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ORIGINAL ARTICLE

What do palliative care patients and their relatives think about research in palliative care?—a systematic review

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Abstract
Introduction Research in palliative care patients has been controversial and is often challenging. It is important to know the views of potentially eligible patients themselves in order to determine the appropriateness of research in the palliative care population and to develop realistic studies that are practical and achievable in this population. This systematic review aims 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.
Methods A systematic literature review was undertaken to identify what is known to date regarding the views of palliative care patients and their relatives towards research participation. Eight relevant studies were identified.
Discussion There is an increasing body of evidence considering the views of palliative care patients towards research in palliative care. However, only three studies have considered the views of their relatives/caregivers. Several common themes emerged from the literature including the potential for personal gain, altruism, the wish to avoid complex studies and a desire to retain autonomy. Trial-related factors were also important determinants of willingness of patients and relatives to participate in research. The views expressed by palliative care patients towards research are similar to those of other patient populations.
Conclusion Research to date in the palliative care setting has suggested that patients are interested in participating in research and may actually benefit from doing so.

Keywords Palliative care patients · Terminally ill · Caregivers · Hospice · Research participation

Introduction

Despite the current need in medical practise for evidence-based medicine, many treatments that are widely used in palliative care have never been proven to be effective, and their use is based on anecdote and physician preference alone [1]. It is widely acknowledged that research in this patient group is difficult and therefore is often not attempted. Challenges include the fact that patients are often unwell, fatigued, emotionally and psychologically fragile and have multiple co-morbidities. Cognitive impairment may lead to difficulties with consent. In addition, families may not support participation as studies may be time consuming and fatiguing. Moreover, it has been argued that research in the terminally ill is inappropriate [2] as patients with palliative care needs are potentially vulnerable.

Much of the debate about the concerns of dying patients regarding research participation has been defined by, and filtered through, the views of family, carers and healthcare professionals or has involved patients who have chronic illnesses but are not close to death [3]. It is important to know the views of potentially eligible patients themselves

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in order to determine the appropriateness of research in the palliative care population and to develop realistic studies that are practical and achievable in this population.

This systematic review aims 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.

Methods

A literature review was undertaken to identify what is known to date regarding the views of palliative care patients and their relatives towards research participation.

A computer search of MEDLINE (1950 to May 2008), EMBASE (1980 to May 2008) and the Cumulative Index to Nursing and Allied Health Literature (1982 to May 2008) through the Ovid gateway was performed using MESH terms: "attitudes", "motivation", "willingness", "preparedness" and "clinical trial", "randomised controlled trial". This identified 10,061 citations. With the additional limits of English language and studies on human adults, the list was narrowed to 3,465. The titles of these citations were reviewed and included if they considered relevant topics including attitudes towards clinical trials or participation in clinical trials. Studies were excluded from further review if they had no relevance to the topic under investigation, e.g. motivational interviewing, attitudes towards treatment preferences and attitudes towards screening. Eighty-two citations appeared relevant. These abstracts were reviewed and were excluded if not relevant to the topic using the same criteria or did not consider the palliative care population. Those of uncertain significance underwent a full paper review. Six relevant studies were identified. Publications known to the research team were also included. The reference lists of relevant publications were reviewed for further related articles. This was combined with a hand search of palliative care journals (*Palliative Medicine*, *Journal of Pain* and *Symptom Management*) to specifically identify publications concerning attitudes towards participation in palliative care patients. This strategy identified a total of eight studies considering the views of patients and/or their carers on participating in research. Each paper was reviewed and the general themes extracted, labelled and combined into common themes.

