55%)

Although when recruiting, achieving a proportionally representational sample was not the aim, what the table does show is that an appropriate number of patients with differing variables such as age, sex, diagnosis, trial and trial site were interviewed.

## **Chapter 5. PRE-TRIAL EXPERIENCES**

This chapter examines the experiences of patients before the start of the trial. There were three main topics that arose from the interviews regarding the period of time between when the patients had their first contact with the trial staff and when they started the trial. These three topics were:

- Personal prior experience in a trial or prior knowledge about clinical trials
- The reasons why patients took part in this trial
- Patients' views on placebo medication and taking part in a placebo controlled trial

They are discussed consecutively in this chapter.

### **5.1. Prior experiences of clinical trials and deciding to take part**

#### **5.1.1. How aware of clinical trials were patients before they are approached?**

The awareness of the concept of clinical trials varied amongst the patients studied. Some patients had never heard of clinical trials. Other patients had spoken to friends who had heard of clinical trials. Some patients had been on other clinical trials in the past or had known friends or relatives who had taken part in clinical trials. Those patients interviewed who had been aware of clinical trials before taking part in this one had various views towards them. Many patients believed in clinical trials and the benefits that they can have, both to current and future patients. As these opinions and others were linked to their views of the clinical trial they had just taken part in,

this is discussed in more detail in chapter 9.2.

Within the group of patients who had been aware of the concept of clinical trials, the extent of their knowledge varied. Some patients had a good understanding of clinical trials while others had only a broad overview. Pt10 gave a good example of how her knowledge changed before and after the trial. Before starting the PBT, she thought that it was only novel agents that were used in clinical trials.

*'Tom: Are you, were you aware of the concept of clinical trials before.....they'd spoken to you?'*

*'Pt10: ...yes, I always thought they were a brand new, eh, well obviously there are some brand new drugs, and, and you don't know what the side effects are going to be however, this, eh, was something that had already been in use...'*

To me this showed that she had processed both her initial knowledge of clinical trials and her new knowledge about this particular clinical trial to realize that her initial knowledge was only limited to novel drugs.

### **5.1.2. How did the patients first hear about their trial?**

My first thought on patients in these trials was *'Where do they come from?'* From a patient's perspective the question may be turned round; *'How do patients first encounter trial staff?'* Patients described being approached by trial staff after oncology out-patient appointments. Sometimes patients had been told by their oncologist that they might be contacted by the trial staff; at other times patients met the trial staff for the first time without being aware that they were eligible for participation in the trial.

*'She made contact. Um, it wasn't something that was a consideration, I mean it's not something I went looking for, um, but she made contact' (Pt16)*

Some patients however did actively offer their services for suitable trials.

*Tom: Had, had you heard about clinical trials before they approached you?*

*Pt11: Yes, yes, I heard about them, know what I mean, I heard about clinical trials and I told [Clinical doctor 1] that I was prepared to do any clinical trials that he wanted me to do.'*

Although a lot of patients had not considered taking part in a trial before they were first contacted, the association of the trial staff with the oncology department made patients at least consider taking part more carefully. The ways in which the trial staff seemed to be associated with the oncology department were by meeting patients in oncology out-patient clinics or by mentioning that the patient details had been given to them by an oncologist. Patients described other clinical trials that they had rejected when they had been contacted without warning by post or telephone, feeling that these trials were not connected with their current care. This opinion was strengthened after speaking to one particular patient. He told me that because I was first introduced to him by one of the trial nurses that he knew, he was happy to be interviewed for my study because of the faith he had in the trial nurse.

*Pt9: the other thing, last Monday, you turned up with [Trial Nurse 1]....*

*Tom: yeah...*

*Pt9: Now, because I trust [Trial Nurse 1], it was easy when you said 'I want to do this,' it was easy to say 'Oh right fine we're in the same team here'...*

*Tom: yeah...*

*Pt9: Let's go, you know, you said 'Would you like to read this?' and I said 'No no, just make an appointment'. So because of the trust issue with [Trial Nurse 1] and [Trial Nurse 1] introduced me to you, it was quite easy for me. Now if you had phoned me up and said, 'I'm Tom Middlemiss, and I'm doing a survey...' I'd have probably said 'Yes' but because of how it was done, it was easier for me to say yes.'*

At the first meeting, patients could be approached by one or more members of the trial staff. This was usually described as a straightforward event for patients. For

some patients though, this first encounter came as quite a surprise:

*'the first day they spoke to me they actually hijacked me.....as I was getting, clothes back on and getting sorted, one of the girls said 'Oh, there's two research people waiting for you.' And I came out and they were sitting and said, they both came up and said 'Hello' and I felt 'Wow! Wow!' you know 'Boom' you know, I've just walked out of there and I'm here. Well, then we went off to a room and we did what we had to do,' (Pt9)*

Pt9 subsequently chooses to re-phrase his choice of words, but the term *'hijacked'* is an evocative one. Other patients used *'confronted'* and *'persuaded'* when talking about their initial contact and entry into the trials. The impression I received from these patients was that it was a slightly unsettling experience. This may have been due to the number of people waiting to see the patient or the way in which they were approached in a sudden manner. A combination of both may have created their feelings. Although the episode was clearly not enough to put these patients off taking part in the trial, it made me aware that the first meeting with trial staff had the potential to be stressful for the patients.

### **5.1.3. Patient understanding of the trial they were taking part in**

Trial staff spent time with patients to explain what was required when taking part in a trial. Patients were also given an information sheet that explained their prospective trial, and any potential side effects that could occur, in plain English. Patients were then given time to consider taking part in the trial with the opportunity of contacting the trial staff with further questions if necessary.

In the group of patients that I studied, my overall impression was that patients had a good understanding of what the trial consisted of and what was required of them.

*'...it was all pretty plain sailing... I don't, I can't remember anything out the*

*ordinary... that happened or I expected, or didn't happen or that, you know. It was just all, get the tablets, take the tablets, finish them or hand them back or whatever and speak to the, speak to the girls. No there was nothing out of the ordinary.'* (Pt12)

However some patients did have misunderstandings about parts of the trial. Pt5 thought that in the randomization part of the trial, he would receive a combination of real and placebo medications with the daily pain scores indicating to the researchers which one of the two he was on each day.

*'Pt5: Probably, I think there were a hundred drugs in it, the chance is fifty-fifty. (laughs)*

*Tom: That's right*

*Pt5: You know, so....*

*Tom: You were happy with that?*

*Pt5: I was happy with that, taking, you know, if I can get three good ones, three nights in a row, or you could get five good ones, and then, you know.'*

This same misunderstanding was reiterated by Pt18 later in the interview process. It may be expected in clinical trials that a proportion of patients will show misunderstandings when questioned at a later date.

Patients did remember receiving the information sheet but their recollection of its content could be poor. They may have only read it once, confused it with many other information sheets they have been given or not read it at all.

*'Tom: I think you were given an information sheet?*

*Pt12: Probably, I've been given so many ...during that...*

*Tom: Do you particularly remember it?*

*Pt12: Not particularly no, being honest, no.*

*Tom: Are they the sort of thing that you do read?*

*Pt12: Oh yes, I read them, I read them, oh don't get me wrong. Although I can't, I can vaguely remember getting it, actually, but oh no I would read these things.*

*Tom: You do read them.*

*Pt12: I do read them. Yes.*

*Tom: And do you remember the content of it, or, or...?*

*Pt12: No. (chuckles)*

A view held by some responders was that the researchers had explained everything to them, negating the need to read the sheet. Anything serious regarding the trial would have been explained to patients. Others, such as Pt20 want or expect everything to be explained to them:

*'Pt20: Oh, don't put it down on pieces, pieces of paper because I don't, I won't understand half of what you put down on pieces of paper.*

*Tom: Really.*

*Pt20:....well I, you need to tell me, face to face what's going on, and I will ask you face to face, tell me what I'm doing, I prefer you to tell me what's going on, then I can take it in better, then I know what's going on, yeah, if you explain to me, then I'm quite happy, if somebody explains to me what's going on, I'm quite happier.'*

Pt20 was expressing the desire for more discussion rather than the information being transferred by a written document. However, she did go on to say that she would give the information sheet to her husband or son to consider before agreeing to take part in a trial.

Knowing the trial as intimately as trial staff do, it may be hard to imagine that a patient would want anything other than a desire for a complete understanding of the intricacies of the trial. However some patients seem happy to have a vague

understanding of what they are taking part in and to place their trust in the trial staff to guide them through the process.<sup>1</sup>

#### **5.1.4. How patients decided to take part in the trial**

How did patients decide to take part in the trial? Clearly, there were many reasons for taking part and these are discussed in chapter 5.3. Before deciding however, some patients discussed the trial with other people. Some patients talked over the decision with their GP while others spoke to family members.

*Tom: did you um think about it, or discuss about it, discuss it with anyone else before agreeing?*

*Pt10: Ah, yes, I spoke to my husband, my son, uh, my Dad (laughs) , ahm, but eh, really it was a no brainer, it was eh, it was the idea of pain relief is always a brilliant thing and eh, um, I do agree with the principle of why they're looking at it.'*

The people that patients discussed taking part in the trial with had the potential to act as a significant influencing power. Patients described GPs looking over the information sheet and allaying any concerns they might have. For example, patients reported that their GPs reassured them that the medication being trialled was one that was already in common usage with a good safety record behind it. Conversely, patients described times when their GP had advised them not to take part in other trials that they had been contacted about.

Other patients needed no time to consider their options and had no need to discuss their decision with anyone. To them, the severity of the pain merited taking part in the trial.

*Tom: What were things like at the start?*

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<sup>1</sup> The issue of trust in relation to researchers is discussed in detail in chapter 8.4.3 *Trust of the staff*.

*Pt17: Oh, it was awfy sore you know....Especially from my bottom. I don't know what that wee bone is called at the bottom of your....*

*Tom: Coccyx...*

*Pt17: ....spine. Coccyk, yeah, that' it coccyk, I mean I was having terrible, terrible pain in it. It's alright if I lie down....but as soon as I get up, sit in a chair, oh, it's murder...*

*Tom: mmm*

*Pt17: Ken what I mean, I could sit in the chair for about five or ten minutes, then I've got tae get up and use my walker [..], then come back to my bed..*

*Tom: mmm*

*Pt17: Just can't take the pain.*

*Tom: mmm*

*Pt17: But I thought that maybe the pill, that the pill, be able to shift, something to do without. It would maybe take the pain away, you know.'*

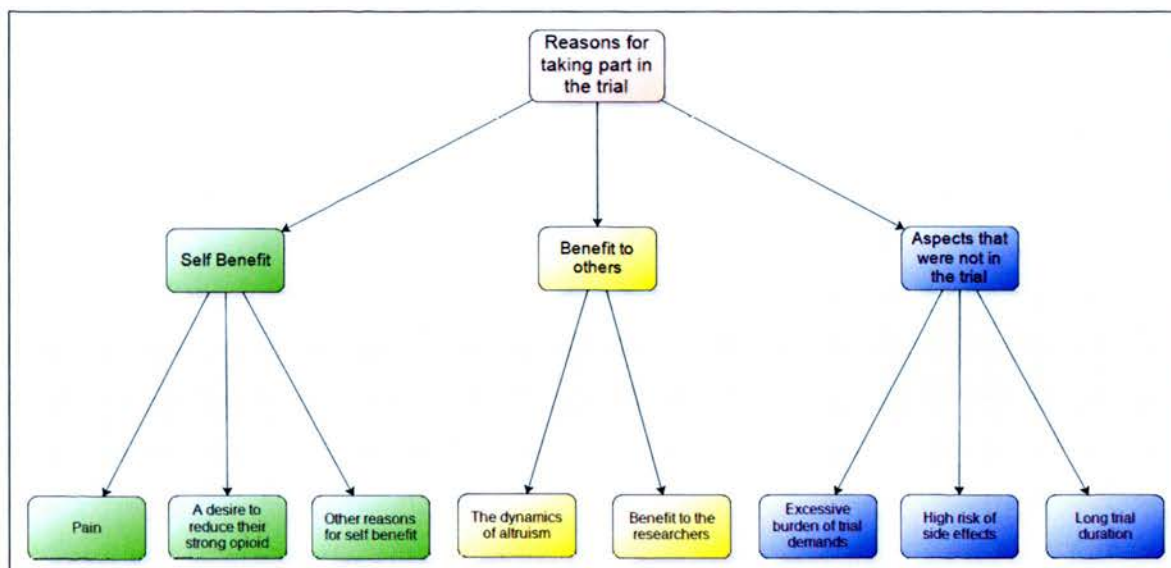
Other patients were very relaxed about taking part, '*...what the heck, I'll do it'* (Pt16).

## **5.2. Conclusion – taking part in a trial**

The patients were approached by the research team, given information about the trial, allowed time to think about the trial and then recruited onto the trial if they were willing to take part. Patients had a wide range of previous experiences of clinical trials prior to taking part and varied in who they discussed the trial with before consenting.

## **5.3. Reasons for taking part in the trial**

A summary of patients' reasons for trial participation is shown in Figure 3.



**Figure 3 - Reasons for trial participation**

Pt20 stated *'I would never say no to a trial.'* Such an absolute statement was rare but what were the other reasons for patients wanting to take part in this or in any trial?

As can be seen in Figure 3, the reasons that patients stated for taking part in the trial were numerous. Some reasons were common and were predicted before interviews began. Other reasons were individual and surprising.

The all-inclusive reason for a patient taking part in a trial was for someone to benefit. The person to benefit could have been the patient themselves, someone else, or both at the same time. The relative importance of who benefits varied between patients. A patient could be happy knowing that they and others benefited at the same time.

This part of chapter five looks at the patients' reasons for taking part in a clinical trial and who benefits from them taking part. When patients discussed others benefiting, they were referring to both other patients and the researchers themselves. This section also looks at elements of the trial that were not present which acted as

motivating factors for patients to take part.

### **5.3.1. Self benefit**

#### **5.3.1.1. Pain**

Patients recruited into the trials had not had satisfactory pain control up until that point. If they had, they would not be eligible for the trial. Patients had to have a consistent level of pain to enter either trial and in addition to this, also had to maintain a significant level of pain after a period of optimal pain management with conventional treatment medications<sup>2</sup>. So when the option arose to control the pain by entering the trial, some patients were willing to take it. As to be expected from such a subjective topic, the degree of pain that patients felt varied. Some patients did not recall having any pain at the start of the trial while others described pain so severe that it made them question whether their life could be tolerated.

*'I was waking up during the night an', just wanting somebody to do away with me...that how much pain I was in.'* (Pt5)

Pt6 also remembered his pain in similar terms:

*'I'd 'a given anything a go at that point because the pain was ridiculous.'*  
The origins of pain and what pain meant to patients, was beyond the scope of this study and was not explored in detail. However patients were encouraged to describe the impact of pain on their lifestyle. Patients reported that family dynamics altered, relationships with partners were strained and social activities were curtailed.

*'Tom: How do you, how do you find it when your family see you in this situation, when you're being affected by the pain...*

*Pt6: I don't like it. I don't like them seeing me. I don't mind being in, I don't say I don't mind being in the pain, but I can live with being in the pain*

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<sup>2</sup> More in depth details of both trials can be found in appendices B and C

*(cough) when they're at school because they don't see me struggling, they don't see me. But it's when they come home at night, you try and reverse everything, you try not to be in pain, you try not to show them that you're in real agony and you're struggling.'*

Patients struggled to leave their houses when racked with pain. One patient's guitar playing fluctuated with the degree of pain he was in. The increased number of hours spent playing the guitar indicated that his pain medication was working.

### **5.3.1.2. A desire to reduce their strong opioid**

Patients talked about the strong opioids that they were taking in addition to the trial drug. A fear of opioids and its connotations existed in this patient population. It is something which I have also encountered anecdotally in my clinical work and is recognized in the literature (Sun et al., 2007, Davis and Walsh, 2004). As in my clinical experience, this fear of opioids was countered by the acknowledgment of their effectiveness. Patients were concerned that they may become immune to opioids in the future or that their effect would run out.

*Pt7: I don't like taking them, I try not to take them.*

*Tom: Why is that?*

*Pt7: I dunno...I think in case I maybe need them later on, you know. If the pain is really.....*

*Tom: Do you think they will run out, or, or ...?*

*Pt7: I think you'd get sort o' immune to it, you know.'*

The addictiveness preconception that is well recognized in the literature was also present in the patients I studied (Sun et al., 2007, Davis and Walsh, 2004).

*Tom: So, so am I right in saying that morphine's a drug that you don't really enjoy taking?*

*Pt11: No I don't, no. It's just not doing any harm at all, it's just the name, I think it's just the name.*

*Tom: Do you think, what, what d'you, can you elaborate on that, on that a bit?*

*Pt11: Because it's morphine. Because it's a heavy, heavy doses and different things, you know what I mean? Because of its addictiveness.'*

Patients described their experiences of common opioid side effects, such as over-sedation and constipation.

There was a hope expressed by patients that being on the trial medication would allow them to reduce the quantity of opioid that they took. Trial drugs could be seen as the lesser of two evils.

*'Tom: What are you going to get out of the pregabalin trial?*

*Pt14: Well, I mean to say, it did the, could stop the, the, the pain., the...*

*Friend: Morphine.*

*Pt14: ...morphine. Eh, that'd be quite a good thing because I mean to say, it's, they're powerful drugs.*

*Tom: Mm, mm.*

*Pt14: The pre model.. whatever they call it...*

*Tom: Pregabalin.*

*Pt14: Pregabalin, I mean to say, it's quite a powerful drug an' all, but it's not nearly as powerful as the, as the ...*

*Friend: Morphine.*

*Pt14: morphine.'*

Patients described feeling happier on the trial medication rather than on an opioid. Pt7 was 'more fun' according to his wife on ketamine rather than on his opioid as he was able to have an evening drink. Pt10 and Pt11 had fewer concerns about driving while taking pregabalin than when taking opioids.

### 5.3.1.3. Other reasons for self benefit

Some patients felt that their care lacked a coordinated effort by healthcare staff. Pt11 took part in the trial with the desire of creating a better '*structure*' of care. He gave the example of feeling uncertain about his medication regimen. He felt that taking the correct medications was his responsibility and this created an anxiety in him:

*'I felt that I was self-medicating....So this gave me the chance, [Research doctor 1] gave me a chance to structure the drugs.'* (Pt11)

Some patients showed a lack of insight into the aim of the trial by wanting to control symptoms of nausea as the primary reason for taking part in the trial. Other patients saw the trial as something else to add on to their treatment:

*'It might be good for me, it might not, so let's go for it.'* (Pt9)

The experience of taking part in other clinical trials was also a motivating factor for some patients. They felt that they received additional input from trial staff during a clinical trial and this motivated them to take part in this trial. A good experience from a previous trial was either related to the outcome of the trial, or simply from getting more attention, which was reported as a welcome experience in itself.

*'Pt9: ...So, then to be told that you're just being monitored, you think, 'Wow!' However, I'm happy because, I'm getting the attention...*

*Tom: yeah*

*Pt9: ...that a lot of people aren't getting because I'm being monitored every 6 weeks. So, it's a bonus.'*

It did not necessarily follow, however, that bad experiences of previous trials put off patients from taking part in this trial. Pt17 described a bad experience that he had had in the past with a different trial and yet he was still willing to take part in this trial.

*Tom: So....you'd been on that trial, of that....pill, that 'nearly killed you,' like you say...*

*Pt17: Uh-huh.*

*Tom: ....and it was after that, that you were approached, by the research team to on to this pregabalin trial, is that right?*

*Pt17: Uh-huh.*

*Tom: ....after having had such a...bad experience with the first trial....*

*Pt17: mmm-hmmm*

*Tom: ....were you anxious what might happen to you on that trial?*

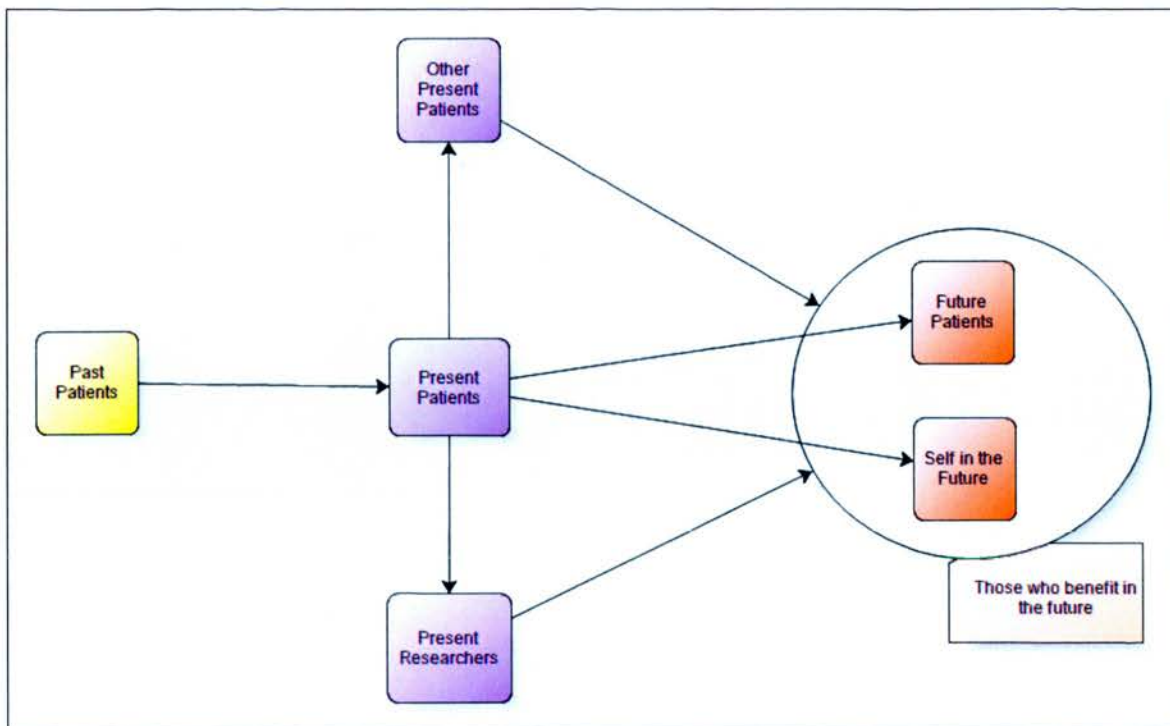
*Pt17: No I wasn't anxious....no, not at all...I was still of the mind, that I might find something you know, to help...'*

### **5.3.2. Benefit to others**

Apart from patients' desire for self benefit, a strong motivating factor to take part in a clinical trial was for the benefit of others. An action that benefits others can be described as altruistic. For some patients this was the only stated motivation for taking part, particularly if they felt that there was no personal pain to relieve, but this viewpoint was unusual. If a patient did feel that their actions were for the benefit of others, it was usually in association with benefit to themselves. The mutual benefit sat easily with patients and the fact that others were benefiting at the same time seemed to be comforting.

