Progress in Palliative Care

Challenges of recruiting hospice patients with advanced cancer to research: reflections on a delirium screening study

--Manuscript Draft— (accepted 6 March 2014)

Manuscript Number: PPC214R1

Full Title: Challenges of recruiting hospice patients with advanced cancer to research: reflections on a delirium screening study

Article Type: Original Research Paper

Keywords: Palliative care; advanced cancer; Research recruitment; Inpatient hospice; Challenges of recruiting; Delirium; Gatekeeping; Study design.

Corresponding Author: Suzanne Rainsford, MBBS MFM(Clinical)

Calvary Health Care ACT

Barton, ACT AUSTRALIA

Corresponding Author Secondary Information:

Corresponding Author's Institution: Calvary Health Care ACT

Corresponding Author's Secondary

Institution:

First Author: Suzanne Rainsford, MBBS MFM(Clinical)

First Author Secondary Information:

Order of Authors: Suzanne Rainsford, MBBS MFM(Clinical)

Tracey Bullen, DCP/ MSc

John Rosenberg, PhD, RN,MACN

Order of Authors Secondary Information:

ABSTRACT

Introduction: Delirium research in palliative care, particularly in the dying phase, is possible but is frequently met with ethical and methodological challenges. This paper describes the challenges faced in a previous delirium screening study.

Methods: Within 72 hours of admission to an acute inpatient specialist palliative care unit one hundred consecutive patients over 18 years of age with advanced cancer were invited to be screened for delirium using validated screening tools.

Results: Of the 100 consecutive admissions 49 patients were unable to participate including seven who did not meet the inclusion criteria and nine (six families and three patients) who withheld consent. The remaining 33 patients were more unwell and closer to death than those who were recruited. Reasons for non- participation included being too unwell (ten), unresponsive (nine), died (two) or discharged (three) before recruitment and exceeding the 72hour time limit (nine).

Conclusion: Gate keeping and physical condition of patients were the main obstacles to recruitment and is consistent with barriers faced in previous studies involving palliative care and dying patients. While it is possible and necessary to conduct studies in palliative care, including the terminal phase, as reflective practitioners we must maintain the balance between the demands for evidence-based practice and our compassion and respect for our most vulnerable of patients.

Challenges of recruiting hospice inpatients with advanced cancer to research: reflections on a delirium screening study.

Introduction

A recent editorial by Sheila Payne[1] challenges palliative care professionals to continue to question, debate and reflect on the 'ethical, practical and methodological dilemmas' of recruiting palliative care patients to research studies. In essence it is finding the balance between the science and the art of caring.

Studies undertaken in palliative care, including inpatient hospice settings, aim to establish evidence-based practice to improve the quality of life of patients and the care-giving experience however, researchers face numerous challenges.[2, 3] Obtaining informed consent from very ill patients can be ethically and legally challenging but possible.[4] While a systematic review by White and Hardy[5] suggests that patients with life limiting illnesses are willing to participate in research, the ethics of recruiting such patients, especially those who are very ill or in the terminal phase, remains contentious[6]. Historically patients in the terminal phase have been considered too vulnerable, too unwell, too exhausted or with limited cognitive ability to provide informed consent to participate. Thus health care professionals often act as 'gatekeepers' excluding these patients in the belief they would find any request to participate as intrusive as they have little to gain personally from the findings and therefore need protecting.[7,8]

Ethics[9] is not the only barrier to recruiting palliative care patients as methodological and logistical factors can impede recruitment. The disease trajectory of palliative care patients frequently presents with complex symptoms, which can include extreme mental and physical fatigue, and poor performance status which creates its own challenges. Of those who do consent to participate in research trials patient attrition[10] becomes an obstacle as patients often die or become too unwell to continue in studies. The difficulties of recruitment and attrition frequently results in small sample size,[11] recruitment of subpopulations and

selection and missing data[12] biases, particularly in the dying patient cohort,[13] that questions the generalizability of results. Despite these barriers conducting research in palliative care is feasible[14] especially if strategies are implemented to ameliorate these problems during the development phase of a research study.[7,15]

Delirium studies at end-of-life can be particularly challenging as decision-making capacity can be impaired. Fluctuation and subjectivity of symptoms can make delirium, especially the hypoactive subtype[16], difficult to recognise[17]and while screening increases detection currently there is no consensus as to the best tool to use.[18,19] A previous delirium screening study by the authors[20] found nearly half of the targeted patients either declined to participate or were excluded due to their physical condition. This paper reflects on the challenges encountered and while the barriers were not unique to this study to the authors' knowledge there are limited papers specifically describing the challenges of recruiting patients with advanced cancer to delirium studies.