Results

Eight studies were identified as being relevant, and all were included. Table 1 gives a summary of all the included studies. No randomised controlled trials were identified, and all studies identified were in questionnaire, focus groups or interview format, or were a retrospective review of participation in previous research studies. All of the studies included in this review are relatively small and encompass a heterogeneous patient and carer population (as described in Table 1). Some included patients within days of death [3], whereas others involved patients earlier in their disease trajectory [4, 5]. Some studies were conducted purely in patients with cancer, whereas others included those with advanced non-malignant disease. Two of the carer studies involved people who were still actively caring for their relative [4, 6], whereas one involved bereaved carers [7]. No studies used the same questionnaires or questioning format. Three studies used self-administered questionnaires, one of which was designed through focus groups and interviews [4]. The methods used for the design of the other two questionnaires were not described [6, 7]. One of the qualitative studies was in the form of a structured interview [8] and the other a semi-structured interview with detailed analysis performed by several researchers [3]. One study involved focus groups with patients and carers, recordings from which were thematically analysed using an interpretive approach [9]. Two studies considered those who had previously been invited to participate in research projects and analysed retrospectively the reasons why patients participated or declined to participate [5, 10]. Not all studies considered all of the themes identified, but all themes were supported in more than one study with the exception of the impact of the views of others that was only considered in one study.

Themes identified from these studies were (1) views of patients and carers on participating in research in general, (2) the potential for personal gain, (3) altruism, (4) trial-related factors that may encourage or inhibit participation, (5) the desire to maintain autonomy, (6) the influence of the opinions of others and (7) the specific barriers to participation.

Discussion

What is known about patients' and relatives' views on research in palliative care?

There is an increasing body of evidence considering the views of palliative care patients towards research in palliative care. However, only three studies have considered the views of their relatives/caregivers. Several common themes emerged from the literature, including views on participating in research in general, the potential for personal gain, altruism, the impact of trial-related factors, a desire to retain autonomy, the influence of the opinions of others and the potential barriers that there may be to participation.

Table 1 Characteristics of included studies considering the views of patients and/or their carers on participating in research (in order of publication year)

Reference	Year of publication	Study population	Type of study	Country	Sample size	Summary of findings
White et al. [4]	2008	Palliative care patients with malignant disease in a hospital setting	Questionnaire	Australia	101 patients, 100 relatives	Over 75% of participants expressed altruistic views. Ninety-two percent of patients would participate in studies involving simple interventions, whereas only 26% would consider studies of complex interventions. A similar pattern was observed for relative support. Financial burden and possibility of side-effects was off-putting to many. Concepts of “randomisation”, “placebo-control” and “blinding” deterred approximately 50%. Many were prepared to complete short questionnaires, accept extra medications, investigations, hospital visits or admissions within a trial context. Patient age was the only statistically significant predictor of willingness to participate.
Kendall et al. [9]	2007	Researchers, patients with cancer and carers	Qualitative in-depth interviews	International researchers, patients and carers in Scotland	32 researchers, seven patients with cancer, four carers	On researching “the good death”, both the researchers and patients suggested that many people nearing the end of life do want to be offered the chance to participate in research, providing it is conducted sensitively.
Terry et al. [3]	2006	Palliative care hospice patients	Semistructured interview	Australia	22	Patients were generally keen to participate in research. Reasons expressed included altruistic views, enhancement of a sense of personal value, the assertion of persisting autonomy and the values they placed on a commitment by doctors to optimising care by research.
Williams et al. [6]	2006	Palliative care hospice patients, caregivers and ambulatory senior citizens	Questionnaire	USA	142 patients, 194 caregivers, 88 ambulatory senior citizens	Caregivers showed the greatest interest in research participation with hospice patients slightly less so. Responses were independent of patient characteristics except for age. Caregivers of hospice patients perceived being “too sick” as a barrier to participation more frequently than the patients themselves, and they were also more concerned about emotional distress or pain for the patient.
Ross and Cornbleet [8]	2003	Palliative care hospice patients	Structured interview with patients	Scotland	40 patients	Patients were asked about their willingness to participate in research in general and in three hypothetical trials. Patients were generally agreeable to participate in research. The most invasive hypothetical study involving venepuncture and random drug allocation had the least favourable response with a trial of reflexology attracting most. The most frequently occurring positive themes to research included: “to help other people”, that “research is important”, “to help myself” and “because the staff have been good to me”.
Hudson [7]	2003	Caregivers of palliative care patients	Questionnaire	Australia	45 caregivers	Considered the experience of caregivers who had participated in a longitudinal research project. 71% reported benefits of being involved in research, and 89% cited no negative aspects associated with participation.
Dobratz [10]	2003	Palliative care home hospice patients	Retrospective analysis	USA	113 potential participants, 97 completed testing	Patients expressed gratitude for being able to provide information that might possibly benefit others.
Ling et al. [5]	2000	Palliative care hospital patients	Review of all patients referred for trial participation over 4 years	England	1,206 referred, 362 entered a study, 248 completed a study	Reasons given for unwillingness to participate were a wish to defer to a later date, a deterioration in condition, distance from home to hospital, a lack of interest, transfer to another unit, inability to give consent and family objection.