#### **5.3.2.1. The Dynamics of Altruism**

The dynamics of altruism are summarized in Figure 4.



**Figure 4 - Dynamics of Altruism**

When some patients were reflecting on their care and treatment, they realized that they had benefited from similar altruistic actions of patients in the past.

*Pt6: At the end of the day, if you didn't have people to try trials, you didn't get this guy who had cancer, I wouldn't be at this stage with my pain, so you've gotta, there've gotta be guinea pigs along the line somewhere.*

*Tom: So you're happy to be one?*

*Pt6: I'm quite, I was quite happy to be one on that case study, yeah.'*

At any time, there was a dynamic process of altruism. Firstly, patients were benefiting from previous patients' efforts. At the same moment, patients were offering a benefit to other patients, both in the same process as them and other patients, including themselves, in the future. I will explain this in more detail.

All patients have benefited from patients before them, whether through structured clinical trials or by anecdotal evidence and the experience of their doctors. A drug

that a patient takes has been used with good effect by someone before them. Pt6 realized this fact as shown in the quote above. His insight allowed him to see those who had gone before him and gave him the desire to act as a 'guinea pig' for the benefit of others in the future. He acknowledged that his desire was to help himself but at the same time he showed his desire to help others. Patients commonly cited their own children or grandchildren as the people who might benefit in the future.

*Tom: did you um...did you have any um...did you take part in the trial for any reason apart from yourself?*

*Pt19: Um, well you never know if it might do some good somewhere along the line, you know what I mean?*

*Tom: Yeah*

*Pt19: And um, I mean, this is the secondary breast cancer and I've got five daughters so (laughs), so I've got an interest in how the...um,....everything goes for that you know. So yeah..*

*Tom: Was that a sort of motivating factor as well?*

*Pt19: Mmm'*

I think that 'helping others' is quite vague and so for some patients, putting their own family in the category of people who may need help in the future allowed them to personalize the altruistic act.

Pt4 stated that part of the reason for taking part in the study was for the benefit of others. While the benefit of future patients was a common, and expected motivating factor, she stated that she felt she was helping other patients in the same trial as herself. Her rationale was that if she was to receive the placebo, others in the trial would be more likely to receive the active drug. This was a new concept that I had not considered.

*Tom: Okay. And so who, who were you helping, or who did you feel you were helping by taking part...*

*Pt4: Myself as well. Any maybe other people that were going to do, do a survey, I mean, if that drug helped me, I would say "Brilliant, that, I had the proper drug and it's helped me." ...*

*Tom: Yeah.*

*Pt4: ... and things like that, you know.*

*Tom: But...*

*Pt4: But that, but that drug just didn't help me.*

*Tom: Did you feel that there were other people you were helping as well, apart from yourself?*

*Pt4: Yeah, other people that were gonnae do the survey eh as well. Maybe they got the proper drug.*

*Tom: Right.*

*Pt4: You don't know.*

*Tom: Okay.*

*Pt4: If they would get the proper drug...'*

Pt10 wanted her own pain to improve as well as wanting to help others in the future who had the same pain. She counted herself as one of the people in the future whom she hoped would benefit from the current trial:

*'There was the idea of helping people in the future and hopefully me in the future, selfish little so-and-so that I am! Because I know my cancer's going to come back and keep coming back for many, well hopefully, touch wood, many years...and um, um hopefully I'll be able to get some of this pregabalin as a proper drug....in the future,' (Pt10)*

Again I had not considered that patients would view the benefit to themselves both in the present and in the future.

Although not asked by myself to quantify specifically the division of where the

benefit lay, several patients stated spontaneously that the motivation was evenly split, 'fifty-fifty' between the benefit to themselves and to others.

### **5.3.2.2. Benefit to the researchers**

*Tom: ....the potential reason for that (having no benefit from the trial) may be that you've been on the placebo....*

*Pt3: ...indeed...*

*Tom: ...how you feel about the fact that there's a possibility of you going onto a trial with no benefit?*

*Pt3: Well there is a benefit, to the people running the trial....'*

Pt3 described another beneficiary of the research apart from the patients themselves. Although the ultimate gain from researchers benefiting is to benefit future patients, he also described the current benefit to researchers.

### **5.3.3. Aspects that were not in the trial**

When considering whether to agree to take part in a clinical trial, patients weighed up what the trial would involve for them. Was it worth it? To be 'worth it' a trial had to have a greater perceived benefit than burden. In the eyes of the patient, and as discussed above, the benefit from the trial did not have to be solely for the individual taking part. Conversely, patients only considered the perceived burden that they themselves would encounter. Patients described three areas of the trial that appeared favourable when considering what the trials did not contain rather than what they did. These three factors were an apparent lack of excessive trial demands, a perceived lack of possible side effects and the lack of a lengthy trial period.

#### **5.3.3.1. Excessive burden of trial demands**

Patients spoke of fatigue in their current state. Their mobility was reduced, their day

could be dominated by pain and their usual activities were curtailed. A clinical trial which did not create an additional and excessive tier of complication to a patient's existence was attractive. The clinical trials that the studied patients took part in were designed specifically for their target patient groups. Each had a deliberately small number of hospital visits, blood samples and complex assessments. Patients understood this and were attracted by the lack of these burdensome activities.

Pt15 had breast cancer with axillary node clearance from one of her arms, rendering that arm unusable for blood tests. Her concern about the frequency of blood tests had made her reject clinical trials in the past despite a desire to take part.

*'If I can do it, I'll do it. Um...the blood test's the, you know, I'd kind of read through it and if it says, bloods, or blood tests every two weeks or something, I'm no' interested....'(Pt15)*

The two main requirements of the trial from a patient's perspective were to take the prescribed tablets and to receive telephone calls from the research staff when arranged.

*'I was persuaded a bit more by the fact that it was only going to last for a short time and it wasn't going to really, cause me any hassle, in the sense of having to go anywhere, or go to the hospital, get ah...it was all going to be done locally or on the end of a telephone.'* (Pt3)

### **5.3.3.2. High risk of side effects<sup>3</sup>**

A topic that I thought I would have to concentrate on at the start of the study was the risk of medication side effects. With my medical background, the topic of side effects of any drug is continually pertinent. I would think this to be particularly the case in clinical trials. The counter argument to this, however, is that ketamine and

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<sup>3</sup> The occurrence of actual or perceived side effects is discussed in chapter 6.2.2

pregabalin are already licensed drugs, with a good safety profile, and are used commonly in the treatment of pain in the palliative care setting. Ethics committees are stringent regarding the potential harm that could occur to patients who participate in clinical trials and one of the most common concerns is that of the potential side effects of medications given. Although the potential side effects were explained in the information sheet that patients were given at the start of the trial, the recollection of these potential side effects is variable. Pt10 pointed out that the trial medications were already established drugs in general usage for other purposes. This information gave her the peace of mind not to be overly concerned by the potential of side effects. Some patients showed an informed attitude towards the balance of risk and benefit in clinical trials. They were willing to accept a degree of risk given the potential benefit. *'Well, having been on so many drugs, if you read all the forms, you wouldn't go on any drugs and you would just die!'* remarked Pt9.

Other patients showed a lack of awareness of side effects.

*'Tom: Ah was that described to you? The potential side effects of the pregabalin?*

*Pt8:uhhhh.....*

*Tom: Were you made aware of that?*

*Pt8: No. I knew it had something to do with nerves, but eh, the nuts and bolts of it no.*

*Tom: No? OK, OK. So that wasn't a concern of yours that there wasn't any side effects?*

*Pt8: I was just assured by the fact that it would have no adversal [sic] effects, by adverse I include pain, or anything which is of an uncomfortable or unpleasant nature.'*

I was concerned that Pt8 seemed to have such a low concern for the potential side effects of the medication that he might be taking. However the medications used in

both trials are ones that I use regularly in clinical practice. Although both drugs have a recognized and encountered side effect profile, this does not prevent their usage. Perhaps patients have been told about the risks of side effects with these medications in the way that I might discuss it with a patient in the clinical setting. I describe the risks to patients but do not portray these risks in a manner beyond the severity with which I perceive those risks. In this case, perhaps I should not necessarily expect the trial patients to be overly concerned in the trial setting either.

### **5.3.3.3. Long trial duration**

Patients were attracted to the trials by the short nature of their duration (four to five weeks). Despite entering into a randomized controlled trial (RCT) with the possibility of receiving a placebo, patients were also aware that a poor response to the trial medication might result in a trial of the active drug after the trial had finished. Pt16 described his initial encounter with one of the research staff:

*'...my questions obviously were 'Is it liable to have any kind of effect on my quality of life?' and the answer was negative. Regardless of anything else we knew this particular drug trial wouldn't really necessarily affect my quality of life, however, were it to do such a thing I would, they would stop it immediately and that would be it, finished and done with.'* (Pt16)

## **5.4. The placebo arm**

Placebo drugs are common in double blind RCTs examining pain medication. RCTs are considered the form of clinical trial that generates the most robust evidence. The presence of a placebo is one of the key components to this. Placebo is a word that is familiar outside the medical world and the 'placebo effect' is also a well known concept.

All patients who go into an RCT are told that they may not get any treatment at all, yet they are still willing to take part in the study. The general reasons for this group of patients taking part in a study have been discussed above. This section looks at patients' attitudes towards placebos before they started on the trial.

#### **5.4.1. Patient awareness of the concept of placebo**

During interviews, patients would often say the word 'placebo' unprompted before I had raised it. If patients were aware of the concept of placebo before starting the trial, this was for a variety of reasons. This may have been through general knowledge, such as doing crosswords, as one patient remarked. Patients or their relatives may have taken part in clinical trials in the past which had used placebos. Pt6 stated that he was aware of the concept of placebos having worked in a hospital environment, albeit as an electrician. I asked Pt8 if he was aware of the concept of placebo to which he replied '*Of course.*' This demonstrates that along the spectrum of patients' awareness of placebos, there is a group who would consider awareness to be almost "a given" within the realms of normal life.

Some patients had never been aware of clinical trials or placebo medication before starting their trial. Whilst some went on to demonstrate their newly informed understanding of clinical trials and placebo medication, other patients showed a potential misunderstanding of the concept of placebo medication. I have already discussed the misunderstanding of Pt5 regarding placebo medication in chapter 5.1.3.

The conversation with Pt18 further illustrates the point.

*'Tom: ...but did you, did you go down one route or the other, or did you get a different sorts on different days? What was your understanding of the, of the way the dummy drugs were given to you?'*

*Pt18: ...so much o' them was dummy, and so much o' them, I don't know what ones.....*

*Tom: so a proportion of the ones you were getting....*

*Pt18: Aye*

*Tom: ...some were real and some of them were dummy....*

*Pt18: Aye, some were, some must have been real and some o' them were dummy, as far as, 'cos the pain wasnae, I wasnae getting great pain, know what I mean, some time.*

*Tom: So on the days that your pain was, better...*

*Pt18: Aye.*

*Tom: ...do you think that was the days you got a real drug rather....*

*Pt18: ...aye must have been a real one, you know what I mean, I must have got (laughing).'*

Despite the interaction with research staff and information sheets, there is still the possibility of misunderstanding regarding how the placebo is administered to patients.

#### **5.4.2. I did not mind being on a placebo**

A preconception of mine that I wanted to explore was the patients' attitudes to being on a placebo; how they viewed this possibility. Several times I asked patients if they thought that it was 'unfair' to be on a placebo. Patients were quick to deny that they thought this might be unfair.

*'Tom:..What did you think about the fact that you might be on a placebo?*

*Pt15: Well, no' much, you know, somebody's got to be. It's the only way they can find out.'*

Patients showed a relaxed attitude to being on placebo. At the very least they understood that the drug they took may not have any effect on them. Yet there were still benefits to the trial from the patients' point of view. As discussed earlier, some

patients felt a benefit would be for researchers or other patients. They reiterated their belief in clinical trials for the future and as a way in which medicine had progressed to this point.

Although some patients did not mind being on a placebo, some patients, and their family members, were curious to find out which arm of the trial they had been on. Pt16's wife came into the room where we were talking halfway through the interview. When she found out that I was not there to discuss the result of the trial, she was a little exasperated that the uncertainty remained. Pt19 was withdrawn from the trial because extreme fatigue was having too large an impact on her daily life. As no other medication had changed, she was sure that the culprit was the trial medication. However, this assertion was complicated when the fatigue continued for several weeks after the trial medication had been withdrawn. She was left with no clear idea which medication she had been on.

*'Pt19: I'd be interested to find out which one I was on, ken, I think [Research Nurse 1] said something about the summer, before I get to find out but yeah, it'd be interesting to, see which one I was on....'*

#### **5.4.3. Conclusion of the placebo arm**

The awareness of the placebo being the central point of the trial seems to be well understood. I was surprised that patients could take a relaxed attitude to being on a placebo. Some patients showed a poor understanding of the concept of placebo by thinking that the drugs they received throughout their own trial could vary.

## **5.5. Conclusion of pre-trial experiences**

I have discussed patients' attitudes and experiences of trials, the reasons why patients wanted to take part in the trial and patient opinions of placebo medication before they went onto their trials. Some patients were aware of benefits from taking part in a trial, including some benefits which were independent of which drug they would receive. Patients with previous experiences of trials felt that they would still get a higher degree of attention and input than if they were not on a trial. Another patient knew he would still get the organization of his medications which had prompted him to participate in the first place. Some patients were aware that they may be given the active drug after the trial period if they were still reporting significant pain.

The next chapter looks at the patients' experiences of being on a trial.

## Chapter 6. EXPERIENCES OF BEING ON A TRIAL

This chapter examines the descriptions patients gave of taking part in a clinical trial. It looks more at the physical process rather than their thoughts on either taking part or on the benefits they received from the trial. Patients described both positive and negative aspects of being in a trial. As well as this, they described features of a trial that had no great impact on their life in a positive or negative manner. The two most significant features of taking part in a clinical trial, pain and interaction with research staff are discussed in greater detail as separate entities in chapters seven and eight.

### 6.1. Positive features

When patients spoke positively about being on the trial, it was frequently with warmth and affection.

*Pt1: ...it's just been, perfect, it's, I've no negative thoughts at all, about anything.*

*Tom: Nothing at all?*

*Pt1: No.'*

I found it was easy for me to get caught up in the emotion of the positive feelings they had for the trial. Although I was not involved in the trial, I have worked with the staff who have been and know them individually. Along with an affiliation to your profession, these positive responses made me feel proud of the impact that the trial had had on patients. Everyone likes to hear positive responses and I was no different.

Patients described receiving clear instructions of what to do during the trial. The

patient who had entered the trial looking for structure in his medication regimen felt he had received that. Another patient enjoyed the occasional interaction with other patients who were on the same trial as her. These chance meetings in waiting rooms helped her decide to go onto the trial in the first place and also gave her confidence in the trial while she was on it. She enjoyed sharing a connection with others in a similar situation to herself.

Patients felt secure within the process of the trial. They did not feel pressurized into remaining on the trial and knew that they could withdraw at any time.

*Pt2: Easy to talk to, they've explained every situation, every part of the trial and they've always made sure that I've known that if I wanted to withdraw at any time, that's my prerogative.*

*Tom: Is that, is that an important piece of knowledge for you to have?*

*Pt2: Well it's good to know that you're not being pushed into something.*

*Tom: Yeah. And they were clear about that, were they?*

*Pt2: Oh yeah.'*

Patients felt the security of being able to contact a member of the trial staff if needed. On the information sheet were several numbers to call in an emergency. Although this brought some anxiety as to what may take place that required the calling of the numbers, having the numbers available was comforting. Patients responded to the security that this provided. Security of the trial is discussed in greater detail in chapter 8.4.2 in the context of the research staff.

Some patients found the participation in the trial to be an educational event. '*Fascinating*' as Pt15 put it when describing the neurological equipment used for assessing peripheral nerve function.

Another aspect that patients described on one site was the environment of the hospital.

*'It's like a different world.....They were just so friendly and, they spoke about things and just, made you feel dead comfortable.....It's so relaxing (Pt1)*

Another patient continued on the same theme,

*'..the [Hospital 1]'s even got this little car park for patients now which is fantastic, eh cos that was always a worry, you know, 'Where am I going to park the car?'' (Pt10)*

The atmosphere was compared favourably to other hospitals that patients had been to. Advanced cancer patients are experienced health care consumers and have spent enough time in waiting rooms and hospitals to be able to appraise the atmosphere of a health care facility. It should be noted however that as the regional cancer centre, this particular area that Pt10 describes was not specific to the clinical trials. It is small details that meant a lot to patients like Pt16:

*'Tom: Can you tell me why that's so important to you?*

*Pt16: Och it is important to people who are feeling sorry for themselves and don't know what direction they're going in. You're looking for, you're no' looking necessarily for reassurance, but you're looking for (sighs) a bit o' light-heartedness, I dunno. I've not really considered that aspect of it but that's what it's about, it's just the general demeanour of the chap who's always...always seems to be there in the, the arrival lounge area at the [Hospital 1], so nice and chatty "Can I help you get a coffee, or can you manage to get one yourself?" and it makes a difference.'*

I think that the clinical environments that the trials took place in is relevant, even if the environment was not exclusively used by the trial staff or that the trial staff were not able to influence the environment significantly. It is important because the patients described it as a positive feature of being on the trial and something that should be taken into account when considering the experiences of the patients.

## **6.2. Negative features**

Why is it important to know the features of a trial that patients thought could be improved? My view is that the answer lies in anxiety. Negative aspects that patients describe cause an underlying anxiety which researchers should be trying to avoid. Minimum anxiety may reduce patient attrition within a trial and also provide patients with an opportunity to enjoy taking part in a trial.

Advanced cancer patients have a limited life expectancy. The intention of palliative care is to address any symptoms that may cause distress, whether they are physical, emotional or spiritual. Anything that was to cause distress, or anxiety, would be against the principle tenets of palliative care. Anything that causes anxiety should be discovered and considered in an effort to reduce this if possible.

No patient interviewed stated clearly that they did not like being on the trials. As is discussed in chapter 10.4.2.1, there may be reasons for not interviewing these patients, if there is a group who had this experience. However, patients did describe aspects of the trial that they found difficult. I enquired about these difficult aspects of the trial, without the intention of highlighting negative features of the trials, but instead to look for balance in the study and therefore a full description of all experiences.

### **6.2.1. Difficult questions**

Throughout the trial period, patients were frequently contacted by the research team to describe their pain on that day. This might have been daily or several times per week. There were two main types of questioning: a numerical scoring of zero to ten

regarding the severity of their pain and a positive or negative reply to descriptive adjectives describing their pain (for example, 'burning' or 'aching'). Some patients described these questions as challenging to answer. However it would appear that if a patient did have difficulty in answering the questions, it was with only one type of question. They found the other type much more straightforward.

Being asked to describe his pain numerically was difficult for Pt3 to do. This was something that he felt he *'was not very good at.'*

*'Pt3: I find that a very difficult thing to do, I mean, I don't know whether I have typical severe pain, or, mmmm, so how, how, how, whether it's between zero and ten, whether it's five or, seven, I really don't know. And I have to, (inhales) try and give really a calculated guess of that....and hopefully, could do that, but eh, I wouldn't know for sure whether I was being accurate or not on that.'*

Although retired, Pt3 was an accountant by trade and I speculated that numbers in his life were very rigid things with fixed meaning. The subjective scoring of pain along a scale that was specific to him only, may have been a difficult concept to accept.

Pt10 showed another thoughtful attitude on the same difficulty:

*'Tom: How, how did you find that concept of scoring pains?*

*Pt10: Umm, it's, it's a good idea, cos it is one of those things, although different people have different pain tolerances, ahm, so it's a, it's a difficult science to work that one out, what is a, what is a 'three' really? (laughs) and eh, um....yeah, it's, it's quite hard to work out, you know whether it's a three or a four or a .....*

*Tom: So yourself you find it difficult?*

*Pt10: Yeah, uh-huh, but then I think everybody will, it's not an exact science, it's not like um, you know, it's not something you can put on a measuring scale...'*

The tone and style of her words suggested that this was not as much a source of

difficulty for Pt10 as it was for Pt3.

With regard to patients having to describe their pain, this too caused difficulty. It is unclear whether this was a source of anxiety to patients but Pt9 put across clearly the difficulty he had with this concept.