Description of the delirium screening study

The aim of the study was to determine the prevalence of delirium within 72hours of admission to a 19-bed acute specialist inpatient hospice (363 admissions in 2013; 83% with a malignant diagnosis; average stay 18.2 days; median stay 11 days) in Canberra, Australia (population 383,400[21]), in patients with advanced cancer and to determine if the use of a validated screening tool increased the recognition of delirium.

Two validated tools were chosen, (1)the Delirium Rating Scale: Revised 1998 (DRS-R98)[22] requiring patient participation for at least 15- 20 minutes and (2)the Confusion Assessment Method shortened diagnostic algorithm (CAM)[23] taking less than five minutes to complete by either the patient or carer. The longer tool has the advantage of classifying patients into hyperactive, hypoactive or subclinical delirium potentially tailoring management to improve patient care.

Between February and June 2013 one hundred consecutive patients over 18years of age with advanced cancer admitted to the inpatient hospice were considered for participation in the study. Within 72 hours of admission, the one investigator approached the patient and/or their family informing them of the study and inviting them to be screened for delirium. Written consent from the patient, or their proxy (enduring power of attorney or next of kin as identified on admission records) where the patient was not capable of providing consent due to cognitive impairment, was gained from 51patients. Consenting patients were screened for delirium using the DRS-R-98 and CAM. The investigator then carried out a review of the medical charts of participating patients to determine the rate of delirium recognition by the treating team prior to screening, based on DSM-IV[24] criteria.

While it may have been possible to screen the patients as part of routine clinical practice and then conduct a quality improvement audit, to comply with the policies and procedures of the hospice Human Research Ethics Approval was obtained. This had the benefit of engaging the onsite palliative care research centre and carrying out the study under research conditions using two validated tools. Non-English speaking patients and those with dementia or co-morbid psychiatric disorder were excluded.

Data were collected on patient demographics and screening scores, entered into SPSS-20 and summarized using descriptive statistics including means, standard deviations, ranges and frequencies. The investigator, a palliative care medical officer who at the time was not part of the treating team, made a descriptive record of the difficulties faced with individual patients.

Results

The remainder of this paper focuses on the challenges of recruiting inpatient hospice care patients with advanced cancer to a delirium screening study. Having previously worked in the inpatient unit the authors felt they were familiar with the staff and general characteristics of the patients so recruiting patients seemed achievable however, of the 100

consecutive advanced cancer admissions 51 patients agreed to participate. Of the remaining 49 admissions seven did not meet the inclusion criteria, nine withheld consent (six patients and three families) and 33 did not participate for reasons shown in Figure1. These 33 patients were more unwell and closer to death than those who participated; mean age 65.2 years (SD 16.9; range 30-95); 16 (48%) were female. (Table 1)

The reasons given by the treating team that the patient was too unwell to be screened included uncontrolled symptoms such as pain, nausea and breathlessness. On two occasions the nursing staff requested the investigator not approach the patient as they were very unwell and the family was distressed. The investigator also made the decision not to disturb two very frail sleeping patients. According to the treating team none of the above four patients had a recognisable delirium and unfortunately there was no further opportunity to screen them within 72 hours of their admission. Of the remaining six patients considered too unwell to participate three potentially had a diagnosis of delirium according to the treating team.

INSERT FIGURE 1 ABOUT HERE

INSERT TABLE 1 ABOUT HERE

The reasons given for withholding consent included “I’m not interested”, “No thanks, I don’t have a delirium. I’m not confused.”, “My Dad’s too tired today” and “I’ve just arrived please come back tomorrow”. The latter two refusals occurred at the end of the week meaning it was not possible to return and screen the patients within 72hours of admission. With the exception of one family who was angry by our request to participate, most families were apologetic their family member could not participate.