Participation in research in general

Hospice patients in Scotland who were interviewed were generally agreeable to participate in research with 66% “quite happy” or “very happy” to take part [8]. In semi-structured interviews with hospice patients in Australia, patients interviewed did not feel that there were serious practical or ethical difficulties with research in the terminally ill [3]. The patients in this study understood that research is seen by the community as a means to improve care. They understood that the alternative to research is guessing and that, if there is no research in palliative care, it may be that for dying patients, guessing is regarded as “good enough”.

In research on “the good death”, both the researchers and patients affected by cancer who were interviewed suggested that many people nearing the end of life do want to be offered the chance to participate in research, providing it is conducted sensitively. However, there is the potential for bias as these participants had all agreed to be involved in this piece of research. While acknowledging that such research can be demanding, most of the researchers, who were from an international background and had experience in end-of-life research, believed it to be no more problematic than many other areas of research and that the challenges identified could be overcome [9].

Personal gain

Patients near the end of life receiving palliative care are not offered any chance of cure by participation in clinical trials but might still hope for some therapeutic benefit not available “off trial” [8]. Ross and Cornbleet (2003) found a desire “to help myself” a frequently occurring theme amongst patients interviewed in a hospice setting [8]. Australian hospice patients believed that research participation offered “important, immediate benefits”. These patients identified the benefit of making a useful contribution despite their terminal illness [3], suggesting a potential psychological benefit of participation. Hospice patients in the USA were more likely than ambulatory senior citizens to identify the potential to improve their symptoms, the opportunity to have a sense of purpose and the potential to be followed more closely by their doctor or nurse as potential benefits of research participation [6]. This suggests that personal gain was an important consideration in this population.

In a questionnaire assessing the views of caregivers who had participated recently in a longitudinal research project in Australia, 71% carers reported on the benefits of being involved in research. The majority (89%) cited no negative aspects associated with participation [7]. Over 60% reported a direct benefit to themselves, as caregivers, from research involvement and felt that it assisted them in coping in their situation and reduced their feelings of isolation. Over 40% of caregivers cited the support and assistance given to them by the researchers as a major benefit, and over 20% reported that their involvement in research improved their ability to care for the patient [7].

Altruism

Kendall and colleagues (2007) interviewed international researchers who were involved in end-of-life research. These researchers commented that participation in research was often seen by patients as an opportunity to “give something back” in return for the care they, or their loved ones, have received. It also provided an opportunity to improve services and support for people in the future [9]. Confirming this, home–hospice participants in the USA expressed gratitude for being able to provide information that might possibly benefit others [10]. Similarly, the most frequently occurring positive theme from a questionnaire asking Scottish hospice patients about participating in research in general was a desire “to help other people” [8]. Terry and colleagues (2006) also found that Australian hospice patients valued the benefits to others that research offers and felt that participation enabled them to give something back to their families and carers and to the community. Others interviewed in this study expressed the view that participation in research when they were in the unique position of knowing they were dying gave them a special gift to give to others [3]. In a questionnaire study from Australia involving over 100 patients and their relatives/carers, 82% of patients in a hospital palliative care department and 76% of their relatives expressed altruistic views towards research participation in that they were interested in studies that may help others but not themselves [4].

Carers have also expressed altruistic views towards research participation with over 30% of caregivers in another Australian study identifying as important the knowledge that their involvement in research would assist future caregivers [7].