*Pt9: Because, the statements that were written, you know, that you had to choose from, you know, the words etc etc, that was something that, you know, you had to think about and the pain is extreme and I've never felt pain like this before. You know, you've had a pain in your leg, or a pain in your back and all the rest of it, but this was something else, you know.....And it was just an annoying pain and, you know, you can't say it's like toothache because it's not like toothache, it's just extreme pain and some of the expressions I did say, 'Yes' it was like, but I found it difficult to relate what the pain was....*

*Tom: ...did you feel that your pain didn't fit in with the descriptions that were being given to you?*

*Pt9: Some of them it did, but, you know, because it was just something that was, something because you'd never felt this before... you had sort of various words in front of you and, yes it was like some of them but it was more extreme than a lot of them....*

*Tom: ...right....*

*Pt9: ....so....that was difficult....*

*Tom: ....mmmm.....*

*Pt9: You know, you picked something that you think 'Well'. When you were scoring it was easy, when you had to pick something, I found that difficult when you had to put something in the boxes.'*

The difficulties were there for patients. Should you be able to, or want to, predict the type of patient that might have difficulty with this? From this study it may seem that patients who are more thoughtful and reflective have a greater difficulty in answering the questions about their pain. Patients can develop an anxiety about the answers that they are giving. My speculative thoughts that would go through a patient's mind

would be questions such as: *'Is it the right score that I am giving?'*, *'How does this compare to others?'*, *'Should I be scoring this pain as high as this?'*

### **6.2.2. Side effects**

The experience of side effects encountered in the studied population ranged from none at all to having to withdraw from the trial. For many patients, their relaxed attitude to the prospect of side effects was matched by the lack of side effects during the trial. It may have been that their retrospective attitude towards the prospect of side effects was because they had not experienced any side effects while they were on the trial.

Some patients reported mild side effects of hallucinations or somnolence. However, this was not met with anxiety or irritation because their pain improved at the same time, balancing the impact of the side effects.

Two interviewed patients had to stop the trial early because they experienced side effects of hallucinations and excessive somnolence. Even when Pt19 described the fact that *'I could have fallen asleep on a knife edge'* she did not remember being overly concerned about the side effect.

*'Tom: ...when you were on the trial, and you found yourself becoming more sleepy, what did you think then, having thought at the start it wasn't going to, do any harm, you know?'*

*Pt19: Um. Oh, I wasn't um, I wasn't worried about it, um, I told [Research nurse 1] everything, you know so um, I left it in her hands as to what to do, ken.....so um, yeah, when, when she said 'I think the best thing is that you come off it,' I figured, 'Yeah', I agreed with her on that because we did seem to have tried.*

*Tom: And, and you said it was a relief, when she said that.*

*Pt19: Yes it was, because I thought 'Oh, this tiredness will go now.' You know. Of course it didn't straight away, um, and I think now it's probably um, fatigue to do with the chemo and everything as well, you know.'*

The situation regarding Pt19's side effects was complicated by the fact that her sleepiness did not resolve once she had come off the trial. This made it unclear for her, as she states above, whether it was the medication or other factors that was making her so tired.

In the case of Pt20, on the KPS, the visual and tactile hallucinations which she described were in keeping with sensitivity to an escalating ketamine dose. This is supported by the fact that the symptoms resolved when she reduced the dose of the trial medication. Despite the side effects, Pt20 reported that she would have continued to take the drug, despite the side effects, if the trial staff had asked her to.

*'Tom: But. Was it you, did you wait until they rung you for you to decide to stop taking it or what happened there?*

*Pt20: Probably. If they hadn't said to me 'Stop taking it' I'd a taken it.*

*Tom: But, if they'd said that earlier, you would have then said to them....*

*Pt20: [...] I was gonnae stop taking it. I thought I should stop taking it, but if they had said to me, would you, would I have done another night for them, I would, I would have said yes. I'd a given it a go.'*

Her disappointment seemed to be more with having to come off the trial and not being able to get to the maximum dose of ketamine than experiencing the side effects.

### **6.2.3. Pills**

By the time a patient reached the fourth week of a study, they could be taking up to

eight trial tablets in a day. This fact was raised in different manners but I think with the same intention of bringing this up as a comment about the trial.

*Pt10: ...and then it went up to four in the morning and four at night....*

*Tom: mmm, mmm*

*Pt10: .....so I didn't need much supper! (laughs)*

*Tom: ....ah, so how, so so, what happened, what happened when you started taking the tablets?*

*Pt10: umm, well I didn't actually notice much difference, well actually no difference at all really, other than just needing less breakfast...(laughs)*

*Tom: mmhmm, mmhmm....because there's so many tablets?*

*Pt10: Well I already have plenty other tablets to take as well....*

*Tom; yeah yeah*

*Pt10: umm, so it was lining them up on the work top and making sure I counted out the right number of everything...yep, mmhmm'*

As corroborated by Pt16:

*'Tom: You said maybe it was the commitment?*

*Pt16: Well it's just the thing of, when you see the amount of tablets I've gotta take every bloody day, and you think you've gotta stick an extra four onto that in the morning and four onto it at night, you go through a tumbler o' water just trying to swallow all this bloody stuff, so that's the sort o', that's a kind o' commitment.....And that's the sort o' thing, I mean if they can get you these, these tablets, instead of having these great big bombs, if they could get them down to something the size o' half your pinkie, then ...in one tablet, then I'm sure it would be more acceptable to everybody...'*

It is interesting that patients can downplay the issue of the size and quantity of tablets. This could have been in the form of a joke or as something that did not concern the patient personally as Pt3 described:

*'Pt3:... I did get instructions beforehand but I don't remember to be honest, getting the fact that build it up to as many as four tablets at a time but eh, that wasn't a problem.*

*Tom: Was it difficult to take the four tablets?*

*Pt3: No, I'm quite easy, I can swallow tablets*

*Tom: ....take a few tablets....*

*Pt3: No I mean I'm quite happy to do that. '*

Although Pt3 did pass this off as something that was not a problem for him, it was still a deliberate point to make when asked about what he thought the trial would involve. My speculation is that patients did not like having to take so many tablets, particularly when they may have been taking a large number of tablets already. However they did not feel legitimate in complaining about this, either because they knew that the tablets might have been doing them some good, it was a requirement of the trial, or they did not feel that they should find taking tablets a difficult task. Therefore they dressed up the criticism as a joke or as something that may have affected others rather than themselves.

#### **6.2.4. Creating your own aids**

Pt4 described the anxiety of taking the right tablets. She said that if it was a genuine drug rather than a placebo for pain control '*you want to get it right, you don't want to be taking too much*'(Pt4). Her drug regimen was explained to her over the telephone and she subsequently described writing these instructions down as she had been uncertain in the past about her drug requirements. After a discussion, although she raised the point that she felt that dosette boxes were stigmatized for the elderly, she would have found one useful to avoid drug errors.

*'Pt4: Yeah. It would be better if likes o' when you're on that drug, say, like there's a box, for older people, mind you saying that I'm getting old myself, but putting them, when you were going to collect them at the Western from Dorothy, say, "Right, there's a box. I've put they tablets in, that's you're*

*tablets for Monday to, till you come back Monday to Thursday” or something like that, so they know.*

*Tom: That wouldn't, you wouldn't have found that um offensive or anything suggesting that you were old? [ ]*

*Pt4: No, no, no. If somebody had handed one o' the boxes I would have probably said “Oh, that's me getting old now, you know, with a box”*

*Tom: Yeah well ...*

*Pt4: But the further I was getting into it I felt “Oh, mind you, I could've done with one o' they boxes”. Cos I, I still say now, in fact I'll probably buy one because my drugs are getting increased quite a lot and I, I do say to myself “oh, have I took that tablet the day”.*

*Tom: S'if they had given you a box from the outset do you think that would have taken out of your hand a little bit of the “Have I taken this, have I taken that?”*

*Pt4: Yeah. Yeah and I needn't o' had to've written it down, I dinnae think. [ ] didn't bother writing it down, I done it for my own good. For myself.*

*Tom: But that might have made that an easier...*

*Pt4: Yeah.*

*Tom: sort of experience for you?. Okay, okay. That's very interesting.'*

The tone of her description suggested an anxiety that she would get something wrong. She was motivated enough by this anxiety to create an organizational system for herself to prevent any errors. She had considered this and other systems that could be incorporated into the trial to prevent herself or others from making similar mistakes.

### **6.2.5. Talking with someone new**

When patients have built a rapport with members of staff, be it in the trial or not, it can be difficult for them when they have to speak to someone else. Pt12 liked to feel that he was well known by the staff that he interacted with. When his regular phone

call came in from one of the trial staff that he had not spoken to before he was a little less relaxed than normal:

*Pt12: As with all organisations, when you get to know people that you're talking to and they're not there, talking to someone else is difficult....There was one of the nurses that I hadn't spoken to the first time I spoke to her and I just answered the questions and that, I didn't say anything... But eh, it was a bit strange, someone come on that I didn't know...it takes one or two phone calls or meetings with people before I do that, I just stick strictly to the rules shall we say. So that the, the nurse that I spoke to on one occasion that I didn't know, eh I just answered her questions....You know, there was no problem at all.*

*Tom: So, you'd've, you'd've rather you just dealt with the same person every time, is that, is that right?*

*Pt12: It's helpful, it's helpful. Or even you know the people, there's maybe one or two that you deal with and, you know, you're fine, you're comfortable, you know, you know you can talk to them.'*

His concern at speaking with someone new also extended to the emergency numbers that are given on the information sheet.

*'I often thought, they give emergency numbers to phone, one of them was Edinburgh, right, and I thought 'I hope I don't have to phone Edinburgh, because I don't know anybody there.' And although they've got it in front o' them, or I assume they would anyway, I just hoped I wouldn't have to phone Edinburgh' (Pt12).*

Although it may not always be possible to have absolute continuity of care, being mindful that some patients can find uncertainty in dealing with a new face or voice is important.

### **6.3. A straightforward experience of the trial**

Some patients seem to take being on a trial in their stride. They looked at it as *'just another part of the treatment'* (Pt2), rather than a significant individual event.

Questions asked about pain were easily answered; the tablets taken were *'like*

*drinking a glass of water'* (Pt8); patients explained their understanding of the trial and their commitments within it in a clear manner. These patients remembered the trial being well explained and events happening as they expected.

For some patients being on the trial fitted into their current lifestyle with no impact or bearing at all.

*Pt6: So during the trial it didn't alter, I just took my, it was another tab, tab or drink that I took during ma, ma, I dunno, ma daily routine. But I just, all I done was took the tablet, got up in the morning, get dressed, put the telly on and lie on the couch and watch TV and that's what I done all day, everyday.*

*Tom: And that was normal for you regardless of the trial?*

*Pt6: Whether I was on the trial or not that was just my daily life and still was up until last Wednesday.'*

It struck me that some patients were approaching their participation in the trial *'like an obedient puppy'*. To me this node, which I named rather than the phrase coming from the data, represents the unquestioning trial participant who holds the view that *'it was just do as you were told, when you were told'* (Pt3). When writing about this in an early memo, I wrote the sentence *'This may be an acceptable approach to taking part in a trial.'* It occurred to me later on that to deem this *'acceptable'* was suggesting that this was a substandard approach to a clinical trial. If this was substandard but acceptable, what would have been better? In my mind, as a medical physician, I would expect my understanding and subsequently patients' understanding of a trial to be comprehensive. Some patients did not seem to see this as a priority in their participation in a trial. Reflecting on my own interpretation, I viewed these patients' position of compliance without full understanding as sub-optimal. Even the node *'Obeying like an obedient puppy'* is somewhat derogatory. I

actually changed the node to *'Followed the instructions'* because I was unhappy with the negative tone of the original title. If I were a lay person conducting this study, I may not hold this viewpoint of the patients, expecting them to have a good understanding of the trial. I would be in a similar position to them, lacking a previous grounding in medicine and clinical trials.

#### **6.4. Experiencing something you did not expect**

Pt3 described the difficult task of having to score his pain every day as *'landed upon me rather than knowing in advance.'* My interpretation is that he found this a difficult chore or a burden within the trial. I wondered if other patients had found that things were *'landed upon them'*. It suggests that things had not been explained to them or that they had not taken in what was explained. In my mind, a surprising event during a clinical trial would not be a pleasant one, such as that which Pt3 described. I asked subsequent patients if they had *'experienced anything you didn't expect'* during the trial. Some patients, as described already, had not expected the tactile stimulation to test for peripheral nerve function. However, rather than being an unpleasant surprise, this turned out to be an enjoyable one. I was surprised to occasionally encounter a positive response to the question when I was expecting patients to describe something negative.

*'Tom: Ah, was there anything during the trial that happened that you hadn't expected?'*

*Pt10: Umm, well I think the whole extra help from [Research nurse 1] and [Research nurse 2] ehm, I hadn't expected that and that was just really nice, having somebody...because when you do all these things, ehm, you get a bit scatter-brained, and um, and so you think of something and you think, 'I must ask the doctor the next time I see them.' And eh, I know I can send emails to [Clinical doctor 2] anytime but I don't like to pester her, because she's such a busy lady and I certainly can't just ahm, phone up my GP, unless it's an*

*important thing as well, cos they're all so busy, so um, I have to sort of try and write down my questions and then the next time I'm seeing somebody, then I can ask my silly little question, but it may be that something I just want to know now, so, having all these daily phone calls was fantastic, uhm, for the extra silly little questions, it was very nice. Quite enjoyed it actually.'*

## **6.5. Conclusion to being on a trial**

Patients that I interviewed found the trial to be either a positive experience or one that they found straightforward. I have discussed aspects of the trial that patients found difficult. The sections that generated the most discussion were the analgesic effects of the trial on patients' pain and the interaction with the research staff. These are discussed separately in the following chapters, seven and eight, because of their central significance to patients' experiences of the clinical trial.

## **Chapter 7. PAIN**

Pain is central to everything in the studied trials in which the patients participated. The primary aim of the trials was to reduce pain; patients were referred to the trial staff because of the pain that they had; the trial staffs' primary research interest was what happens to the pain during the trial. For the most part, patients discussed their pain with me more than any other topic.

Pain is a subjective entity and clinicians can only base their opinions on what the patients tell them. The International Association for the Study of Pain defines pain as *'An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'* ([www.iasp-pain.org](http://www.iasp-pain.org)). Scoring tools have been devised to give clinicians a quantitative insight into this pain. The tools can screen for a particular type of pain or measure the severity of pain. The scoring tools assessing severity allow clinicians to follow the fluctuation of a patient's pain, but only within the context of the individual.

This chapter looks at pain as patients describe it, how the patients view their pain and the impact of the trial on that pain.

### **7.1. Pain at the start**

As discussed in chapter 5.3.1.1, patients described pain as one of the major reasons for taking part in their trial. There was a group of patients who described their pain as severe at the point of starting the trial, even to the point of wanting to die rather

than tolerate the pain. Another group of patients described significant pain but without the same sense of desperation. A third group remembered minor or no pain at the start of the trial. Pt8 remarked that he had been led to believe that cancer pain was unbearable. He was quite surprised by the lack of pain that he had suffered and the tolerability of the little pain which he did have. His views, if shared by others may suggest that some patients expect a level of pain relating to cancer.

## **7.2. Cause and impact of the pain**

For most patients, the pain that they described was related to their cancer. There was the occasional patient who felt that the origin of their pain was arthritis. Pain could be caused by the cancer itself or as a result of cancer treatment, most commonly chemotherapy-induced neuropathy. Among those patients that were suffering from cancer related pain, it was often pain from bone involvement that was described to me. This was not surprising considering that the aim of the PBT was to study cancer related bone pain. The KPS addressed a wider spectrum of underlying causes of pain but they were always neuropathic in nature.

Patients would describe the impact that the pain had on their lifestyle and their relationships: shopping trips, meals out and visits to relatives were restricted; partners took on increased duties for the patient and for the household; patients described strained relationships with family members.

## **7.3. How is the pain viewed?**

*Pt8: ...although I knew somewhere around there it would come back.*

*Tom: It was, it was, the pain was around?*

*Pt 8: It was around, yeah.'*

The pain was around. Although not always explicitly described by patients, this was the underlying tone throughout the study on the topic of pain. Even if something reduced the pain, it was never far enough away that it might not return. Patients described the recurrence of the same pain or of another pain in a different site.

For some patients, the pain was part of their disease process and something to contend with. For others, it signified deterioration in their overall condition, and even an indication towards the terminal phase of their illness. Pt15 had breast cancer ten years prior to her current breast cancer.

*'Pt15: I always thought I was quite good with pain but...I think um, I think part of it was fear you know...with... 'Is this the beginning of the end', you know,... as if it's gonnae spread through my body and you know....*

*Tom: mmm-hhmm*

*Pt15: I know it is but...it's like I'm no' ready yet... you know, ten years time I'll probably be more ready yet but...'*

The pain can hold different significance for different patients studied but whether the pain was present and dominating their life or under control, it was always around.

## **7.4. Response to the trial**

### **7.4.1. Reduction in pain**

The most straightforward response described was from those patients who felt that there was a dramatic reduction in their pain while on the trial medication. *'Relief beyond relief'* was the description by Pt5 when his pain diminished. For these patients, whether they were on a placebo or not seemed to be a separate and less significant matter. Two patients, one of whom was Pt5, described their

misunderstanding of the way in which a patient could encounter a placebo. Whether a patient was on a placebo or not was of less importance than the fact that the pain had reduced.

Other patients described a pain reduction when the active drug was started after the blinded part of the trial. This suggests that the patient may have received the placebo during the blinded period of the trial.

*Pt4: Eh, and then when I did get that ketamine, I knew right away eh it was working.*

*Tom: You did.*

*Pt4: Oh aye, oh I knew right away, aye.*

*Tom: Yeah. And what were you, what did you feel then?*

*Pt4: I felt relieved. Well, really relieved, aye that I had something that, that got, I mean I go out to the shops and that.'*

The boundary of where the trial started and finished was blurred for patients. Although strictly off-trial when the active unblinded drug was given to patients, it was still the same trial staff who managed them. I think that for some patients this was still regarded as part of the trial period. Their primary concern was the reduction in their pain, whatever period of the trial they were on.

#### **7.4.2. Failure to reduce pain**

Then there are those patients who had no reduction in their pain. As the trial was still blinded through the course of this thesis, it was not possible for me to know why their pain did not reduce. From my perspective, I believe that being as equally blinded as the patients was beneficial. If I had held a greater amount of knowledge than the patients experiencing the trials, I think that my levels of induction would

have been less. I remained able to look upon the trial as the patient looked upon it, rather than as a trial staff member may look upon it. As an example:

*Tom: ...did you say that the pain wasn't diminishing at all?*

*Pt12: Not really. Not really.*

*Tom: So if that was the case, um why would you continue on the trial, continue taking the drug?*

*Pt12: Well it could be the other way, if I stopped taking it the pain might go up.*

*Tom: Mm, mm.*

*Pt12: Maybe it was keeping us at that level.'*

As I was unable to know any more than he, this seemed a plausible point of view for the patient to hold.

How did patients see the failure to reduce their pain? Some patients viewed this with disappointment having had their hopes raised. Others did not have this same sense of disappointment. Instead, these patients felt that the chance of failure was one of the core components of the trial experience. I think that for the most part, patients went into trials with their eyes open. It may not have been that they had a comprehensive understanding of the trial, but they did understand that they may not get a benefit from it. As discussed in chapter 5.4 on the placebo arm of the trial, patients were aware that part of the trial may include receiving a placebo tablet. The reflections of the patients on the failure of their trial to reduce their pain are developed in chapter 9, where patient reflections of the trial in general are discussed. It would be interesting to interview patients at different times of a trial to see if this view changed during the process.

## **7.5. Conclusions**

Pain could dominate a patient's outlook on life and their interaction with others. Similarly, the response to the trial could cause a tremendous feeling of relief and joy. However, the reduction in pain was not the only benefit of the trial. The next chapter describes the interaction with the trial staff.

## **Chapter 8. THE INTERACTION WITH THE TRIAL STAFF**

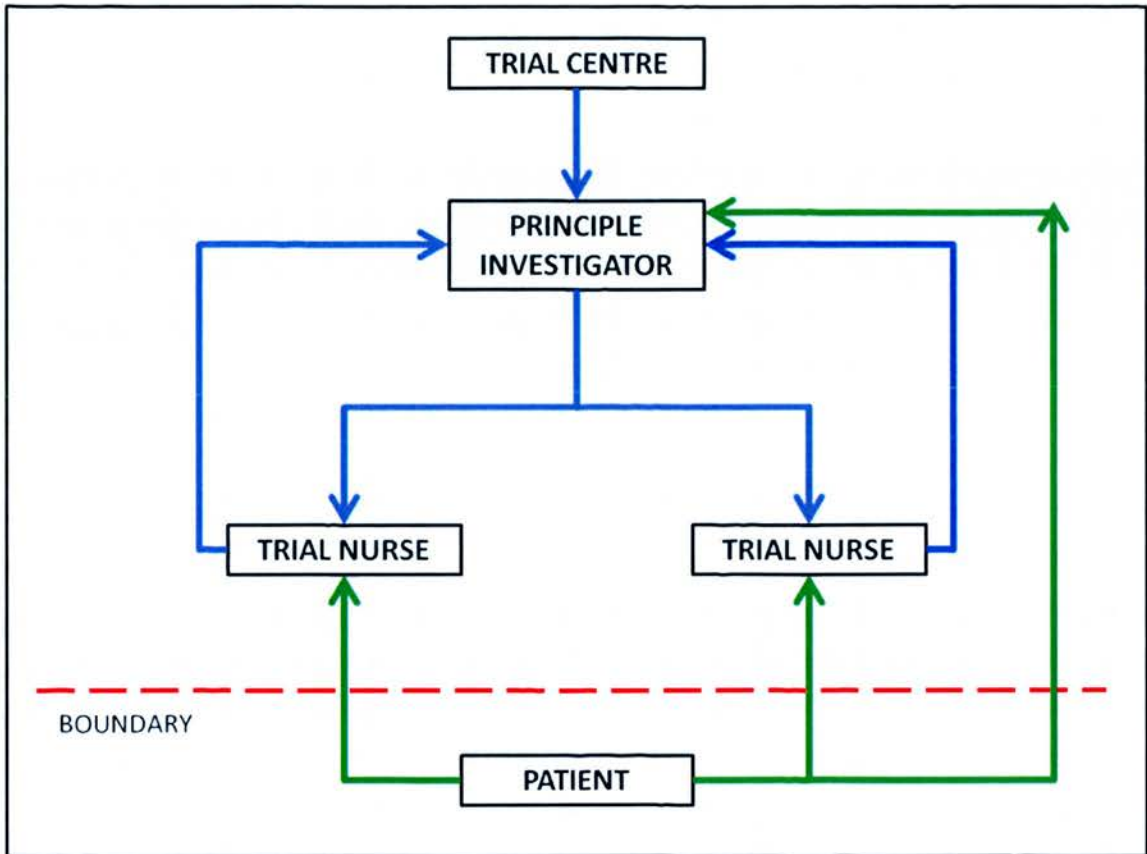
Few patients had met the trial staff before being contacted regarding the trial, yet the relationship that developed with the trial staff is one of the core categories of advanced cancer patients' experiences of clinical trials explained in this thesis.