On three occasions where recruitment to the study was not possible due to the physical condition of the patient the family requested to participate. While the DRS-R-98 was unable

to be used completion of the CAM by the family and medical record audit showed a positive result for delirium for all three patients in the preceding 24 hours. These findings influenced subsequent medical care and treatment planning but were excluded from the final analysis as both screening tools were not applied.

Discussion

Despite this study having strategies recommended in the literature[7] including ethics approval, managerial support, onsite research centre support and collaboration with hospice staff (nursing and medical) there were still challenges in accessing and recruiting hospice inpatients. This paper highlights the challenges experienced with findings consistent with barriers encountered in most care of the dying research.[15,25] Four categories, not necessarily mutually exclusive, were identified including (1) methodological and logistical issues, (2) patient characteristics, (3) 'gatekeeping' and (4) ethical issues.

In an effort to reduce the burden on medical and nursing staff the one investigator carried out recruitment and assessment of all the patients. Whilst this increased the consistency in applying the screening tool it meant it was not possible, due to rostering and long weekends, to access all admissions within 72 hours.

The choice of screening tool was a factor in recruitment as illustrated by the families of the three non-recruited patients who requested to participate. While both tools used in this study had been validated for use in palliative care the use of the longer DRS-R-98 increased the participation burden potentially resulting in recruitment bias contributing to the high non-participation rate and possible under estimation of the prevalence of delirium.

One of the key reasons for non-participation was the physical condition of the patient-clinical deterioration and high baseline symptom burden unrelated to the study. These reasons for non-participation are similar to the reasons given for high attrition rates in palliative oncology trials[10] and are not surprising given the reasons for admission to inpatient hospice.

Recruiting patients on or soon after hospice admission coincides with a time that is often overwhelming to the patient and their family and can be associated with high levels of distress. Following assessments by the nursing and medical teams the additional demands of the presence of an unknown investigator was sometimes perceived as 'a disruption to the settling in process.' Prior to approaching the patient the investigator gained permission from the treating team and on a number of occasions they acted as 'gatekeeper' stating the patient was too unwell, unresponsive or the patient and or family was too distressed to be disturbed. A systematic review by Rinck et al [26] advocated that in order to enhance the quality of palliative care trials patients with very limited life expectancy should be avoided. Whilst it could be argued that the unresponsive patients had nothing to gain by being involved in the study as they were close to death, the literature suggests that delirium is common in the terminal phase.[18] However, if some of the 'unresponsive' patients had an unrecognised hypoactive delirium in the terminal phase screening may have resulted in an improvement in patient and family care by altering clinical management and providing valuable information to the family to enhance their understanding thereby reducing distress.

In some situations not being a member of the treating team created an objective distance on the part of the investigator however, there were times when the investigator was unable to remain detached. While aware of the possibility that some of the very unwell or distressed patients had a delirium and would benefit from recognition and implementation of a specific management plan on two occasions the investigator made the decision not to disturb frail sleeping patients. Lynch et al[27] recognised the risk of the investigator distorting research aims and objectives by blurring the boundaries between research and therapeutic relationships. Whilst it is important to establish a relationship of trust between researcher and participant it is imperative not to take advantage of this trust through an imbalance in 'power.' Whilst these vulnerable patients approaching the end of life need to be protected from undue distress, managing 'gatekeeping' reflects the importance of maintaining the

balance between conducting research that can benefit patients and minimising patient burden and distress.

In any research the ethics of consent must be maintained to ensure advantage is not taken of vulnerable patients, especially those with impaired cognitive capacity. Mindful that delirium is common in dementia[28] and the screening tools used have a high specificity and sensitivity for delirium[22,23] for ethical reasons and the paucity of published dementia studies in advanced cancer palliative care, the decision was made to preclude patients with a pre-existing dementia. The literature suggests consent and capacity are major ethical challenges in palliative care delirium studies[29] however obtaining informed consent in this study was not the main contributing factor for non-participation in eligible patients as in all cases where patients had reduced cognitive capacity their proxy (universally their next of kin) provided consent. While the number of patients for which consent was withheld (9%) is consistent with a previous study by Gibbins et al[14] (8%) the generalizability of this finding is limited as many of the most vulnerable patients were not approached due to 'gatekeeping' and it is uncertain whether patient or proxy consent would have been obtained.