Trial-related factors

Trial-related factors have been shown to be important in determining patients' and their relatives' views towards potential participation in palliative care research. A survey of the views of advanced cancer patients and their relatives towards participation in randomised controlled trials (RCTs) in palliative care in a hospital setting found that the majority of participants were interested in studies of symptom control that would have no impact on cancer progression. This supported an interest in trials that may improve quality and not necessarily quantity of life [4].

Financial cost to the patient was the major deterrent to trial participation in this study. The concepts of random allocation, placebo controls and double-blind trial designs were a deterrent in this study in 40%, 28% and 29% of patients, respectively, and many more were unsure. There was also a striking correlation between the invasiveness of trial interventions and willingness to participate in a hypothetical pain study. While over 80% of patients and their relatives would support participation in simple non-drug trials (pain education, special mattress and aromatherapy), less than 20% would support a trial of an epidural infusion or spinal stimulator. The potential for side-effects was also highlighted as a factor of great importance, with this being a deterrent to participation. Many patients and relatives were prepared to make extra visits to the hospital, spend a night in hospital, answer questions by telephone or face-to-face and complete questionnaires weekly. Approximately one third of patients were willing to undergo weekly blood tests or radiology. Almost two thirds were prepared for extra tablets and over 40% for injections, at least weekly. However, relatives often seemed more prepared for the patient to undergo inconvenience than were the patients themselves [4].

It has been reported that patients were generally unwilling to enrol in placebo-controlled RCTs, but the reasons given in interviews with hospice patients in an Australian study were sometimes confused or contradictory. The authors of this study felt that patients did not understand this experimental design well enough to judge its acceptability and that careful explanation may be necessary. They report that active comparator trials were more acceptable [3].

Similarly, Ross and Cornbleet (2003) found that, while the hospice patients they interviewed were generally agreeable to participate in research, the type of trial influenced their willingness to participate. The most invasive hypothetical study proposed to patients involving venepuncture and random drug allocation had the least favourable response (46% of patients “quite happy” or “very happy”) with a trial of reflexology attracting 77%. Factors deterring patients from participation included the need for record keeping by the patient and concern about the potential emotional strain [8].

How trial-related factors influenced patients' and their caregivers' willingness to participate in research has also been described in a questionnaire study from the USA [6]. Forty-six percent of hospice patients and 60% of caregivers were interested in interview or survey research with 45% and 57%, respectively, expressing an interest in therapeutic research. Younger patients were more favourably disposed towards both survey and therapeutic research participation than those over the age of 75 [6].

Maintenance of autonomy

In one study, patients in a hospice expressed deep concern about the denial of their autonomy by others—about being treated as though already dead [3]. One reason commonly expressed by patients was that their involvement in research would confirm that they were still real people and that they should be regarded as such. The argument that terminally ill patients were more vulnerable than other patients and therefore, had doubt cast on the voluntariness or the autonomy of their consent was refuted by patients in this study. They felt that there was a “freedom” in being close to death so that they could say precisely what they wished and had nothing to lose by voicing their own opinions [3]. Similarly, Ling and colleagues (2000) found that palliative care patients within a large cancer hospital in the UK were quite prepared to “say no” if they did not want to enter a study [5].

Opinions of others

A study of patients with advanced cancer in an Australian hospital setting has demonstrated the important influence of the opinions of others on a patient's decision whether to participate in research [4]. Only 55% of interested patients would participate in a study if their relatives were not supportive, and only 51% of relatives would continue to support a patient's decision to participate in a trial if they were not keen for them to do so. Furthermore, while there was a degree of agreement overall between patients and their relatives, the level of agreement did not reach significance in over half of the questions asked. The opinion of the treating doctor was also important to the majority of participants with respect to trial participation with over three quarters (84% of patients and 75% of relatives) stating that they would be interested in trial participation if their doctor made it clear that he/she was keen for participation, suggesting that coercion is a risk [4]. No other study specifically considered this issue.