The majority of patient interactions were with the trial nurses. Although the trial doctors were discussed, and mentioned here, it was the interaction with the trial nurses that patients discussed the most.

The interaction could be straightforward, with the duties or requirements of the trial being fulfilled to a satisfactory level. Within this relationship, however, some patients found a positive experience beyond the physical outcome of their trial.

### **8.1. Duties of the trial nurses**

The role of the trial nurses was to act as the first point of contact for patients throughout the duration of the trial. They were usually the first person from the trial staff that the patient met, the person they had the most contact with during the trial and the last person the patient dealt with at the end of the trial. The interaction between trial staff and patients is illustrated in Figure 5.



**Figure 5 - Interaction with the trial staff**

Before a patient consented to taking part in the trial, the trial staff made contact with them and explained what was involved in the trial into which they were being recruited. Patients were given an information sheet and had the opportunity to contact the trial staff to discuss any questions they had. Unusually for a trial, in the PBT, patients often had to be recruited and consented on the same day as the first meeting with the trial staff. This was because starting the baseline trial assessments, and ideally the trial medication, on the same day as the first dose of radiotherapy was central to the trial. In the KPS, patients had time to consider taking part in the trial before consenting.

Once a patient consented to take part in the trial, there was an extensive initial assessment involving a large number of questionnaires and an examination of the patient's peripheral nervous system. This involved the testing of hot and cold sensation, vibration and light touch.

During the trial, the nurses assessed the patients' pain response to the trial medication. This involved formal questioning on a regular basis throughout the trial. Although less extensive than the initial assessment, the questions asked the patient to score their pain from zero to ten and to answer descriptive questions about the pain. Depending on the trial, the contact was daily, including weekends, or several times a week, for the four to five week duration of the trial. If the patients were having any difficulty during the trial, they were encouraged to contact the trial nurses. There was always one member of the trial staff between both sites (Edinburgh and Glasgow) available 24 hours a day.

## **8.2. The relationship - casually professional**

So what were the patients' experiences of interacting with the trial staff, particularly the nurses? Firstly I think it is important to highlight the quantity of contact the studied patients had had with health care professionals both during the course of their cancer treatment and previous to that. Patients described many clinic appointments, many hospitals and many different staff members. I was told about friendly porters who remembered patients from several months previously and evasive consultants who avoided difficult questions. Patients glowed when talking about appointments that had gone well and shuddered at hospital admissions that had not. I was left with the impression of a group of patients who had a lot of experience of dealing with the

health profession, who had experienced both good and bad care and could differentiate clearly between the two.

When enquiring about the experiences between patient and trial staff, I asked the patients a broad question to allow them to recall and discuss what came into their minds; *'What did you talk about?'* Pt9 described first of all the social aspect of the telephone conversation.

*'Tom: What did you talk about with her?'*

*'Pt9: Ehm, basically it was 'How are you?'....we spoke about ehm, her having a week off and what she was doing and then we talked about the pain levels, how they were and she monitored my pain levels.'*

Both the patient and research nurse knew that the genuine reason for the conversation was professional, yet the social and often jocular element could hold as much weight for the patient as the clinical aspect and stay in their mind for longer. My interview with Pt12 was limited by his poor recollection of events during the trial. However, I found it interesting that one of the things he did remember clearly was the interaction with the research team.

*'Tom: So you enjoy your talking with the research staff?'*

*'Pt12: Oh yes. Yeah, I did indeed. Yes.'*

*'Tom: What did you talk about?'*

*'Pt12: First of all we got rid o' the, the real stuff...'*

*'Tom: Yeah.'*

*'Pt12: ... you know? And then just in between times it was wee bit banter about things like, 'What did you do at the weekend?' and 'Did you have a nice weekend?' and they asked me, things like that. You know, just general everyday subjects.'*

Aside from the friendly nature of the trial nurses, patients commented on the competency of the trial staff in general. They are described as *'superb'*, *'dedicated'* and *'brilliant'* with *'everything explained thoroughly'*. The overall feeling by the patients was that the trials were run smoothly and efficiently with difficulties being anticipated. Patients felt the staff had a high profile and were easily accessible throughout the process of the trial. I came to think of the trial nurses as casually professional. Patients described the nurses making themselves feel at home in a patient's house, by making a cup of tea for example, while at the same time delivering the required drug prescription and instructing the patient on how to use it.

*'Pt20: She just fitted in to my house, when she came in and took her coat off and sat down, she didn't, I didn't have to say to her can I take your coat dear. [Research Nurse 2] just took her coat off and started to sit down, and to me that's just...*

*Tom: For you that's good for you.*

*Pt20: Uh-huh, she just settled in, and she was absolutely, she was just an absolutely lovely person. She was absolutely lovely.'*

It was this approach that seemed to resonate with some patients and allowed the trial staff to be held in such high esteem.

### **8.3. Actions and characteristics of the staff**

Trial staff became valued for actions which patients may not have come across within the health care profession before. For example, trial nurses would visit patients in their home if that was more convenient for the patient. One less mobile patient cited the staff's willingness to conduct all his trial commitments in his home as one of the motivating factors for taking part in the trial.

*'Tom: So was there any, eh, impact on your life or your lifestyle?*

*Pt3: None at all really, no. As I say, it was only just done, conducted by phone and by one... a visit at the beginning and at the end by Dorothy.*

*Tom: So, was that important to you that it wasn't going to have an impact on your life?*

*Pt3: I think it was, because it would have been more cumbersome and more difficult for me to go to the hospital.*

*Tom: mmm*

*Pt3: Certainly if I had had to go more than once, I mean, I would probably have resisted it. But the fact that it's conducted in the house and not interfering with a lot in my life.'*

Patients would describe trial nurses acting as their advocates when contacting other doctors, dropping off medication rather than patients having to go to the chemist and fielding questions that patients did not want to trouble other people with.

Some characteristics were intangible to patients. Patients knew that the feelings the interactions induced were positive but may not have been aware what the feelings were. The feelings were compared to what patients *were* familiar with. Patients referred to the trial nurses, and doctors, as '*just like a friend*' (Pt1); others suggested a brother or a sister. Who they referred to was a trusted person in their life.

*'Tom: .... can you just describe a bit more the interactions that you had with the staff?*

*Pt2: ....Em, well it was just .. I was going to say it's like normal appointments but it's no' because we actually ended up on first name terms with the doctors and that, that's, I like that, that was good because you feel you can talk better to doctors and that if it is like that you feel there's a barrier dropping doon, you know.*

*Tom: Was that a new thing for you?*

*Pt2: It was, eh. As soon as [Research doctor 1] introduced himself to me, he says 'Call me [first name]' and it was pretty informal, so it's always been like that and it's, it's, I think it's helped.*

*Tom: Would that have made you more, em, keen to discuss problems if you had them?*

*Pt2: I think so.*

*Tom: Because you felt that you knew them better.*

*Pt2: Yeah, yeah. '*

The characteristics that I came to think of when describing the trial staff would be those of versatility and flexibility. Nurses had to call a patient during the day, but if he wanted to go swimming, they were happy to call him afterwards. As mentioned above, if a patient was finding it difficult to get to the hospital or a chemist to pick up a prescription, often one of the trial nurses was able to deliver it to their house. A colloquial term would be 'going the extra mile'. Pt16 described his desire for professional accompaniment as '*riding shotgun*'.

*'As, you know, I thought she was very good, I thought she was very diligent, or whatever's the word, she really (pause).....seriously rode shotgun on the situation, she really did. Very good.'* (Pt16)

A double-barrelled shotgun has both barrels running parallel with each other, facing in the same direction. I had not considered the phrase before but it was one that resonated with its accuracy. The other descriptive term that Pt16 used was being '*aware*':

*'Pt16: They have a lovely attitude, who have a caring attitude and who genuinely are there or appear to be genuinely there to help...*

*Tom: Can you tell me why that's so important to you?*

*Pt16: Och it is important to people who are feeling sorry for themselves and don't know what direction they're going in. You're looking for, you're not looking necessarily for reassurance, but you're looking for (sighs) a bit o' light-heartedness, I dunno. I've not really considered that aspect of it but that's what it's about...they were very helpful, very understanding, very obliging um and, and aware.....I suppose that's it, aware.*

*Tom: Aware (pause). It's an interesting word.*

*Pt16: I would say that's the thing, they were tuned in, they were very aware.'*

I think that *'being aware'* could sum up everything that you would hope for in the relationship between patient and care giver. Pt16 described his vulnerability by admitting to *'feeling sorry'* for himself. The trial staff seemed to be aware of the situation that patients found themselves in and reacted empathetically.

## **8.4. Reasons for positive feelings towards the trial staff**

For some patients, the trial staff were appreciated for being competent and the experience was not highlighted as anything greater than a satisfactory interaction. For some patients, the interaction seemed to be the most significant part of the trial. I will discuss some of the reasons that I think are behind this positive view.

### **8.4.1. Being known by the staff**

The description of patients suggested that they felt cared about. *'It's no' "next please"'*, reported Pt1 when describing his visits to the trial staff in the hospital. Why I like this quote is that it alludes to his previous treatment; the appointment being a small part of someone else's day rather than being the major part of *his* day; all in four words. Patients looked forward to the appointments with the trial staff and wanted to go to the hospitals for them.

Pt12 described his daily interaction with some clinical staff in his local hospital. He described warmly the familiar interaction generated through daily contact.

*'They all know me. Everybody knows my name.'* (Pt12)

As with being invited to call doctors by their first name, being known was important to patients. It nurtured a relationship which could offer more than what appeared

superficially to be a straightforward interaction.

#### **8.4.2. The security of presence of the trial staff**

The description of patient/researcher interaction suggested that the patients felt cared for. However being cared for did not necessarily have to come only from a health care professional. Family and friends provided this role also. What the trial staff could provide, which may not have been available from friends and family, was an aspect of security in their presence. Patients described the contact details of the trial staff that were available to them; they had office and mobile numbers of nurses and doctors and were encouraged to use them. They knew that if they had any questions or ailments they could contact the number and expect a prompt, if not immediate reply, which was comforting. Not all patients needed to call the staff outside of arranged times but the availability to do so was reassuring.

Security has the connotation of someone higher up or more powerful looking after you. I would argue that there is a feeling of experience that comes from the side offering the security. Security can deliver something more than just being cared for. It suggests a protection from the vulnerability that exists when taking part in a clinical trial or with any illness. This is why family or friends could not necessarily provide this same emotion. Some of the trial nurses were experienced in delivery of chemotherapy prior to being involved in trials and were able to use this knowledge when required to with patients.

#### **8.4.3. Trust of the trial staff**

Something that was very important to Pt9 in establishing a rapport with the trial staff

was the transparency of this team.

*Pt9: Oh the research, the great thing about the research staff is... there is no hidden agendas with them.... so basically they told me, who they were, what they were and what they were doing.*

*Tom: What...you say that's the great thing about them. Why is that a good thing?*

*Pt9: Because they were up front.... and you felt that they're not trying to hide anything.....so, for me that was a bonus.'*

This importance of knowing the background of the trial staff speaks about the desire for integrity in the staff you are working with and for. The relationship between patient and researcher is symbiotic as each relies on the other for some benefit. Amongst other things, patients were looking for a reduction in their pain while trial staff needed patients for their trials to exist at all. Pt9 was expressing his satisfaction with the credentials of the trial staff that allowed him to trust them. Trust is hard to win but can last a long time. Actions can also build trust. Pt5 described that he felt that the research team would deliver on promises that they had made.

*Pt5: And that makes a difference, you know, if you're in, distressed or pain or anything like that she was always there. She was always there, which is a lot better you know than...some of them ones.*

*Tom: So you've had previous experiences that are different to that?*

*Pt5: Aye*

*Tom: OK, and so why, why was it, um, so good that you had her number like that?*

*Pt5: I think it makes a big difference. You know, I've got other numbers for like, the [Hospital 2] and the palliative care nurses and what-have-you. They promise all these things, and then they don't follow them up. I found that out, you know.'*

With trust could come confidence as described by Pt20:

*'...I had that belief in it, and don't know, where the belief came from, but the thing was, [Research doctor 1], I really liked. And if I take a, I don't mean*

*'like' like but if I get, I get a.....I don't know, I kind of get a sorta good feeling about people, that I sort of trust. And I trusted him.' (Pt20)*

Her trust was so much that she would have been prepared to increase her dose of ketamine, despite side effects, if asked.

Pt17 had no concerns about the trial because he felt that all his treatment up until that point had been of such a high standard. His trust in the health care profession was transferrable from one situation to another.

Patients would describe their first contact with the trial staff in different manners. Pt9 for example, recalled clearly one of the trial nurses going into detail about the background of the trial staff members. This was important to him to establish his trust in them. Other patients remembered the friendly approach that the trial staff projected. I think that it is unlikely that the trial staff varied what they initially discussed with patients to a significant degree but patients took away what was important to them.

Those patients who did agree to take part in the clinical trial were satisfied enough with what they had heard to want to take part in the trial. Establishing trust was one of the important factors of this first meeting. A sense of trust also contributed to the security of presence discussed above.

## **8.5. Conclusion**

The interactions with the trial staff prompted patients to refer to them as like a friend or sibling. A trust and sense of security developed, leading patients to hold the staff

in high regard for their professional approach. The patients who reported this were from all areas of the studied population regardless of sex, trial or pain response. Not all patients were as effusive, with some being positive about the trial staff in a measured way.

I can only speculate on the attitudes of the trial staff and nurses in particular. Anything else is beyond the scope of this study. Were the nurses aware of the impact of their approach on the research patients? Were these conscious actions or unconscious ones, derived from a combination of their personalities and getting to know the patients over a period of time? Whatever the background to the staff's interactions with the patients, it had a large impact on the patient group studied.

## **Chapter 9. PATIENT REFLECTIONS ON TRIALS**

Previous chapters have examined specific aspects of patients participating in a clinical trial. This chapter examines the general reflections patients had of the trial they participated in and also their views on trials in general.

As I have done throughout the results section, rather than relating the complex and sometimes conflicting reflections of individual patients, reflections about the trial are discussed in collective sections.

### **9.1. Patient reflections on their own trial**

#### **9.1.1. A positive reflection on their own trial**

Positive reflection about their trial came from patients both with and without a reported reduction in pain. I will discuss these two groups separately.

##### **9.1.1.1. Positive reflection on their trial after a reduction in pain**

This group of patients had a clear, positive attitude towards the trial they had taken part in and its benefits. They felt a strong conviction that everyone should go onto a trial because of the potential benefit. Pt5 had said *'I'll take my chances here'* before going on to tell me of the relief that the pain reduction had brought. I began subsequently to see this group of patients as those who had taken a gamble that had paid off. Patients were aware of the possibility of having no response but it had not happened to them; taking part in the trial had been a success.

These patients were also able to see and discuss the other benefits to being on a trial but the primary outcome for them was their pain reduction.

#### **9.1.1.2. A Positive reflection on their trial after no clear reduction in pain**

Some patients spoke positively about their experiences on their trial despite not having a reduction in pain. This came as a surprise to me. Before starting to interview patients I thought that patients would fall into two categories: firstly, the patients who showed an analgesic effect would be very positive towards their trial; secondly, those who did not show an analgesic effect would be wistful at best at what could have been, or even dismissive of the trial as waste of their time. When coding the patients who still spoke warmly about trials, despite it having no effect on their pain, I created the node '*stoicism in the face of 'failure' of the trial.*' Failure was in inverted commas as it was to suggest that the only 'success' was a reduction in pain. When it became clear that patients were taking other positives from the trial, rather than just pain reduction, this node became increasingly interesting.

Within these patients who showed '*stoicism in the face of 'failure' of the trial*' there are two factors that seem to be central to their viewpoint: taking benefits from the trial other than a reduction in pain, and the manner in which they viewed the failure of the trial to reduce their pain.

#### ***Taking benefits from the trial other than a reduction in pain***

In chapters 6 and 8 I have already outlined several benefits that patients felt could be gathered from taking part in a trial other than pain reduction. In summary, these benefits included the altruistic reasons for taking part in the trial, an increase in the

structure of care and an increased contact with health care staff that being in a trial offered.

***The manner in which patients viewed the failure of the trial to reduce their pain***

When it became clear over the period of the trial that a patient's pain was not reducing, a common response was of acceptance, albeit with a proportion of disappointment as well.

*Tom: So then when you got a little bit down the line and it wasn't working... did that not bother you?*

*Pt6: No. It just, it I mean just, it was just something I've tried and it didn't work. And, but it was just unfortunate.*

*Tom: What did you think about that, having no relief?*

*Pt6: It still... didn't matter. You still, you're still on the assumption that you've still gotta try anything and everything if you're going, no matter what it is you've still gotta try and beat whatever pain you're in, whether it's pain or cancer or whatever, I'm still on the assumption if another trial come up, I've actually been put forward, I'm on a trial now for the cancer. I'm still doing a trial. I still would give trials a go, I don't shrug them off because that one didn't work.'*

The acceptance of knowing that the trial might not be successful was also connected to their awareness of placebo medication.

*Tom:....it may have been that you were on the placebo.*

*Pt2: That's right.*

*Tom: Is that, did that strike you as unfair that you ran the risk of..*

*Pt2: No, no because that's part and parcel of these trials anyway. You know that before you go into the trial you know.'*

Some people shrugged it off, 'just my luck', as Pt19 said. Others did not mind given the fact that the possibility of a treatment failing was part of the nature of trials.

Despite the stoical approach, an element of disappointment was present, either as a

spoken emotion or as an undercurrent to the situation. Pt4 stated that she was not disappointed because she knew she was in a trial but added the caveat that she would have been *'over the moon'* if it had worked. As described above, Pt6 was not disappointed because *'you've got to try anything and everything that comes along...It was just unfortunate that it didn't work'*. While patients denied that they were disappointed sometimes their follow-up statements, as shown in these quotations, suggested there may still have been some lingering disappointment underneath.

When Pt2 described the pain and its inability to be controlled as *'part and parcel'* of his disease, it occurred to me that disappointment might be something that had accompanied patients since being diagnosed with cancer. To get to the point of having a terminal illness, overall failure, or consistent failure and disappointment, must have been present along the course of the disease. If this is the case, the emotion of further disappointment in response to a trial not producing the result that a patient had hoped for may be measurable within the context of previous disappointment. It may be that this familiar emotion of disappointment makes dealing with the failure of the trial a little easier to tolerate. Taking other positives from the trial might be a technique that patients had developed in the past in other situations during their cancer journey.

### **9.1.2. Patient anxieties**

A small group of patients expressed a view about the suitability of their place in the trial. I was alerted to this when Pt10 stated that *'I wasn't a very good candidate'*. Pt10 thought this because her more sedentary lifestyle (due to her pain) limited the painful episodes that needed controlling, thus scoring her pain lower than she might

do otherwise. Pt3 did not recall having pain at the start of the trial and so was not sure if he needed the drug at all.

*Pt3:..but again I wasn't actually particularly looking for a benefit but I didn't have any great pain....*

*Tom: ..right...*

*Pt3: ....that we were trying to cure, I was just, eh, it was an additional thing that...it didn't....it didn't bother me if I was on a placebo or not to be honest.'*

He reconciled this in his mind by stating that he was not doing the trial for himself anyway.

What do these two descriptions say about patients in trials? I think that they suggest a potential for some patients to feel anxious; that they should not be in the trial. The feelings may be those of being found out as a fraud or that their poor response to pain may twist the results of the study. I think in Pt10's case there was an underlying anxiety while Pt3 held a slightly more detached view that he was in the trial for different reasons to what the researchers thought he was in it for. He gave me the impression that he felt he knew better than the researchers but was still doing them a favour.

### **9.1.3. Would patients take part again?**

#### **9.1.3.1. A willingness to take part again**

My findings from this study indicated that patients showed a willingness to participate in the same trial again or in another trial if they were offered to take part in one in the future. This view was expressed by patients whether they had had a reduction in their pain or not. Pt4, who did not have a reduction in her pain, stated:

*'Yeah, I would do it again. Aye. Because maybe next time I would get it.'*

She was referring to her view that she had received the placebo and so was hoping that in the next trial she may receive the active drug. Being on a trial and not getting the pain reduction that they had hoped for had not put patients off trying a different trial. Patients put the failure to achieve analgesia down to not receiving the active drug. There is also the possibility that the active drug did not have an effect on their pain. Other patients said that they would do another trial again because of the need to try all available options.

### **9.1.3.2. A reluctance to take part again**

Some patients did describe a reluctance to repeat their trial. In their opinion the trial had not worked so they did not see the benefit in taking part again. Pt3 did not want to take part in another trial, and had indeed rejected another trial because he felt that his body was telling him that it had had enough. He did also describe that this had been the opinion of his oncologist which may have played a significant contributing factor in his decision:

*Pt3: I possibly might not on the grounds that ....I think we're beginning to feel, um, that I've been interfered with enough. And I don't mean that I've been over interfered with but I've just had so much.... stuff put into me and things you know....*

*Tom: mmm-hmm*

*Pt3: ...so when you're taking an additional eight tablets a day, you were thinking 'Gosh, your putting a lot of.....*

*Tom: mmmm*

*Pt3: .... 'other stuff into your body.'*

*Tom: yeah*

*Pt3: And perhaps it's time you gave your body a rest.'*

He gave a firm example, the only one during the study, where he stated he had been

offered to do another trial and he had refused. The other patients held speculative thoughts. Some others thought that they had then '*done their bit*' (Pt16) so therefore did not need to contribute more. Pt16 was interesting in the fact that he brought up the topic of doing another trial spontaneously. At the start of this quote he is clear that he does not want to do another trial but only a few sentences later he reflects on the need of someone else and could not rule out the possibility of doing another one.

*Pt16:....I have, I have no axe to grind about it, I wouldn't necessarily go and do another one instantly, but um I certainly have no regrets whatsoever.*

*Tom: Right, why would you not do another one? Why would you not do another one?*

*Pt16: (sigh) I suppose the commitment and, I again it's more up here than to do wi' ma body, because you know, ma body's....knackered anyway so it doesn't really matter. But I, I dunno. Could be ma selfishness, maybe I say 'I've done one, I've done one and that's enough, to hell wi' it I'm not doing any more'.*

*Tom: Uhm.*

*Pt16: But, I, I don't know. If somebody came along and there was a good enough reason, a good enough excuse, and there was a better, or another possible ongoing benefit for some other poor blighter, then I may very well do it, but out of, straight off the top of ma head is that I've done one, that's enough.'*

This highlights the fact that even if patients think that they may or may not take part in another trial, when they are given the option to take part, their entry into another trial cannot be predicted with any certainty. It also shows the value of interviewing patients who have actually participated in trials rather than asking patients about theoretical trials. Patients have the potential to say one thing and do something different when the actual opportunity arises, such as taking part in a trial.

#### **9.1.4. The trial as a burden**

I was interested in whether patients found being on a trial a burden. Patients did not feel that being on their trial was a burden and some could not understand why other patients might think it was a burden.

*Tom: So you didn't find it a burden at all being on the trial?*

*Pt10: No I found it great fun.'*

Is it genuinely the case that there was no element of burden to taking part in a clinical trial? Burden is quite a strong word. If I were to think of another word to describe things that might be less emotive, it might be 'down-sides', or 'difficulties'. To my mind, 'burden' means having a serious impact in your life which I do not think has been described by the patients studied. Even Pt19, who had to be withdrawn from the study, did not see the trial as a burden.

*'Pt19: Um, well apart from the tiredness it didn't really affect me in any other way so, and, you know, I'd agreed to go on the trial so, I couldn't really, if I'd expected to come out of it, with nothing changed, it's not much of a trial is it, if you know what I mean. You expect something to, to happen, you know, obviously it wasn't going to be anything serious (coughs), but um, expect changes to be made.'*

Patients did describe difficulties however which I have gone into in more detail in chapter 6.2. These included the size and quantity of pills to be taken, struggling with the questions asked and the possibility of speaking to someone new.

#### **9.1.5. After the trial finished**

After some patients had spoken so positively about the benefits of being in a trial, I wanted to know what happened after a trial finished. Some patients were still under the care of the trial staff and receiving the active drug. Others had not seen the staff

for some time and were happy dealing with the community palliative care team who had looked after them before the trial started.

*Tom: You mentioned that um, during the trial, um, you could ring up [Research Nurse 2], on a Sunday, and things like that...*

*Spouse: Yep*

*Tom: ...to answer questions...do you have someone like that now, who you can still ring up?*

*Spouse: I can ring [Community Nurse 1] ...*

*Pt17: [Community Nurse 1] ...*

*Spouse: ... [Community Nurse 1] ....Marie Curie lady...*

*Tom : yeah, yeah....*

*Spouse : [Community Nurse 1]...can ring her...*

*Tom: yeah, you can ring her any time ...*

*Spouse: Yes...*

*Pt17: mmm*

*Tom: she can, sort of, she can fill that role that....*

*Pt17: mmm*

*Tom: she, was she doing that before the trial started as well?*

*Pt17: mmm, mmm'*

There were some patients who did seem to miss the trial staff. Pt11, who had been pleased with the added structure of care the trial offered, felt that this structure had fallen away since the trial finished. Another patient, who had not had a good pain response during the trial, was still in pain when I interviewed him. He did not seem to be sure when his pain would be reviewed except for an oncology appointment a few months away. This particular patient posed a difficulty for me as I felt that his pain control could have been improved. After the interview we discussed options

that might be available to him. I suggested that I could ask his local community palliative care team to visit him but he was reluctant for me to do this.

Having heard of the potential positive impact the trial staff could make, I felt that there could be a negative side to this after the patient was no longer in contact with them. Would there be a void in the place where the trial staff had been? Some patients were still in contact with the trial staff, with the contact variably maintained by either the patient or the trial staff. This suggests a more complex situation of the relationship between trial staff and patients after the trial had finished.

## **9.2. Patient views toward trials in general**

In chapter seven and eight I have described the benefits of the trials to patients regarding a reduction in their pain and the interaction with the research staff. Concerning patients' overall opinions of clinical trials, Pt6 summed up one of the firmly held beliefs:

*'You've got to have trials.'*

These patients realized the treatment they had received during their illness was at least partly attributable to trials that had taken place in the past. Some felt that they had a debt to pay back to all the people who had taken part in trials in the past which had benefited them.

*'Pt6: At the end of the day, if you didn't have people to try trials, you didn't get this guy who had cancer, I wouldn't be at this stage with my pain, so you've gotta, there've gotta be guinea pigs along the line somewhere.'*

*Tom: So you're happy to be one?*

*Pt6: I'm quite, I was quite happy to be one on that case study, yeah.'*

Pt16 described his view of the importance of clinical trials.

*Pt16: I just think that these sort o' things, I do appreciate that these sort o' things are important. I really do. And I only wish to God that more people probably saw the importance of this sort of thing. I really do.*

*Tom: What do you mean by that?*

*Pt16: Well, there's so many areas, especially involved in cancers that are such a bloody total mystery still and they can only be sorted out through trial and error, through people trying different things, that's the only way it's gonnae work. Because no-one going to, well, maybe they will come up with some huge bloody brainstorming things or genes they can stick up everybody and blooming 'Whack', away it goes. I don't see it happening, not in my lifetime, that's for bloody sure.*

*Tom: Mm.*

*Pt16: But I don't see it in yours either for that matter. No, I believe the only way we're gonnae get on top of this whole thing is through research, through checking, through trying, through drugs that've been slightly modified or, or cross-used or what the hell.*

*Tom: Great.*

*Pt16: No I think it's a great, I'm in favour of it, hence the, it's one o' the reasons I did it, you know.'*

This belief crossed the boundary of the analgesic effect of the trial. Some of the strongest opinions in favour of clinical trials came from patients who had had no reduction in their pain during the trial. When asked, patients were also of the opinion that they would recommend taking part in a clinical trial to others. Pt5 would tell them *'Go for it, it will work for you. It worked for me.'* The created node *'Tell the world about trials'* came as a response to Pt1's comment, *'just put me in a room'* so enthusiastic was he to encourage others to take part. Patients' reasons for feeling strongly about trials were either due to the benefit they had received themselves or because of their overall opinion of the necessity of trials.

### **9.3. Conclusions**

Patients expressed positive views towards the trial that they had taken part in and towards trials in general. Those who were positive about their trial came from both groups of patients, those with good and those poor pain response. Patients seemed to favour the possibility of taking part in another trial in the future and would happily recommend taking part in a trial to other people. This was also independent of their response to pain. Other patients describe a fatigue towards trials or a reluctance to go through another one.

There were still aspects of trials that patients did not like or which caused them some levels of anxiety. Individual patients expressed views of both a positive and negative nature rather than having a fixed opinion on the trial as a whole.

## **SECTION 4 – DISCUSSION**

## **Chapter 10. DISCUSSION**

In this discussion chapter I will look at the central theory of the study, contextualize the findings with the current published literature, critique the study and suggest areas for future research before drawing my final conclusions.

### **10.1. The central theory of wellbeing**

#### **10.1.1. Summary of themes**

There were two main reasons why patients took part in one of the clinical trials studied: to reduce their pain and to benefit someone else. Patients described altruistic feelings towards patients in the same trial, patients in the future, including themselves, and towards the trial staff. Patients were also attracted by the lack of invasive measures and the apparent simplicities of the trials.

The trial process was found to be straightforward at least, if not even enjoyable. There were aspects that were difficult, such as taking a large number of tablets, but patients indicated that they had not found being on the trial a burden.

Some patients had severe pain before the trial started. There were many ways in which the pain impacted on their lives. Those patients who did have a positive analgesic response to the trial were very pleased with the outcome. Those who did not get a pain response still tried to take a positive outcome from the trial, such as in the solace of an altruistic act. Patients were aware that while on the trial, failure of

pain reduction was a possibility. Some patients could be stoical about the lack of response while others showed an underlying disappointment.

Some patients took a great amount of pleasure and benefit from their relationship with the trial staff. These patients were made up of both those who had a good pain response and those who had a poor pain response during the trial. My opinion is that this relationship was independent of a patient's pain response. Some patients described the interaction as similar to the one they would have with family or friends. They described the fun of taking part in the trial and of the beneficial structure that the trial offered. It seems that patients developed feelings of trust towards the trial staff and felt a sense of security from their presence and availability. However, some patients were less effusive about the trial staff and again this was independent of their response to pain. It was not clear to me why some patients would be so positive about the trial and its staff while others were almost complimentary just to be polite and did not describe the trial having any significant impact on their life. Some patients would also talk of other relationships with either relatives or other health professionals that they valued highly.

Patients were happy to have taken part in the trial. Some were happy to consider taking part in another trial again while others thought that their body had had enough. Patients did not tend to see the trial as a burden overall. They felt that trials were important and needed to take place.

### **10.1.2. The central theory of wellbeing explained**

Over the course of the interviews, I found that that many things could have a positive impact on a patient. The patients spoke of the relief of having their pain reduced, of the compassion that had been shown by a trial nurse or of the security that being in a trial could offer. Yet nothing was universal. A trial nurse could make a tremendous impression on one patient and be described in measured terms by another. Patients who did not have a reduction in their severe pain still described the experience as a positive one and would take part again. I felt there was something that linked these differences together; something that each participant shared which I had not considered.

It struck me that the experiences of taking part in a clinical trial made an impression on a patient's wellbeing. It was this wellbeing that was central to everything else.

I think of a patient's wellbeing as something that is unique to them. As the word describes, it is a 'wellness' of their whole being. It is an equilibrium that is sensitive to internal and external influences. The internal factors could be physical, emotional or spiritual. The external factors could be the interaction with others or the loss of an activity, such as driving. Like pain, to compare two patients' states of wellbeing would be meaningless.

I will describe positive and negative impacts on a patient's wellbeing (see Table 3), the impact of the trials on a patient's wellbeing as well as discussing the individuality of wellbeing.

### ***A positive impact on wellbeing***

A patient's wellbeing is intangible yet we can intuitively see if something has an impact on it. When Pt5 said that a reduction in his pain was '*relief beyond relief*', it was clear that this was having a positive effect on his wellbeing. The security of the presence of the trial staff made patients less anxious, which had a positive impact on their wellbeing. When Pt16 spoke of the '*awareness*' that he felt, he seemed to be speaking of an awareness of patients' wellbeing. The staff appeared to be willing to do things that boosted or maintained patients' wellbeing rather than diminish it.

### ***A negative impact on wellbeing***

Aspects of the trial, or care in general, could have a negative impact on a patient's wellbeing. Being faced with eight new tablets on top of the usual thirty tablets is one example. Patients spoke critically of previous experiences in clinics and hospitals regarding the manner in which they were spoken to or how they were looked after. The instances patients recalled could have been many years previously yet they were still told with fresh hurt or anger. These episodes had such a negative impact on patients' wellbeing that they still recalled the incidents with clarity.

### ***The overall impact of the trial on wellbeing***

What was not clear initially was the juxtaposition between patients describing parts of the trial which might have had a negative impact on their wellbeing and yet still being positive about the trial in general? As I described in chapter 9.1.1.2, a patient's pain may not have improved during the trial yet they were still positive about taking part in the trial. In these cases there were other reasons for the patient to be positive

about the trial. An example was Pt19 who felt that being on the trial may have a potential benefit to her five daughters in the future. Despite having to withdraw from the trial before her pain improved, by taking part in the trial and so potentially helping her daughters in the future, she was able to take an overall positive view of the trial and subsequently feel an increase in her wellbeing. Table 3 lists some of the potential influences of the trial on a patient's wellbeing.

**Table 3 - Examples of positive and negative influences from a trial on a patient's wellbeing**

POSITIVE INFLUENCES	NEGATIVE INFLUENCES
Pain reduction	Taking too many pills
Altruistic acts	Failure of the trial to reduce pain
Trial staff input	Difficult questions to answer
The structure	Side effects
	Becoming annoyed by the trial

***The individuality of wellbeing***

Influences from different aspects of the trial had different significance for different individuals. For example, the fluctuation in a patient's pain state could increase or decrease patients' wellbeing by different amounts. Similarly, the benefit received from the input of the trial staff may be greater in some patients than in others. When all of the variable factors of the trial are taken into account, the overall outcome of the trial, whether positive or negative, is likely to vary between individuals. This might suggest why some patients found the trial to be a very positive experience, while for others it was something that fitted into their daily routine without having much impact.

The fluctuation of a patient's wellbeing is dynamic. I do not think of it as directly proportional to factors such as disease state, or physical condition. Instead I think that these factors play a contributory role in the state of a patient's wellbeing. If the positive influences on a patient's wellbeing, perhaps emotional or spiritual, have a greater effect than the negative influences, potentially physical, it may explain why a patient, who had no reduction in their pain, was willing to continue to take part in a clinical trial.

### **10.1.3. Conclusion - central theory of wellbeing**

I have described the concept of a patient's wellbeing which I believe is the central theory of advanced cancer patients' experiences of clinical trials. I have described how positive and negative features of a trial can influence a patient's wellbeing and how one can have a greater bearing than another towards the overall wellbeing.

However, the total influence from the clinical trial on a patient's wellbeing is finite. Everything that goes on in a patient's life can increase or decrease their wellbeing. The influencing factors from a clinical trial could have a very small or very large impact on a person's overall wellbeing. The context of the trial in relation to a person's overall wellbeing is beyond the scope of this thesis. What has been considered is the impact that being on a trial has on a person's wellbeing.

## 10.2. Considering the study findings in relation to the current literature

### 10.2.1. The literature describing wellbeing

The concept of wellbeing in terminally ill patients is extensively discussed in the literature. Some authors describe psychological wellbeing while others describe psycho-spiritual wellbeing. I think that the overall concept is the same. I have chosen two main papers to discuss in the context of this study.

Lin and Bauer-Wu have written a comprehensive and integrative review of the literature on psycho-spiritual wellbeing in terminally ill patients. Their aim was to *'synthesize the literature and develop generalizations about substantive issues that contribute to psycho-spiritual wellbeing in patients with advanced cancer'* (Lin and Bauer-Wu, 2003). The proposed themes that they presented were: self-awareness, coping with and adjusting effectively to stress, having satisfying relationships with and connectedness to others, sense of faith, sense of empowerment and confidence, and living with meaning and hope. Some of their findings resonate with the findings of my own study. An example of this was discussing patients' interactions with health care staff. Yeung's paper found that *'health care professionals who used empathy, understanding and reassurance contributed to positive psychological outcomes for patients'* (Yeung et al., 1999, Lin and Bauer-Wu, 2003). The authors' concluding comments are also pertinent to this study:

*'The studies suggest that psycho-spiritual wellbeing is a concept that can be enhanced or diminished in patients with advanced cancer, and that those who have an enhanced sense of psycho-spiritual wellbeing are able to cope more effectively with the process of terminal illness and find meaning in the experience. Open communication and positive relationships with health care*

*professionals have been shown to be important in enhancing psycho-spiritual wellbeing. However, there is a paucity of research on specific interventions in this area....qualitative studies are also needed to understand more fully psycho-spiritual wellbeing among these patients'* (Lin and Bauer-Wu, 2003).

It was after I had written my conceptual description of patients' wellbeing that I read this paper. To read such similarities to what I had observed and described was heartening and confirmatory of my findings. Although the clear primary aim of the clinical trials studied was to reduce pain, it could be argued that for some patients, a side benefit and therefore a specific intervention, was an improvement in patient wellbeing. I would also argue that this study has gone some way to describing elements of a trial that can have an impact on patients' wellbeing.

Folkman and Greer describe a theoretical framework for psychological wellbeing during a serious illness and the variables that contribute to the psychological wellbeing (Folkman and Greer, 2000). In my findings, I speculate that patients who did not find an analgesic benefit from the trial tried to find a benefit from other sources, such as performing an altruistic act or benefiting from the interaction with the trial staff. This may have been consciously or unconsciously. Folkman and Greer describe '*meaning based coping.*' This '*generates positive affect, which provides a psychological 'time out' from the distress and motivates further coping. An important feature of this positive affect is that it can co-occur with negative affect, perhaps not at the very same moment, but certainly close in time.*' I think that patients in this study were showing examples of meaning based coping when they spoke of other parts of the trial that held benefit for them beyond just the pain response.

As shown above, current literature has already described components of patients' experiences that have an influence on their wellbeing. Given the degree of complementary elements that I have described in this thesis compared to the described elements in the literature, I feel that within this studied group, the clinical trials had the potential to influence the patients' sense of wellbeing. As the concept of patients' wellbeing is something that emerged from the data as the study progressed, I was not able to measure or assess patients' wellbeing over the course of their trials. However there are scoring methods such as the Positive and Negative Affect Scale that have been designed for this function (Watson et al., 1988). Including this scoring scale in future trials may show the evolution of a patient's wellbeing as a trial progresses.

### **10.2.2. The literature describing research in the advanced cancer trial population**

To my knowledge this is the first study that has explored the experiences of advanced cancer patients who have taken part in symptom control trials, therefore I am unable to compare this study directly with anything of a similar nature. However there is merit in comparing the findings with advanced cancer patients' opinions on palliative care research and their experiences in early phase chemotherapy trials.

#### **10.2.2.1. Comparison with previous studies involving advanced cancer patients' opinions on research**

There are some similarities with the published studies that interviewed patients to explore their opinions on research in palliative care. The theme of altruism is similar to that described in the systematic reviews discussed in chapter two (Todd et al.,

2009, White et al., 2008). It is interesting that one of the main negative features described by Todd, that of anxiety relating to placebo medication, has not been borne out in this study. Terry had found that information about trials should focus more on discussion than on written information which was corroborated by some patients that I interviewed (Terry et al., 2006). When I asked patients about the manner in which they had received information regarding their trial, their responses were varied. Some patients had a good idea of what the trial entailed and others seemed to have largely misunderstood the main aims of the trial. Patients also showed poor recollection the information that they had received and some held a preference for spoken over written information.

#### **10.2.2.2. Comparison with phase I and II clinical trials of chemotherapeutic agents**

During the literature search for this thesis, papers were excluded that had studied life-prolonging treatments such as chemotherapy. However, as the study progressed, I become more aware of similarities between these trials and my own area of interest. The clearest similarity is in the studied patient population. Generally, phase I clinical trials involve patients with advanced incurable cancer; the same population that I have studied. Therefore there is merit in studying papers that have involved patient experiences of chemotherapy trials, particularly phase I trials, to compare these findings with my own.

There are four main authors who have contributed to exploring patient experiences in oncology clinical trials (Cohen et al., 2007, Cox, 2000, Madsen et al., 2007a, Madsen et al., 2007b, Wootten et al.). Their work comes from North American, Europe and

Australasia. The authors have all explored patients' experiences around the time of a clinical trial. I was aware of Madsen's work before starting my data collection due to the similarity of the grounded theory approach that he adopted (Madsen et al., 2007a, Madsen et al., 2007b). His work is also discussed in chapter 2. However, I was not aware of the other three. I will discuss the differences and similarities between the oncology trials and the trials that I studied separately.

### ***Differences between Phase I and II trials and my studied trials***

The fundamental difference between these trials is the complex issue of offering life-prolonging treatment. Patient motivation in taking part in the chemotherapy trials is especially complex. Cox describes patients taking a more positive attitude to the life prolonging nature of the trial than may have been presented to them by the trial staff (Cox, 2000). The patients in the KPS and PBT were fully aware that the trials being offered to them would not prolong their life.

Another difference is the physical change that patients may feel while on the two types of trial. Often within phase I trials, the outcome may be measured by tumour reduction rather than any subjective feeling of the patient. This makes a tangible positive outcome from phase I trials less apparent to patients. With a clinical trial aimed at pain reduction, patients are much more able to 'feel' that the trial is having a positive impact. For the phase I clinical trials, patients are more likely to experience the negative aspects of trials in the form of side effects than any positive outcome (Cox, 2000).