Barriers to participation

Patients and their relatives were also able to identify potential barriers to participation other than the trial-related factors previously discussed. Williams and colleagues (2006) [6] found that USA hospice patients were more likely than ambulatory senior citizens to see the following as barriers to trial participation in a self-administered questionnaire: being “too sick”, having too little energy and a concern for creating an additional burden on their caregiver. Caregivers of hospice patients perceived being “too sick” as a barrier to participation more frequently than the patients themselves did. They were also more concerned about potential emotional distress or pain for the patient. While hospice patients themselves were concerned that research might create a further burden for their caregiver, caregivers themselves were less likely to see this as a barrier to any participation [6].

Are these views similar to those of cancer patients at an earlier stage in their disease trajectory?

The views expressed by palliative care patients towards research are similar to those of other patient populations. Patients in a UK cancer hospital were asked why they accepted or declined to participate in RCTs of cancer therapy [11]. Seventy-two percent of patients who were offered RCT participation agreed to participate. The main reasons given were that “others will benefit” and “trust in the doctor”. One of the main reasons for declining participation was concern about randomisation. An important factor influencing decision making was whether the trial offered active treatment in all arms of the study. The most important aspects with respect to trial participation for cancer patients in another questionnaire study in the UK were the likelihood of being treated by a specialist, having progress monitored and contributing to research knowledge that might benefit humanity [12].

The views of both cancer and non-cancer (inflammatory bowel disease) research participants and non-research participants in Denmark were assessed by questionnaires. Attitudes toward clinical research were found to be positive in all groups with non-participants being the least positive. Both personal and altruistic motives were highly rated. Primary reasons for non-participation were fear of “the unknown” and/ or unease with randomisation. The majority of both cancer and non-cancer groups rated a desire to get access to a new drug or diagnostic tool as important. The wish to obtain a good relationship with the department performing the study was of limited importance [13].

Other studies considering cancer patients' willingness to participate in research have demonstrated an aversion to randomisation with one Canadian study reporting 63% of patients refusing trial entry because of this [14]. In contrast, a UK questionnaire study demonstrated that, while some cancer patients were initially deterred by randomisation, careful explanation of the need for randomisation and its implications increased participation [15].

Conclusion

There has been controversy about the appropriateness of involving palliative care patients in research [2, 16]. Research to date in the palliative care setting has suggested that patients are interested in participating in research, and may actually benefit from doing so [8, 10, 17, 18]. It also appears that the views of palliative care patients are similar to those considering participating in trials in the oncology setting.

The variety of methodologies employed and the heterogeneous nature of the patient and carer groups included in studies to date weakens the conclusions that can be drawn from a review of the published literature. However, a number of common themes emerged. Patients and carers were generally in favour of research in general, irrespective of the likelihood of personal gain. Altruism was strongly expressed along with a desire to maintain autonomy. The influence and opinions of others, both carers and doctors, are very important. All the studies support at least some of the themes documented here, and none refuted the findings of the others.

Although many of the studies in palliative care have involved small numbers of participants [8, 10] and are qualitative in nature [3], they have highlighted some areas in trial design that must be reconsidered in order to make trials more acceptable to patients and their relatives. Trial designs must be as simple as possible so that the patient can understand the methods and concepts used (for example, careful explanation of any randomisation, placebo use, blinding etc.). The data collection methods employed should require minimal record keeping on the part of the patient. Active comparator trials seem more acceptable than placebo-controlled trials. Ideally, there should be no financial burden for the patient, and trials that are less invasive appear more likely to accrue patients than those that are invasive. Side effects were a deterrent to patients, whereas inconvenience, e.g. attending hospital appointments, seems less so.

By addressing the concerns of patients and their relatives and designing trials that are acceptable to them, it is likely that research trials will accrue more patients and that improvements in palliative care will be made through clinically relevant research.

Authors' statements regarding contribution and conflict of interest Clare White: I declare that I participated in the study design, implementation, collecting of results, analysing results and write up and that I have seen and approved the final version. I have no conflicts of interest.

Janet Hardy: I declare that I participated in the study design, implementation, collecting of results, analysing results and write up and that I have seen and approved the final version. I have no conflicts of interest.

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