The end point of chemotherapy phase I trials seemed to be very different to the KPS and PBT. In the phase I trials described, the most likely endpoint was when patients were withdrawn from the trial due to side effects or deterioration (Cohen et al., 2007, Cox, 2000, Wootten et al.). This differs from the KPS and PBT where the majority of patients studied completed the trial with little difficulty. Being withdrawn from the trial had a negative impact on patients who were then forced to face difficult questions regarding future treatment options and the status of their disease (Cox, 2000, Wootten et al.). This issue did not seem to arise in the population that I studied.

Patients did not feel that they had a choice whether to go in to the trial or not and they also felt that they were 'living their life on hold' while being involved in the trial (Cox, 2000). From these papers, the experience of taking part in a phase I or II trial appeared to be very onerous. Patients were very graphic about the severity of side effects that they had to put up with or the demands of the trial participation (Cohen et al., 2007, Cox, 2000, Wootten et al.). Quality of life issues were discussed and described in a negative context (Cohen et al., 2007). This also differed from KPS/PBT findings which suggested that patients felt that they were able to reject trial participation and did not feel that their lives were negatively impacted while on the trial.

### ***Similarities between phase I and II trials and my studied trials***

During my reading I discovered, patients gained a lot from chemotherapy trials other than the response to the medication. They described the positive benefit of

performing an altruistic act, enjoying the relationship with the research staff and the amount of attention that they received (Cohen et al., 2007, Cox, 2000, Madsen et al., 2007b, Wootten et al.). Madsen describes the differences in patient satisfaction between two trials where the number of doctors and the continuity of patient contact is very different (Madsen et al., 2007b). The patients who were cared for by the same small trial staff gave a much more favourable description of their interactions with the trial staff than those trial participants who were cared for a large and variable group of researchers.

I had speculated that throughout the time frame of the trial, patients might change their opinion as to the reasons why they were taking part in the trial and the relative importance of each reason. This was corroborated with one of the studies:

*'When hope of symptom relief and cure were not met participants re-evaluated the benefits of their participation and attached a stronger meaning to altruistic aspects of participation.'* (Wootten et al.)

Some patients in the phase I and II trials had difficulty with the information that they were given (Cox, 2000, Madsen et al., 2007b). Some had either misunderstood the point of the trial or had put an incorrect amount of hope in the possibility of a cure for their disease. I described misunderstanding of the aim of the trials also and particularly on the use of placebo medication. In similar comments, patients described the various merits of written information and spoken information with trial staff (Cox, 2000, Madsen et al., 2007b).

Patients did seem happy to have taken part in phase I and II trials and would do again in the future (Cox, 2000). Although this opinion was similar to my findings, what

was interesting was that the patients who felt this had also had a very difficult trial experience with a large number of side effects and significant impact on their lifestyle. I think that this highlights the power and significance of the undercurrent of life-prolonging treatment in phase I and II trials. Despite going through very challenging trial periods, patients appear willing to take part because of the overall potential life-prolonging benefit.

Another similarity is the issue of what happens after a trial finishes. Patients in these papers give vivid descriptions of distress and abandonment after they finish the trial, having either completed the course of treatment or been withdrawn from the trial (Cohen et al., 2007, Cox, 2000, Wootten et al.). This was an area that I was only able to touch on and speculate about but the descriptions in these trials add a greater weight to this topic.

### ***Conclusions***

I have found several differences and similarities with my own findings when studying the experiences of advanced cancer patients who have taken part in phase I and II trials. I am pleased that I conducted this search of the literature after I had completed my own data collection and analysis so that I was less aware of others' findings before I was able to engage in the topic myself. I believe that the similarities carry greater weight and resonance due to my lack of awareness of them before starting my own data collection.

### **10.3. How is this study useful beyond the scope of the studied participants?**

The population studied was a broad section of patients with advanced cancer. Attempts were made to sample a wide range of patients with different experiences. Although all patients studied had metastatic cancer, for the most part they would not be classified as in the end of life phase of their illness. At the end of the research period, only 9 of the 21 patients interviewed had died. A lot of the patients were still mobile outside of their houses and were still carrying out activities of daily living. Only four patients had an ECOG score (Eastern Cooperative Oncology Group) of three at the time of interview. Some patients were limited in their mobility within the house although this may have been related to pain rather than overall progression of their illness. At the start of the study, I thought that a lot of the patients would be in a similar position to those that I encountered in hospices, spending over 50% of their days in chairs or bed for example. However, this was not the case. The patients studied were community based palliative care patients rather than in-patient based, end of life palliative care patients. The group of patients studied was similar to the types of patients that are frequently encountered within the palliative care community. Therefore I think that the findings from this thesis hold interest for all practitioners of palliative care. As well as holding interest for the palliative care community, several findings of the thesis hold interest for any clinical trial practitioner and those who interact with patients in general.

In this section I will discuss the findings that I think are useful beyond the scope of the studied participants. These are the concept of wellbeing, information given to patients, recruitment of patients and transition of care.

### **10.3.1. The concept of wellbeing**

When a patient's wellbeing is kept in mind during trial design, this may increase the potential for the patient to find the trial a positive experience. In turn this is likely to result in a reduced attrition rate. There is a potential benefit that lies in the relationship between patient and trial staff. In these trials, by providing an atmosphere of trust, security and familiarity for patients, the trial staff created an environment that had the potential to increase their patients' wellbeing. Following this model may be of benefit to others designing clinical trials in the future.

The concept of patients' wellbeing is not limited to clinical trials. Pt16 described the environment of the regional oncology centre when someone met him and offered him a cup of coffee.

*Tom: Can you tell me why that's so important to you?*

*Pt16: Och it is important to people who are feeling sorry for themselves and don't know what direction they're going in. You're looking for, you're no' looking necessarily for reassurance, but you're looking for (sighs) a bit o' light-heartedness, I dunno. I've not really considered that aspect of it but that's what it's about, it's just the general demeanor of the chap who's always...always seems to be there in the, the arrival lounge area at the [Hospital 1], so nice and chatty 'Can I help you get you a coffee, or can you manage to get one yourself?' and it makes a difference.'*

This is an example of a positive influence on a patient's wellbeing. Whether these actions are conscious or unconscious, patients have shown the potential value that they can hold.

### **10.3.2. Information given to patients and patient understanding of the trial**

Patients described a variable knowledge of the trials in which they participated. Some patients were not aware of the process by which placebo medication was administered; some had a poor understanding of the risks of side effects; others had a complete grasp of the trial and its implications. Patients also had variable recollection of the information that they were given. There was a group of patients who had little inclination to read or comprehend the information sheet. They expressed a preference for information being explained to them verbally and held a belief that anything particularly serious would have been explained in this manner. This calls into question the way in which information was given to patients and the checking of patients' understanding of the trials they were undertaking. This was similar to the findings studies involving phase I chemotherapy trials (Cox et al., 2005, Madsen et al., 2007a). Putting greater emphasis on explanation rather than information sheets may be considered in the design of future studies.

A pertinent question is why some patients appear to have a poor understanding of the trial process. Certainly, by the time of interviewing a patient, it may have been a few weeks to a few months since the trial finished and the finer details may not be as clear in their mind. Patients did admit that they were sometimes confused about the different information sheets that they had been given for various trials and procedures. Looking at the situation in another way, the patients may have happily ceded responsibility of being in a trial to the research team. If you have trust in the research team, your knowledge requirements may be reduced.

### 10.3.3. Recruitment of patients

There are many factors that have been described in the literature regarding barriers to taking part in a clinical trial (Mills et al., 2006a). As all patients interviewed took part in the trial, my comments describe some of the factors that patients discussed around the time of patient recruitment, rather than barriers to taking part.

Some patients described being '*hijacked*' or '*accosted*' when first encountering trial staff. Although it is difficult to know the actual situation and whether these patients were distressed by these incidents, their choice of words suggests that there was the potential for this first meeting to be stressful for patients, whether they agreed to take part in the trial or not. The patients who reported these feelings of anxiety at the time of recruitment all took part in the PBT rather than the KPS. A difference in design of these trials is that the PBT generally started on the same day as the radiotherapy treatment. If patients did not start their medication on this day they were unable to take part in the trial. A standard requirement of an ethics committee is for patients have 24 hours between initial contact and recruitment onto a trial to consider the information they have received. As this was not always possible in the PBT, an exception to this requirement was approved, so that patients could be recruited and started on the trial medication on the same day. Some patients may have been responding to this lack of time that is usually afforded to them. This suggests that the standard requirement is beneficial for patients; to have the time to consider what is being offered.

It may be that these episodes of stress during the first encounter are less significant

than I have stated. Pt3 gave contradictory reports of his pain status during his interview but he did maintain at times that he had no pain. As a result he felt that the benefit of taking part in the trial was not for himself but for the researcher. In his words, he was '*persuaded*' to take part, even with no pain. To be entered into the trial a patient has to have a significant degree of pain. Although Pt3's memory may be different to what he reported at the time, his perception at the time of interview is valid. Trial staff have to recruit patients for their trials to be a success. It may be that some perceptive patients feel this pressure being transferred on to them.

#### **10.3.4. Transition of care.**

Patients highlighted the benefit that they can derive from the interaction with the trial staff during the trial. However they also mentioned the difficulties that may arise when this short yet intense relationship comes to an end. At the end of the trial some of the aspects of the trial that the patients found so beneficial, such as the security of presence and regular contact with the trial staff came to an end. Some patients described restarting or increasing their contact with their community palliative care team. Other patients appeared to be less clear where they were able to obtain a similar style of support. Perhaps there is a greater detriment to the patient by the loss of these benefits, than receiving them in the first place. Perhaps trial staff should be aware of this potential during the trial and make greater efforts to prevent the occurrence of this sense of loss. This is beyond the scope of this study but is worth highlighting for future work (as discussed in chapter 10.5.2). Work on this transition has already been conducted in early phase cancer trial population (Cox et al., 2005).

## **10.4. Reflection on the whole study**

Throughout the study, I have conducted reflexive practice to be aware of my position within the research process. While examples of this are described throughout the thesis, I will collate the most salient points here. I will also look at aspects of the study that may have had an impact on the findings that have been presented.

### **10.4.1. Personal impact**

As I have described in chapter 4.2.1, I am a 32 year old, middle-class, Caucasian male doctor with an English accent. I think that these characteristics have played an influential role in the outcome of the study. As a palliative care doctor, I assumed a role of authority when patients were questioning an aspect of their care. Patients would ask me technical questions which I was able to answer. Whilst I was able to help patients with their questions, and so hopefully gain their trust, I was also putting myself above them in the power dynamic. Although I tried to distance myself from the trial staff, thus ensuring the confidentiality of the patients' views, I was still often viewed as part of the trial staff. I think that this may have made patients slightly reluctant to discuss negative aspects of their experiences as I was not a completely independent body. Being part of the health care profession immediately puts me on that side of the balance and I think that my findings are swayed towards viewing the patients' experiences from this angle. Had the research been conducted by someone who was not related to the health profession, their view may have been quite different.

Although I made efforts to create an equal power dynamic, in reality this was not possible while I presented myself as a doctor. I would not have felt comfortable

concealing this information from patients so I acknowledged and accepted this imbalance for what it was and the impact that it had.

Anxieties of novice researchers are to be expected and I was no different. Although I made efforts throughout the interview process to develop my interviewing technique, I still look back at interview transcripts critically with views of how the process could have been better. Similarly with data analysis, had the study been conducted by a more experienced qualitative researcher, the findings may have been different. However it is accepted within the literature that there may be limitations of novice researchers. Glaser described grounded theory as a learning process.

*'It is okay when the future is the continuing skill development in doing grounded theory.'* (Glaser, 1999)

Similarly, Heath and Cowley offered advice which I followed throughout the process:

*'The novice researcher should set aside "doing it right" anxiety, adhere to the principle of constant comparison, theoretical sampling and emergence and discover which approach helps them best achieve the balance between interpretation and data that produces a grounded theory.....It is wise to remember too that the aim is not to discover the theory but a theory that aids understanding and action in the area under investigation.'* (Heath and Cowley, 2004)

I believe that I adhered to this advice and am able to be satisfied with the results that have been generated.

## **10.4.2. Areas in the study that could be improved**

### **10.4.2.1. Patient recruitment**

Patient recruitment in palliative care research can be challenging for reasons such as gatekeeping, attrition rates and ethical limitations (Dean and McClement, 2002).

The difficulties in this study were: gatekeeping, the manner in which patients were approached and recontacting patients after they had been given the information sheet.

### ***Gatekeeping***

One of the exclusion criteria for the study was if patients were ‘in the dying phase of their illness.’ This was decided by discussion between me and the trial staff. As described in chapter 4.1.2, the description ‘in the dying phase’ of their illness is deliberately ambiguous. Indeed it is not possible to quantify. However, by deciding a patient was too unwell to be approached, the trial staff and I were making an assumption on the patient’s behalf that we could not be sure was their wish. On one hand, there is a risk of offending them and their family by requesting that they give up more of their time when they are at the end of their life. However, by assuming that they were too unwell, we may have been preventing patients from making a contribution that they would have liked to make. I can see the double-standard of being aware of the hindrances of gatekeeping in palliative care research and still acting in the same manner myself. I think that this highlights the delicate balance of this area. As a researcher, either you take part in gatekeeping to whatever degree you feel is appropriate, or you run the risk of offending or upsetting a percentage of patients by asking them to take part in research. Clearly this level is different for different researchers. Out of 22 patients that Terry interviewed for his study, 14 died within 48 hours of the interview (Terry et al., 2006). In the same situation, I might have excluded these patients as being in the dying phase of their illness.

### ***The manner in which patients were approached***

There were several ways in which patients were approached to consider taking part in this study. Some patients were telephoned by me with no prior mention of the study by the trial staff. Others were given the information sheet or had the study discussed with them by the trial staff before I contacted them. Certainly for the latter approach, and even sometimes for the former, I felt that in the eyes of the patients, this positioned me strongly alongside the trial staff. Although I made efforts to distance myself from the trial staff, I felt that this was a significant factor. However, during interviews, some patients had described their displeasure at being 'cold-called' by other trials or studies. These patients may not have taken part in this study if they had not been contacted, or at least been made aware of the study, by the trial staff.

I have already discussed the limitation of not being able to interview a patient who the trial staff felt had not been happy during the participation in the trial. These patients seemed to be rare. On one occasion when a patient of this nature was approached, it was by the trial staff who it was felt he was not happy with. This may have been a contributing factor to him rejecting the offer to take part in the study. Had I called him, he may have been more amenable to agreeing as he may not have seen me as part of the same team. More effort needs to be spent considering how these patients can be included in studies like this one. It is very important that the patients who have a poor experience of clinical trials are able to share these experiences. The manner in which they are approached could be vital in succeeding in recruiting them and learning from the aspects of a trial that they did not enjoy.

### *Re-contacting patients after they had been given the information sheet*

The ethics committee were very clear that patients were to be contacted only once to discuss recruitment. Although I agreed with the sentiment of not pursuing patient recruitment when it was uninvited, this did pose difficulties. There were times when patients stated they had a chest infection or were not feeling well that day but asked me to call back another time. I was unsure whether this was genuinely the case or they did not want to take part in the study without actually saying so. I was in a similar dilemma when leaving a message on patients' telephone. Throughout the process I tended to err on the side of not recontacting patients. I felt that I would rather be in the position of not recontacting a patient who had wanted to take part than pursuing patients excessively who did not want to take part but did not want to say so explicitly. I felt that if a patient was very keen to take part, they would contact either me or the research team.

#### **10.4.2.2. The trials being studied**

The studied trials contained a small number of patients over two sites that were being run by the same medical team. This introduces several limitations. Although the trial nurses were different between Edinburgh and Glasgow, they had been trained and nurtured by the same two doctors. It may be that this team is exceptional at their delivery of patient care and the medical influence has rubbed off on the trial nurses. If patients were recruited from different parts of the country which had entirely different research teams there may have been a wider range of experiences, particularly regarding the interaction with the trial staff.

The trials are also relatively undemanding for patients and use medication that is well established and is largely known to have a low side effect profile. These facts may put a distortion on the findings of the patients that may not be reflected in other symptom control clinical trials.

#### **10.4.2.3. Data Analysis**

##### ***Supervising staff***

The main point of supervision was Dr Laird who was also heavily involved in the running of the trials. He is described by the patients and is the initial medical link for the trial nurses from Edinburgh and Glasgow. He would read the interview transcripts and we would discuss themes that I was developing. Within this relationship there is a conflict of interest between the running of the trial and the development of this study. By reading the early interview transcripts, his approach to later patients could have changed which might in turn influence their experiences of trials. However, during the data analysis, the work was my own and the themes that I developed were done independently. It is a limitation that he participated in this study while being so involved in the trials. However I feel that it is a relatively small one due to his limited contribution to the data analysis process of the study.

##### ***Methods for data analysis***

During the theoretical sampling of patients, the change in patients' pain, measured by the Brief Pain Inventory and McGill Pain Questionnaire, was used to select suitable patients. As well as completing these pain scoring tools, patients also completed a depression screen and a quality of life tool (the Hospital Anxiety and Depression Scale (HADS) and the Euroqol quality of life thermometer). These could have been

implemented during the data analysis as a point of triangulation for patient responses and descriptions of the trial. Once the concept of wellbeing during the trials was forming, it would have been possible to have gone back and looked at patient HADS scores and Euroqol ratings at the start and end of the trial. This may have added weight or challenged the views that patients held.

The decision was made close to the start of the study not to conduct focus groups. If patients had had the opportunity to meet collectively and discuss their own and each others' experiences of being in a clinical trial it may be that new light could have been shed on the topic.

#### **10.4.2.4. The interview process**

##### *The style of format of the interview*

I have described the flexible nature of the interview process. Patients were allowed to bring up topics which were important to them. However, the frame of the interview was predetermined by me and I led patients along this frame rather than allowing them to initially lead the interview. I think that this decision restricted the opportunity for patients to describe what they had remembered about the trial and directed their responses towards my agenda. This may have diminished the potential for new discovery from patients.

##### *The choice of having only one interview*

Another point of discussion was the choice to have only one interview session with each patient. The advantage of this is that it is less time consuming for patients. Again this was something that was important for the ethical approval of the study. By interviewing a patient once at the end of the study, I received a snap-shot of their opinion at that time. While these opinions remain valid, had I interviewed patients at different points of the trial their responses may have been very different in three main ways. Firstly, I have speculated that their opinions on hope for the trial and their reaction to a failure to reduce pain may have changed as the trial proceeded. Secondly, I think that as patients got to know me better, we may have been able to have more in-depth conversations on topics that they did not feel comfortable talking about during a first meeting. Finally, there were times when I would have liked to have discussed issues with patients that they brought up in interviews once I had a chance to analyse their views in the context of themselves and other patients. By being limited to only one interview, this option was not available to me.

As patients' experiences of trials and studies were not known, on reflection, I think that the approach of one interview per patient was appropriate for this study. However, with this studied group suggesting that taking part in research was not a burden, a more longitudinal approach might be more appropriate for a future study.

### **10.5. Further studies to be developed**

The findings and process of this study has suggested other studies that could be conducted in the future, either by me or by others who could use my findings as guidance for their own work.

### **10.5.1. Changes to this study if it was repeated**

With the knowledge that I have gained from conducting this study, if I were to repeat it, there are several aspects that I would do differently.

#### ***Single interview of patients***

Patients have described their experiences of taking part in a clinical trial. However their opinions were sought at the end of the trial, once their participation had finished. My speculation is that their opinions may change as the trial proceeds. This speculation has been borne out in other studies (Wootten et al.). An example of this is what patients were hoping to get out of the trial. The results generated suggest that patients wanted an improved level of pain control but they were also motivated to a certain degree by the altruistic nature of the trial. It may be that at the start of the trial the patient's main focus was on pain control with altruism playing a small or negligible part. As the trial progresses, and potentially their pain does not diminish, the altruistic nature of the trial starts to play a greater role in their mind. Multiple interviews along the course of an illness, common in the wider spectrum of social science, can give a better picture of a patient's experience (Murray et al., 2009). However, this approach is thought to be underused in medicine (Lewington et al., 2007, Murray et al., 2009).

The decision to interview patients only once was made when it was unclear what patient experiences of clinical trials were like. Having found these trials to be of relatively little burden to patients, I think that it would be reasonable to interview patients at different stages of a trial. At the least, it would be beneficial to interview patients before they started the trial, while they were taking part in the trial and after

they had completed the trial. In this manner, any change in opinion could be monitored.

The disadvantage of this approach would lie in the selection of patients. It would be harder to sample patients who might offer differing experiences if they were recruited before the trial started. Because of this, it might be appropriate to have a combination of patients who were recruited at different parts of the trial, depending on their response and involvement in the trial.

### ***Use of concurrent tools***

As described in chapter 10.4.2.3, I would take a greater benefit from the scoring tools that patients completed. In particular these would be the HADS and Euroqol thermometer. This data could be compared with the views that patients were giving to stimulate further discussion.

### ***Running of the trial***

As I have described in chapter 10.4.2.1 there were several limitations to the way in which patients were recruited and how I as the researcher was seen by the patients. I think that it would be important to try and have a greater distance between myself and the trial staff. They would not be involved in discussing this study with prospective patients and would not be involved in the selection of patients who were to be approached. This would run the risk of contacting patients who may be in the 'dying phase' of their illness but it may be that these patients would welcome the opportunity to discuss their experience of the trial.

I would also have supervision from someone who was not related to the trials. This would allow a more independent view on the data that was being generated without the risk of influencing, either consciously or sub-consciously, future patients who were taking part in the trials.

As discussed above in chapter 10.4.2.2, there would be benefit in studying patients from different trial sites which were being run by different trial staff. This would allow for a wider range of patient experiences.

### **10.5.2. Future studies of a different nature**

There are several areas of interest that have been generated from this study that I would like to explore further.

#### ***Relating to wellbeing***

The concept of wellbeing has been developed over many years. Its role in relation towards patients with advanced cancer specifically is also well documented (Lin and Bauer-Wu, 2003). What I think would be interesting would be to try to measure how this wellbeing may change over the course of a clinical trial. There are several scoring tools to measure wellbeing. The Warwick-Edinburgh Mental Well-being Scale and the Positive and Negative Affect Schedule are just two (Tennant et al., 2007, Watson et al., 1988). These could be incorporated into clinical trials in the manner in which other scoring tools such as the HADS frequently are. This would allow the change in patient's wellbeing to be assessed as a trial progressed. This

would inform researchers in the design of future studies as to what may have the maximum positive impact on a patient's wellbeing while taking part in a trial.

***A study to investigate patient experiences after trial completion***

In my findings, I commented that patients may have difficulty coming to terms with the loss of the regular medical or nursing contact once a trial comes to an end. Cox also discusses this sense of abandonment at the end of a phase I trial (Cox, 2000). Cox has subsequently looked at the implementation of nurse-managed phase I trial conclusion with positive findings (Cox et al., 2005). There is scope to investigate this period further for advanced cancer patients who have complete symptom control trials. At this time in their illness trajectory, several patients will benefit from specialist palliative care input beyond the capacity of the trial staff. Patients described instances of this service being implemented but other patients described still being in pain and uncertain who might be able to assist in their management. Are trial patients being hindered from accessing palliative care services because of their participation in a symptom control trial? The input that patients receive during a clinical trial from trial staff is greater than can be expected for all patients in the final period of their illness. Does the fact that patients experience this for a period of time before returning to a more routine amount of input have a negative impact on the patient? It would be interesting to conduct a longitudinal study of patients who have completed a trial to see how they experienced their healthcare after the high intensity contact offered during a trial.

*A study to investigate the attitudes of healthcare professionals towards symptom control trials for advanced cancer patients*

One of the most striking findings of the study was the potential benefit that patients could receive from the relationship with the trial staff. I am interested in what it is about these staff member that make such a difference to patients. Do they differ from other members of the palliative care community? What are their similarities and differences of the trial staff to each other? Does the attitude of the senior clinicians have an impact on the staff below them? One variable that should also be taken into account when studying the attitudes of research staff is the amount of time they spend with patients. This simple act may be more significant than the manner and attitudes of the research staff.

The other interesting factor is how do these trial staff members differ to other health care professionals who may not be involved in clinical trials or palliative care? The success of clinical trials can often depend on the willingness of other professionals to refer patients towards the trials. Excluding palliative care physicians, those referring patients could be oncologists, general practitioners or district nurses. What are their opinions towards clinical trials in palliative care and what are the barriers that might prevent them from referring patients towards trials? Where would these findings fit in the context of the findings of this study which suggests the potential benefit to patients from taking part in such a clinical trial? A qualitative, interview based study of a wide range of health professionals may shed some light on this subject and inform the knowledge of barriers towards patients taking part in clinical trials.

## 10.6. Conclusion

In this thesis, I have set out to explore the experiences of advanced cancer patients who have taken part in clinical trials. As this has not been done before, there are no findings which I can compare my own with. I adopted a constructivist grounded theory approach with the aim of discovering theory within the data.

Patients were motivated to take part in the clinical trials for several reasons including a desire to reduce pain, altruism and for greater organisation or structure of their care. Patients found the trial to have positive benefits. I have shown that the experience of being in a clinical trial involves many different factors, of which pain reduction is just one. Altruistic reasons for trial participation and interaction with staff during the trial have been among the themes that have held most discussion.

I have described a model of patient wellbeing that is influenced by all aspects of the trial. A reduction in a patient's pain may increase their wellbeing. The interaction with the trial staff may increase a patient's wellbeing. A failure to reduce a patient's pain may have a negative impact on a patient's wellbeing but this may be countered by the interaction with the trial staff to create an overall increase in a patient's wellbeing. The influence of the trial on a patient's overall wellbeing may be large or small, depending on other inputs in their life.

I believe that this model meets the description of a completed theory that '*...provides the best comprehensive, coherent and simplest model for linking diverse and unrelated facts in a useful and pragmatic way.*' (Morse, 1994)

This study has given light to the experiences of advanced cancer patients on clinical trials, has shown direction for future research and gives examples of well received patient centred care.

## APPENDIX A: DATA ANALYSIS

It would not be possible or beneficial to outline the entire analytic process that took place during this study. Instead I will describe the active process that took place, rather than the theoretical ideal and illustrate this with extracts from the analysis. The aim is to show the reader the process that brought me to the results described.

### A.1 Coding

The software package NVIVO (version 8) was used to facilitate data analysis. As well as being able to annotate transcripts and organize memos, the central benefit of NVIVO was to structure my coding. A code as described below is assigned to a 'node' in the package. Nodes that are, or at least initially appear to be independent entities are referred to as 'free nodes'. Once it is clear that several free nodes are related to each other these can be collected under the title of a 'tree node'. An example is the tree node entitled 'Side Effects' with the free nodes that came under this topic.

Side Effects
Being wrong about side effect risk
Discussing the risks of a trial
Experiencing side effects
Failing to remember potential side-effects
Remember being assured of no side effects
Showing a relaxed attitude to side effects
Trials are safe
Was it a side effect or something else

Tree nodes can then be built up further into categories and from categories, developing concepts and an overall theory takes place. I will outline examples of how the stages of my coding developed.

### A.1.1 Initial coding

Initial coding was adhered to for the first 12 interviews. This involved remaining close to the data and where possible using gerunds to describe the data (Charmaz, 2006). By using words that reflect action I attempted to avoid making premature conceptual conclusions before sufficient data collection and analysis had taken place.

In an example from interview 5, I show the initial codes:

Codes	Transcript
<p>Pain was the only reason, Describing pain which required trial meds</p> <p>Describing initial contact made,</p> <p>Coming to decide to go on the trial</p>	<p>Pt5: If it's gonnae get that pain away.  And when you're in agony, the agony I was in, I was waking up during the night an', just wanting somebody to do away with me....</p> <p>TM: Really...</p> <p>Pt5:...that how much pain I was in.  Now, I went in there an', that day at the Beatsons and we met....[research doctor 1] and [research nurse 3]. He says well, 'We got a drug here, a trial drug'. I says, 'Well, I'm your man. I'll do it. I'm...I'll take this.' In a week,</p>

<p>Positive outcomes from the trial</p>	<p>ohh, so much relief.</p> <p>TM: Yeah</p> <p>Pt5: You know.</p> <p>TM: You don't think, you didn't have to</p>
<p>Coming to decide to go on the trial</p>	<p>think too hard about going ....</p> <p>Pt5:...no..</p> <p>TM:...into it. OK.</p> <p>Pt5: I never thought twice, somebody</p>
<p>Taking advice from relatives before agreeing to enrolling,</p>	<p>says.... Me an' [research nurse 3] spoke about it, and me an' my wife spoke about it, and I says look, 'gonnae help me, I'm taking this.'</p>
<p>Coming to decide to go on the trial</p>	<p>TM: Sure</p> <p>Pt5: Nobody's going to change my mind.</p>
<p>Stating happiness to take part</p>	<p>TM: Sure, sure. Why might they have changed your mind?</p> <p>Pt5: They wouldnae a'! Oh they</p>
<p>Stating happiness to take part</p>	<p>wouldnae 'a changed my mind.</p>

As with the originators of grounded theory, Charmaz advocates for line-by-line coding in the initial stages. Implicit concerns as well as explicit assumptions can be identified. An example of an implicit concern was with Pt9. He said, *'You never get*

*to hear of the people who go into the hospital, like me, and went to see the orthopaedic surgeon.....'* The crucial phrase of his sentence was '*like me*'. Although innocuous on paper, the feeling with which he said these words, full of vulnerability yet appreciation, spoke volumes for his opinions of the hospital staff that he was describing. This could only be elicited from the recording, rather than the bare transcription.

At the same time as the initial coding and familiarising myself with each interview, I annotated the transcriptions with thoughts that struck me while going through then to refer back to at a later date.

### **A.1.2 Focused Coding**

As the interviews progressed, I had started to develop tree nodes under which the free nodes were placed. The advantage of focused coding is being able to move quicker through the data compared to the time consuming line-by-line coding. If I came across data that had been covered by another patient I did not code this in a line-by-line manner. If the patient was saying something new I would code that piece of data. Alternatively if I felt that a patient was making a common point but in a particularly eloquent manner, I would code this to be able to use the quote in the future. Below is an example of my focused coding.

<b>Codes</b>	<b>Transcript</b>
All HCPs are great, all of them	Pt17: A' cannae say, a' cannae honestly say, I can criticise the treatment I've had.  Tom: You can't?  Pt17: No really, no really.

<p>Criticising non-research HCPs gently</p> <p>Complementing non-research HCPs</p>	<p>Tom: Happy customer....</p> <p>Pt17: Aye, well, it's just unfortunate that I've got this but I mean, I can honestly say, [clinical doctor 5], and also see that eh, a [clinical doctor 6], on the team, a [clinical doctor 6]....</p> <p>Tom: I don't know.....</p> <p>Pt17: ....She's a urologist...</p> <p>Tom: ....right....</p> <p>Pt17: ...and she's, she's very good. You know. She does have, says, 'How you feeling?' and that, 'Not too bad', 'Any problems with the waterworks?', 'No', 'That's fine.' Then shakes your hand and you're out the door! (laughing)</p> <p>Tom: quick!</p> <p>Pt17: Quick! Very quick. Very quick....[clinical doctor 5], he's very nice and he just explains it to you, you know, he says, 'Oh no, that's what it is.' He'd had a look at me, see this bone scan, and he says 'No it's coming from there, that's what does. That's what an electric shock is' he says, 'That's exactly</p>
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	<p>right'. So then, that, that was more or less it. Then when I was sitting outside, that's when the sisters came....</p>
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## A.2 Development of Categories

Once I had coded the first few interviews, several codes began to group together, for example, the interaction with the trial staff. The responses by patients were overwhelmingly positive both in those who had a reduction in pain and those who had not had a reduction in their pain. As the interviews progressed, I tried to get a fuller picture of what it was about the interactions that patients enjoyed. From here, the issues of trust and security started to become apparent.

This is an informal memo that I wrote at the time, trying to pull together some of the issues that were arising around research staff members:

*'Going through Pt12, trust is a big issue, and it also was with Pt9 too. Their credibility etc. Also Pt2 likes to think about [research doctor 1] as a good man with cars etc, Other people have said it is like talking to a member of family or a pal. Surely you would trust them. So perhaps trust is a really big deal that could link a lot of the other themes together. Esp the therapeutic relationship with the nurses, maybe they are working towards winning their trust. Has this been lost along the way, or have patients been let down. Remember Pt5 saying that people had said that they would do things and never did, thus diminishing the trust or the weight that you might have with others in the future.'*

Another dimension was those patients who were quite measured in their description of their interaction with the trial staff. They were not critical but were also not as enthusiastic as early respondents. This was interesting because I had initially thought that all patients would be this enthusiastic. This more measured description gave a more even balance to the category. I was interested in patients who might have felt

that trial staff were not satisfactory in their performance. As discussed elsewhere, recruiting patients who may have been able to shed light on this aspect of patient's relationships with the trial staff was to prove difficult.

By the time the interviewing and data analysis was complete, I had developed 14 categories as shown below. Some of these categories also had sub-categories. The category 'Being on a trial', which I abbreviated to BOAT, was further split into BOAT positive, BOAT negative and BOAT stride. BOAT stride referred to those patient who had taken the trial in their stride with it having too much of an impact on their life.

<b>CATEGORIES</b>
Being on a trial
Dealing with the placebo issue
Drugs (not trial)
Emotions regarding the trials
How you were when
Interaction with all HCPs
Interaction with lay others
Pain
Pre consent factors
Reasons for taking part
Reflecting on trials
Side effects
What wasn't there
Withdrawing from a trial

### **A.3 Theoretical Coding and Theory Generation**

*‘Thus, I suggest renewed emphasis on actions and processes, not on individuals, as a strategy in constructing theory and moving beyond categorizing types of individuals’ (Charmaz, 2006).*

With this quote as my guide, I wanted to develop theoretical codes and an overall theory regarding the studied phenomenon. The clear initial process was the path through the trial period. Before interviewing started, the process of being recruited, taking part in the trial and then having views on the experience of the trial was one that could be seen.

In October 2010, I wrote the following extract in a memo:

*‘I am thinking about the flow of the story. I can see a timeline with pre/during/reflections. At each step along the way there are bits sprouting off which you can then delve into in greater detail. This could be my big picture...’*

However in February 2011 my views had changed:

*'So you've got the linear pattern of the trial. Pre-trial & reasons for taking part, then BOAT, then reflections.*

*But through that you have the more subtle things like trust, research nurses, being aware, riding shotgun, the structure.*

*The problem with the linear pattern is that you could have worked that out before. The subtle things really have come directly from the data. But can you put these as one of the central themes? They might not apply to all of it.*

*I am trying to find the central category that links it all together. Within that you have to have the subcategories. If you took trust for example as the central category, then you could have underneath it, the trust from those who had a pain response and those who didn't.'*

On a train journey to London I was still wrestling with the concept of the central theme. I started writing my thoughts in a memo and was struck by a moment that I have read about in other researchers' texts but had not necessarily expected for myself.

*'What is the overriding category that can develop into the theory??*

*The current options are trust, the relationship with the researchers, pain. But I can't think how to put all that together. Or for everything to link under it.*

*But!! What about a person's concept of their own wellbeing? And how this is adjusted both up and down. What causes it to rise? What causes it to fall? It is dynamic. People who don't feel that impressed by the research team, perhaps it is because their wellbeing is being maintained in some other way.*

*What examples can I think of?.....'*

As I continued to write the memo I felt that I had made the major breakthrough in developing my central theory and from this point worked the other categories around this. I decided also however that it was important to outline the linear process of taking part in a trial. The detail provided by this outline could then be latterly applied to the central theory of the person's 'wellbeing'.

#### **A.4 Data Saturation**

The issue of data saturation is always contentious. After 21 interviews I felt that I had achieved a satisfactory degree of saturation whereby further interviewing of patients with a similar background to what I had already studied would generate limited new data. I was aware that I had not been able to interview certain groups of

patients and this is discussed elsewhere. For those patients that I was able to interview, I feel that an acceptable level of data saturation was achieved.

## **A.5 Conclusion**

This appendix outlines the analytic process that took place in generating the results from the data.

## **APPENDIX B: KETAMINE PAIN STUDY**

### **Introduction**

Neuropathic pain is difficult to manage and occurs in about 40% of cancer sufferers.

N-methyl-D-aspartate (NMDA) receptors within the spinal cord are known to play a role in neuropathic pain. Ketamine is a non-competitive NMDA antagonist. Ketamine blocks the NMDA receptor which subsequently acts by ‘winding down’ and minimising pain transmission. This is particularly beneficial when a hyper-excitability state exists, as is commonly present in neuropathic pain.

Although ketamine has been shown to be effective in neuropathic pain and pain secondary to critical limb ischaemia, its effectiveness in neuropathic pain of malignant origin has yet to be established.

### **Objectives and Design**

The primary objective of the trial is to determine whether the use of ketamine with best standard pain management improves pain control more than best standard pain management alone. The secondary objectives include comparing the two trial arms in regard to specific neuropathic pain scoring, distress and depression scoring and to measure the side effect profile of ketamine.

The trial is a randomized double blind with an incorporated placebo arm.

The three main components to the trial are the run-in period, the study titration period and the assessment period.

**Stage 1 Run-in period:** The run-in period allows time for optimisation of opioid analgesia using a defined schedule. To progress further in the trial, by the end of the

run-in period patients are on a stable opioid dose and are still scoring pain at a significantly high enough level.

**Stage 2 Titration period:** The patient is randomized and then given their trial medication. During this period the patient does not receive any other analgesic but is allowed to take breakthrough opioids at any point. The dose titration of ketamine or placebo follows a set schedule and increases until analgesia is achieved or the side effect profile is deemed too great to continue. The patient is monitored daily during this stage by research staff.

**Stage 3 Assessment period:** Once the patient is established on a stable dose of medication, there is a 16 day assessment period where the patient is assessed every 4 days.

Patients can optionally consent to have ten millilitres of venous blood taken at two points in the trial for future genetic investigation to response to ketamine.

**Inclusion/Exclusion criteria:** The main inclusion criteria is that patients have to have a confirmed neuropathic pain against a validated scoring criteria and that a traditional neuropathic agent has failed to treat this effectively. Patients are excluded for criteria that include having received chemotherapy or radiotherapy that may affect their neuropathic pain, having a change in their tumoricidal treatment that may affect their pain during the course of the trial or have a life expectancy of less than 2 months.

The total daily dose of ketamine during the titration period is from 40mg up to 400mg.

**Side effects**

In the doses that are used in the trial period, the side effects that may be encountered are those of hallucinations, nightmares and other transient psychotic effects.

**Dose reduction**

If the patient experiences side effects that are likely to be attributable to the trial, titration should go no further. If the side effects are intolerable to the patient, the dose should either be reduced to the previous level or maintained at the current level.

At the end of the trial, the dose of medication is reduced over a period of up to 7 days.

## **APPENDIX C: PREGABALIN BONE TRIAL**

### **Background**

Cancer induced bone pain (CIBP) is a unique state that is different to that of inflammatory pain and neuropathic pain. Its management can have unique challenges to achieve satisfactory analgesia without unsatisfactory levels of side effects. Radiotherapy can be effective, or partially effective for some but not all episodes of CIBP.

At the level of the spinal cord there is a process of central sensitisation. Glutamate is one of the key neurotransmitter involved. While there is good evidence for the glutamate receptor blockade, inhibition of presynaptic release of glutamate is less well studied. Animal models have suggested that the anti-convulsant gabapentin may reduce cancer induced bone pain.

### **Aims**

The principle aim of the study is to assess whether pregabalin and radiotherapy are more effective at managing CIBP than radiotherapy alone. Secondary aims look at quality of life indicators, tolerability of pregabalin and assessments of neuropathic pain.

### **Trial Design**

The trial is double-blind randomized controlled trial of pregabalin. Patients who receive radiotherapy for CIBP are eligible to take part. The trial is made up of two main sections.

#### *1. Run In*

This phase optimises patients' opioid doses before randomisation. This period lasts until the patient starts radiotherapy. If there is a sufficient degree of bone pain after this period, they are able to process to the second stage of the trial.

## *2. Assessment*

On the first day of the assessment phase, patients are randomized to receive pregabalin or placebo. The number of tablets taken is increased on a weekly basis from one tablet twice a day up to a maximum number of four tablets twice a day (equivalent to 300mg pregabalin BD). The assessment phase lasts four weeks. If a patient has to withdraw from the assessment phase, the drug is gradually reduced over a period of a week.

Patients are able to take their regular opioid escape/breakthrough medication during the period of the trial as required.

### **Inclusion Criteria**

The significant inclusion criteria are

Age  $\geq$  18 years

Life expectancy > 2 months

Due to receive palliative radiotherapy for bone pain

Clearly identifiable bone pain

### **Exclusion Criteria**

Current gabapentin/pregabalin use

Significant renal impairment

Change in any tumoricidal therapy before entering the study which may be expected to have an analgesic benefit during the study period

Patients receiving bisphosphonates purely as an analgesic regimen which may be expected to have effects during the study period

Bed bound patients

Patients receiving wide-field irradiation

### **Trial Measures**

At the start and end of the trial patients complete a battery of questionnaires and assessments. They also give a blood sample for assessment. These assessments usually take place in the hospital setting

During the assessment period patients are called at least weekly for assessment of their pain levels and description of any side effects. This is usually conducted by telephone.

# APPENDIX D: PATIENT INFORMATION SHEET



Patients' Experience of Palliative care Research
PEPR

## PATIENT INFORMATION SHEET - interview

A qualitative study using semi-structured interviews to explore patients' attitudes towards research in palliative care.

### **Invitation**

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish.

Part 1 tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the conduct of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

## **Part 1**

### **What is the purpose of the study?**

The purpose of the study is to explore patients' experience of a large clinical trial to demonstrate patient attitudes and recommendations for future research.

### **Why have I been chosen?**

You are being invited to take part in this study because you have been identified by your doctor or nurse as someone who has taken part in one of 3 large clinical trials called either the Pregabalin Bone Trial, the Ketamine in Pain Study or the Menthol in Neuropathic Type Pain study. These trials/studies are taking place in Edinburgh and Glasgow.

### **Do I have to take part?**

No, you do not need to take part if you don't want to. It is up to you whether or not you take part in the study. If you do decide to take part you are still free to withdraw at any time without giving a reason. A decision not to take part or withdraw at any time during the study will not affect the care you receive in any way nor will it affect your participation in the original trial.

### **How long will the study last?**

For you the study will last approximately one hour of your time.

### **What will being in the study involve?**

Your involvement in the study will be an informal interview. This session would last approximately one hour. The interview would be in a place and time of your choosing (usually your home). The topic of discussion will be your thoughts and experiences of research, in particular the trial or study that you have just taken part in. This interview will be with a research doctor who is trained in palliative care. The interview will be discretely recorded by digital recorder to allow the researcher to further examine the material at a later date.

### **Will I need to stay in hospital?**

No- you will not need to stay in hospital.

### **How often will I need to visit the hospital?**

The interview can be conducted at your home, in which case you would not have to visit the hospital. If you would prefer to conduct the interview in the hospital, you would have to visit the hospital once, for the actual interview itself.

**What happens if I decide to take part?**

If you are interested in taking part you will be approached near the end of your trial by one of the research nurses or doctors. At this time you will be able to ask any further questions on the study that you might have. If you would like to take part in the study we will arrange a time to meet to conduct the study. Before you take part in the study you will be asked to sign a consent form to confirm that you agree to take part in the study and that you understand what the study entails.

**What if there is a problem?**

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed.

**Might I be removed from the study?**

Yes, there are two instances where you may be removed from the study. Firstly, if the researcher feels that you are confused for whatever reason (of which there may be many) during the interview he will ask you not to continue with the interview. Secondly, if the researcher feels that you are too unwell to take part in the interview then again he will terminate the interview. You will also be able to remove yourself from the study at any time without explanation required.

**Will my taking part in this study be kept confidential?**

Yes, it is totally confidential. You will be allocated a study number to ensure you remain anonymous. We will only collect details of your age, sex, postcode and the name of your condition.

**Part 2**

**What if there is a problem?**

If you have a concern about any aspect of this study, you should speak to the researchers who will do their best to answer your questions (contact number 0131 777 3529 (Edinburgh Cancer Centre) or 0141 211 3418 (Beatson Oncology Centre). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

In the event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Lothian Health Board but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

**Are there any risks or inconveniences involved in taking part in the study?**

If you agree to take part in study we will arrange a time and place to meet for the interview. Fixing a time in your diary may be an inconvenience for you. Patient's energy levels vary from day to day and you may not feel strong enough to commit to the arrangement. You will be freely able to cancel or rearrange the interview at anytime.

There will be no physical risk involved in taking part in the study. While sharing your experiences you may have feelings or memories that are upsetting. These may be brought back to light when discussing previous treatment. However the research doctor is trained in palliative care and will be able to discuss these feelings sensitively and appropriately.

**What will happen to the information that I give in the study?**

All information will be stored securely and confidentially. If you join the study, some parts of your medical records and the data collected will be looked at by authorized persons involved in the study. They may also be looked at by authorized people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

**Will my GP be informed?**

We will inform your GP by letter if you decide to take part with your consent.

**Will my oncologist (cancer doctor) be informed?**

We will inform your oncologist by letter if you decide to take part with your consent.

**What will happen to the results of the study?**

The results of this study will allow us to find out what patients think about research and also how it can be improved in the future to help patients. The results will be

published in a scientific journal. Some anonymous quotes may be used in published material to illustrate a point.

**How many people will take part?**

We are planning to interview approximately 24 patients individually and a further 12 patients will make up 2 focus groups.

**Who designed the study?**

A group of research doctors and nurses from hospitals within Glasgow and Edinburgh designed the study.

**Who is organising and funding the study?**

The study is being organized by the University of Edinburgh and jointly funded by the University of Edinburgh and NHS Lothian.

Who has reviewed the study?

This study was reviewed by a number of medical specialists during its development. The West of Scotland (1) REC has reviewed and approved this study.

**Who can I contact for further information?**

You will now be given time to make your decision about whether to enter this study. If you would like to discuss any aspect of this study with a doctor not directly involved, please contact Prof John Welsh, Tel: 0141 301 7041. If you have any queries you can contact the researchers in your area responsible for the study.

**Glasgow: Anne Todd (Research Nurse) or Dr Barry Laird (Research Fellow)**

Contact: 0141 211 3418 or radio page 07654 380244

**Edinburgh: Dorothy Boyle (Research Nurse)**

Contact: 0131 777 3529 or radio page 07654380245

**Thank you for taking the time to read this information**

# APPENDIX E: PATIENT CONSENT FORM

## CONSENT FORM

Centre Number:

Patient Identification Number for this study:

Title of Project: Patients' Experience of Palliative care research: A qualitative study using semi-structured interviews and focus groups to explore patients' experiences of research in advanced cancer.

Name of Researcher:

Please initial box

1. I confirm that I have read and understand the information sheet dated.....  
for the above study. I have had the opportunity to consider the information, ask  
questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at  
any time  
without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of my medical notes and data collected during  
the study may be looked at by individuals from regulatory authorities or from the

NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I note that my GP will be informed of my participation in the study

5. I agree to take part in the above study.

\_\_\_\_\_  
Name of Patient                      Date                      Signature

\_\_\_\_\_  
Name of Person                      Date                      Signature

taking consent

When completed, 1 for patient; 1 for researcher site file; 1 (original) to be kept in medical notes

## **APPENDIX F: FIRST INTERVIEW SCHEDULE (AUG 2009)**

### **REASONS FOR PARTICIPATING**

- Can you tell me how you came to hear about the trial.
- What was your initial reaction to the trial and how did you come to be involved?
- What were your reasons for agreeing to take part in the trial?

#### *Areas that could be explored*

Do you remember what your frame of mind was at the time of starting the trial (including mood and emotion)?

How were you coping with your acceptance of your disease at the time?

Was there any motivation to help others in taking part?

Did you feel that taking part would help improve your symptoms?

Could you tell me if taking part in the study affected your levels of hope?

### **EXPERIENCE OF THE TRIAL**

- What were your experiences of the trial?
- How well did you understand what you were participating in?
- Do you feel you were fully informed of the requirements of the trial?
- Had you been involved in previous research/trials?
- Did you have any negative experiences during the trial?

#### *Areas that could be explored*

What were your experiences with the research staff (i.e. doctors and nurses)?

What impact did the trial have on your life?

How did you manage the assessment sessions? (hospital visits, frequency, duration)

Did you feel supported by the research staff during the trial?

### **IMPROVEMENTS OF FUTURE TRIALS**

- What area of the clinical trial could be better for patients like you? (for example trial design, duration of trial, after care, publication of results)
- Would you recommend participation in similar studies to other patients in your situation?
- Do you think when you look back on the trial that you would participate in it again?

## **APPENDIX G: LAST INTERVIEW SCHEDULE (March 2011)**

What do you remember about the trial?

Did being on the trial change how you see yourself as a person?

How do you look back on the period of time when you were on the trial?

What happened after the trial finished?

How did you find the change after the contact with the trial staff ceased?

If not benefit, has the trial been a waste of your time?

Can you remember anything that occurred that you were not expecting during the trial.

What area of the clinical trial could be better for patients like you?

# APPENDIX H: ETHICS APPROVAL LETTER

**WoSRES**  
West of Scotland Research Ethics Service

**NHS**  
Greater Glasgow  
and Clyde

**West of Scotland REC 1**

Ground Floor  
Tennent Institute  
38 Church Street  
Western Infirmary  
Glasgow  
G11 6NT

Tel No. 0141 211 6238  
Fax: 0141 211 1847

10 DEC 2009

03 December 2009

Professor Marie T Fallon  
St Columba's Hospice Chair of Palliative Medicine  
University of Edinburgh  
Edinburgh Cancer Centre  
Western General Hospital, Crewe Road  
Edinburgh EH4 2XU

Dear Professor Fallon

**Study Title:** Patients' Experience of Palliative Care Research: A phenomenological study examining the attitudes and experiences of patients who have participated in research during the advanced stages of their cancer

**REC reference number:** 09/S0703/104

**Protocol number:** 1.0

The Research Ethics Committee reviewed the above amendments contained within your letter dated 9th November 2009.

#### **Ethical opinion**

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

#### **Ethical review of research sites**

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

#### **Conditions of the favourable opinion**

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

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[www.nhsggc.org.uk](http://www.nhsggc.org.uk)

*For NHS research sites only, management permission for research ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>. Where the only involvement of the NHS organisation is as a Participant Identification Centre, management permission for research is not required but the R&D office should be notified of the study. Guidance should be sought from the R&D office where necessary.*

*Sponsors are not required to notify the Committee of approvals from host organisations.*

**It is responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

#### **Approved documents**

The documents reviewed and approved at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Covering Letter		09 November 2009
REC application	amended	09 November 2009
Participant Information Sheet: Focus Group	2.0	09 November 2009
Participant Consent Form	2.0	09 November 2009
Response to Request for Further Information		09 November 2009
Participant Information Sheet: Interview	2.0	09 November 2009
Evidence of insurance or indemnity		27 July 2009

#### **Membership of the Committee**

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

#### **Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

#### **After ethical review**

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email [referencegroup@nres.npsa.nhs.uk](mailto:referencegroup@nres.npsa.nhs.uk).

**09/S0703/104**

**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely



**Dr John Hunter**  
**Chair**

Email: [andrea.torrie@ggc.scot.nhs.uk](mailto:andrea.torrie@ggc.scot.nhs.uk)

**Enclosures:** *List of names and professions of members who were present at the meeting and those who submitted written comments*  
*"After ethical review – guidance for researchers" SL-AR2*  
*Site approval form (SF1)*

**Copy to:** *Dr Barry Laird*  
*Edinburgh Cancer Centre*  
*Western General Hospital*  
*Edinburgh EH4 2XR*

## REFERENCES

- ANNELLS (1996) Grounded theory method: Philosophical perspectives, paradigm of inquiry and postmodernism. *Qualitative Health Research*, 6, 379-393.
- BARBOUR, R. S. (2001) Checklists for improving rigour in qualitative research: a case of the tail wagging the dog? *BMJ*, 322, 1115-7.
- BARBOUR, R. S. (2005) Making sense of focus groups. *Med Educ*, 39, 742-50.
- BERRY, S. R. (2004) For purposes of research, palliative care patients should not be considered a vulnerable population. *Clin Oncol (R Coll Radiol)*, 16, 223-4.
- BLUFF, R. (Ed.) (2005) *Grounded Theory: The methodology*, Berkshire, Open University Press.
- BORGSTEEDE, S. D., DELIENS, L., FRANCKE, A. L., STALMAN, W. A., WILLEMS, D. L., VAN EIJK, J. T. & VAN DER WAL, G. (2006) Defining the patient population: one of the problems for palliative care research. *Palliat Med*, 20, 63-8.
- BRITTEN, N. (1995) Qualitative interviews in medical research. *BMJ*, 311, 251-3.
- CASARETT, D. J. (2003) Assessing decision-making capacity in the setting of palliative care research. *J Pain Symptom Manage*, 25, S6-13.
- CHARMAZ, K. (Ed.) (2006) *Constructing grounded theory: A practical guide through qualitative analysis.*, London, Sage Publications Inc.
- CHOCHINOV, H. M. (2009) The culture of research in palliative care: you probably think this song is about you. *J Palliat Med*, 12, 215-7.
- COHEN, M. Z., SLOMKA, J., PENTZ, R. D., FLAMM, A. L., GOLD, D., HERBST, R. S. & ABBRUZZESE, J. L. (2007) Phase I participants' views of quality of life and trial participation burdens. *Support Care Cancer*, 15, 885-90.
- COX, K. (2000) Enhancing cancer clinical trial management: recommendations from a qualitative study of trial participants' experiences. *Psychooncology*, 9, 314-22.

- COX, K., WILSON, E., ARTHUR, A., ELKAN, R. & ARMSTRONG, S. (2005) A randomised controlled trial of nurse-managed trial conclusion following early phase cancer trial participation. *Br J Cancer*, 93, 41-5.
- COYNE, I. T. (1997) Sampling in qualitative research. Purposeful and theoretical sampling; merging or clear boundaries? *J Adv Nurs*, 26, 623-30.
- CROTTY, M. (Ed.) (1998) *The foundations of social research: meaning and perspectives in the research process.*, Thousand Oaks, CA., Sage Publications Inc.
- DAVIS, M. P. & WALSH, D. (2004) Epidemiology of cancer pain and factors influencing poor pain control. *Am J Hosp Palliat Care*, 21, 137-42.
- DE RAEVE, L. (1994) Ethical issues in palliative care research. *Palliat Med*, 8, 298-305.
- DEAN, R. A. & MCCLEMENT, S. E. (2002) Palliative care research: methodological and ethical challenges. *Int J Palliat Nurs*, 8, 376-80.
- DENZIN, N. K. & LINCOLN, Y. S. (Eds.) (1994) *Handbook of qualitative research*, Thousand Oaks, CA., Sage Publications Inc.
- DEY, I. (Ed.) (1999) *Grounding grounded theory: Guidelines for qualitative inquiry.*, Edinburgh, Academic Press.
- DOBRATZ, M. C. (2003) Issues and dilemmas in conducting research with vulnerable home hospice participants. *J Nurs Scholarsh*, 35, 371-6.
- FLEMMING, K., ADAMSON, J. & ATKIN, K. (2008) Improving the effectiveness of interventions in palliative care: the potential role of qualitative research in enhancing evidence from randomized controlled trials. *Palliat Med*, 22, 123-31.
- FOLKMAN, S. & GREER, S. (2000) Promoting psychological well-being in the face of serious illness: when theory, research and practice inform each other. *Psychooncology*, 9, 11-9.
- FONTANA, A. & FREY, J. (Eds.) (1994) *Interviewing: The art of science.*, Thousand Oaks, CA., Sage Publications Inc.
- GLASER, B. G. (Ed.) (1978) *Theoretical Sensitivity*, Mill Valley, CA., Sociology Press.

- GLASER, B. G. (Ed.) (1992) *Basics of grounded theory analysis: Emergence vs. forcing*, Mill Valley, CA., Sociology Press.
- GLASER, B. G. (1999) The future of grounded theory. *Qualitative Health Research*, 9, 836-845.
- GLASER, B. G. (Ed.) (2001) *The grounded theory perspective I: Conceptualisation contrasted with description*, Mill Valley, CA., Sociology Press.
- GLASER, B. G. (2002) Constructivist Grounded Theory? *Forum: qualitative social research*, 3, Art. 12.
- GLASER, B. G. & STRAUSS, A. L. (Eds.) (1967) *The discovery of grounded theory: Strategies for qualitative research*, Chicago, Aldine Publishing Co.
- GUBA, E. G. & LINCOLN, Y. S. (Eds.) (1989) *Fourth Generation Evaluation*, Newbury Park CA., Sage Publications Inc.
- GYSELS, M., SHIPMAN, C. & HIGGINSON, I. J. (2008) Is the qualitative research interview an acceptable medium for research with palliative care patients and carers? *BMC Med Ethics*, 9, 7.
- HAWRYLUCK, L. (2004) People at the end of life are a vulnerable research population. *Clin Oncol (R Coll Radiol)*, 16, 225-6.
- HEATH, H. & COWLEY, S. (2004) Developing a grounded theory approach: a comparison of Glaser and Strauss. *Int J Nurs Stud*, 41, 141-50.
- HSIEH, H. F. & SHANNON, S. E. (2005) Three approaches to qualitative content analysis. *Qual Health Res*, 15, 1277-88.
- KELLE, U. (2005) "Emergence" vs. "forcing" of empirical data? A crucial problem of "grounded theory" reconsidered. *Forum: qualitative social research*, 6, art. 27.
- KUPER, A., LINGARD, L. & LEVINSON, W. (2008) Critically appraising qualitative research. *BMJ*, 337, a1035.
- KVALE, S. (Ed.) (2009) *InterViews: learning the craft of qualitative research interviewing*, Los Angeles, CA., Sage Publications Inc.
- LEWINGTON, S., WHITLOCK, G., CLARKE, R., SHERLIKER, P., EMBERSON, J., HALSEY, J., QIZILBASH, N., PETO, R. & COLLINS, R. (2007) Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-

- analysis of individual data from 61 prospective studies with 55,000 vascular deaths. *Lancet*, 370, 1829-39.
- LIN, H. R. & BAUER-WU, S. M. (2003) Psycho-spiritual well-being in patients with advanced cancer: an integrative review of the literature. *J Adv Nurs*, 44, 69-80.
- LINCOLN, Y. S. & GUBA, E. (Eds.) (1985) *Naturalistic Enquiry*, Beverly Hills, CA., Sage Publications Inc.
- LING, J., REES, E. & HARDY, J. (2000) What influences participation in clinical trials in palliative care in a cancer centre? *Eur J Cancer*, 36, 621-6.
- MADSEN, S. M., HOLM, S. & RIIS, P. (2007a) Attitudes towards clinical research among cancer trial participants and non-participants: an interview study using a Grounded Theory approach. *J Med Ethics*, 33, 234-40.
- MADSEN, S. M., HOLM, S. & RIIS, P. (2007b) Participating in a cancer clinical trial? The balancing of options in the loneliness of autonomy: a grounded theory interview study. *Acta Oncol*, 46, 49-59.
- MAYS, N. & POPE, C. (2000) Qualitative research in health care. Assessing quality in qualitative research. *BMJ*, 320, 50-2.
- MELVIN, C. S. (2009) When to Refer Patients to Palliative Care: Triggers, Traps, and Timely Referrals. *Journal of Hospice and Palliative Nursing*, 11, 291-301.
- MILES, M. B. A. H., A.M. (1994) *Qualitative Data Analysis*, Thousand Oaks, CA., Sage Publications Inc.
- MILLS, E. J., SEELY, D., RACHLIS, B., GRIFFITH, L., WU, P., WILSON, K., ELLIS, P. & WRIGHT, J. R. (2006a) Barriers to participation in clinical trials of cancer: a meta-analysis and systematic review of patient-reported factors. *Lancet Oncol*, 7, 141-8.
- MILLS, J., BONNER, A. & FRANCIS, K. (2006b) Adopting a constructivist grounded theory: Implications for research design. *International Journal of Nursing Practice*, 12, 8-13.
- MILLS, J., BONNER, A. & FRANCIS, K. (2006c) The development of constructivist grounded theory. *International Journal of Qualitative Methods*, 5, 1-10.

- MORSE, J. M. (Ed.) (1994) *Emerging from the data: The cognitive process of analysis in qualitative enquiry*, Thousand Oaks, CA, Sage Publishing Inc.
- MURRAY, S. A., KENDALL, M., CARDUFF, E., WORTH, A., HARRIS, F. M., LLOYD, A., CAVERS, D., GRANT, L. & SHEIKH, A. (2009) Use of serial qualitative interviews to understand patients' evolving experiences and needs. *BMJ*, 339, b3702.
- POLKINGHORNE, D. (2005) Language and Meaning: Data Collection in Qualitative Research. *Journal of Counseling Psychology*, 52, 137-145.
- PUNCH, K. F. (1998) *Introduction to Social Research: Quantitative and Qualitative Approaches*, Thousand Oaks, Sage Publications Inc.
- ROSS, C. & CORNBLEET, M. (2003) Attitudes of patients and staff to research in a specialist palliative care unit. *Palliat Med*, 17, 491-7.
- SANDELOWSKI, M. (1995) Sample size in qualitative research. *Res Nurs Health*, 18, 179-83.
- SEALE, C. (Ed.) (1999) *The quality of qualitative research*, London, Sage Publications Inc.
- SEALE, C. (2002) Quality Issues in Qualitative Inquiry. *Qualitative Social Work*, 1, 97-110.
- SEIBOLD, C. (Ed.) (1992) New York, Oxford University Press.
- SEYMOUR, J. & CLARK, D. (1998) Phenomenological approaches to palliative care research. *Palliat Med*, 12, 127-31.
- STRAUSS, A. L. & CORBIN, J. (Eds.) (1990) *Basics of qualitative research: Grounded theory procedures and techniques.*, Newbury Park CA., Sage Publications Inc.
- STRAUSS, A. L. & CORBIN, J. (Eds.) (1994) *Grounded theory methodology: An overview*, London, Sage Publications Inc.
- STRAUSS, A. L. & CORBIN, J. (Eds.) (1998) *Basics of qualitative research: Techniques and procedures for developing grounded theory*, Thousand Oaks, CA., Sage Publications Inc.
- SUN, V. C., BORNEMAN, T., FERRELL, B., PIPER, B., KOCZYWAS, M. & CHOI, K. (2007) Overcoming barriers to cancer pain management: an institutional change model. *J Pain Symptom Manage*, 34, 359-69.

- TENNANT, R., HILLER, L., FISHWICK, R., PLATT, S., JOSEPH, S., WEICH, S., PARKINSON, J., SECKER, J. & STEWART-BROWN, S. (2007) The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes*, 5, 63.
- TERRY, W., OLSON, L. G., RAVENSCROFT, P., WILSS, L. & BOULTON-LEWIS, G. (2006) Hospice patients' views on research in palliative care. *Intern Med J*, 36, 406-13.
- TODD, A. M., LAIRD, B. J., BOYLE, D., BOYD, A. C., COLVIN, L. A. & FALLON, M. T. (2009) A systematic review examining the literature on attitudes of patients with advanced cancer toward research. *J Pain Symptom Manage*, 37, 1078-85.
- WALSHE, C. E., CARESS, A. L., CHEW-GRAHAM, C. & TODD, C. J. (2004) Case studies: a research strategy appropriate for palliative care? *Palliat Med*, 18, 677-84.
- WATSON, D., CLARK, L. A. & TELLEGEN, A. (1988) Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*, 54, 1063-70.
- WHITE, C. & HARDY, J. What do palliative care patients and their relatives think about research in palliative care?-a systematic review. *Support Care Cancer*, 18, 905-11.
- WHITE, C. D., HARDY, J. R., GILSHENAN, K. S., CHARLES, M. A. & PINKERTON, C. R. (2008) Randomised controlled trials of palliative care - a survey of the views of advanced cancer patients and their relatives. *Eur J Cancer*, 44, 1820-8.
- WILLIAMS, A. M., CROOKS, V. A., WHITFIELD, K., KELLEY, M. L., RICHARDS, J. L., DEMIGLIO, L. & DYKEMAN, S. Tracking the evolution of hospice palliative care in Canada: a comparative case study analysis of seven provinces. *BMC Health Serv Res*, 10, 147.
- WOOTTEN, A. C., ABBOTT, J. M., SIDONS, H. M., ROSENTHAL, M. A. & COSTELLO, A. J. A qualitative assessment of the experience of participating in a cancer-related clinical trial. *Support Care Cancer*, 19, 49-55.

YEUNG, E. W., FRENCH, P. & LEUNG, A. O. (1999) The impact of hospice inpatient care on the quality of life of patients terminally ill with cancer. *Cancer Nurs*, 22, 350-7.