The challenges faced in recruitment and the use of a single site resulted in a number of limitations including a small sample size and recruitment bias. These limitations not only question the generalizability of the results to other settings but whether the findings of this study are representative of this inpatient hospice population due to non-participation of patient subgroups, however, this reflects the challenges inherent in recruiting patients to research at the end of life. The participation rate may have been increased by using more than one investigator and working more closely with the treating team to allay concerns regarding screening burden while reinforcing the clinical benefits to patient care. It is hoped this study adds to the literature informing future research including consideration of interventional study design and multi centre research.

Despite the challenges encountered the aims of the study were achieved and the awareness of delirium was raised amongst the medical and nursing staff with subsequent

changes to current clinical practice. A process is underway to incorporate delirium screening into routine clinical care in this inpatient hospice unit. While there remains a lack of consensus regarding the choice of delirium screening tool this study supports the CAM as being appropriate. Future studies are recommended to determine if routine screening improves patient outcomes especially in the terminal phase.

In conclusion, whilst it is possible and necessary to conduct studies in palliative care including the terminal phase more work needs to be done to address the challenges of recruitment. The challenges encountered in this study were not specific to delirium but are consistent with the barriers faced in many studies involving palliative care and dying patients- 'gatekeeping' by health professionals and the disease trajectory of palliative care patients (frailty, rapid deterioration and death). Thought must be given in the development phase of research to develop strategies to engage the treating teams and maintain the balance between conducting research that can benefit patients while minimising patient burden and distress.

As reflective practitioners we must maintain the balance between the demands for evidence- based practice and our compassion and respect for our most vulnerable of patients and their carers. The authors hope this paper adds to the continuing debate of finding the balance between science and the art of caring.

Acknowledgements

The authors are grateful to the hospice staff, patients and families for their time and effort in making this study possible. We also acknowledge the support from Dr Andrew Skeels, Medical Director, in his role as clinical supervisor.

Author disclosure statement

No competing financial interests exist.

References

1 Payne S. Recruitment into palliative care research studies: a common challenge. *Prog Palliat Care 2013;*21(5):263.
2 Addington-Hall J. Research sensitivities to palliative care patients. *Eur J Cancer Care* 2002;11:220-224.
3 Wohleber AM, McKitrick DS, Davis SE. Designing research with hospice and palliative care populations. *Am J Hosp Palliat Me* 2012;29(5):335-345.
4 Agar M, Ko DN, Sheehan C, Chapman M, Currow D. Informed consent in palliative care trials: challenging but possible. *J Palliat Med* 2013;16(5):485-491.
5 White C, Hardy J. What do palliative care patients and their relatives think about research in palliative care?-a systematic review. *Support Care Cancer* 2010;18:905-911.
6 de Raeve L. Ethical issues in palliative care research. *Palliative Med* 1994; 8:298-305.
7 Bullen T, Maher K, Rosenberg J, Smith B. Establishing research in a palliative care clinical setting: perceived barriers and implemented strategies. *Appl Nurs Res* 2014; 27(1):78-83.
8 Ewing G, Rogers M, Barclay S, McCabe J, Martin A, Todd C. Recruiting patients into a primary care based study of palliative care: why is it so difficult? *Palliative Med* 2004;18(5):452-459.
9 Casarett D. Ethical considerations in end-of- life care and research. *J Palliat Med* 2005;8(Supp 1): S148-160.
10 Hui D, Glitza I, Chisholm G, Yennu S, Bruera E. Attrition rates, reasons, and predictive factors in supportive care and palliative oncology clinical trials. *Cancer* 2013;119(5):1098-1105.
11 McWhinney I, Bass M, Donner A. Evaluation of a palliative care service: problems and pitfalls. *BMJ* 1994;309:1340-1342.
12 Diehr P, Johnson L. Accounting for missing data in end-of-life research. *J Palliat Med* 2005;8(supp 1) S50-57.
13 Ross C, Cornbleet M. Attitudes of patients and staff to research in a specialist palliative care unit. *Palliative Med* 2003;17:491-497.
14 Gibbons J, Reid C, Bloor S, Burcombe M, McCoubrie R, Forbes K. Overcoming barriers to recruitment in care of the dying research in hospitals. *J Pain Symptom Manag* 2013;45 (5):859-867.
15 Fisher D, Burgener S, Kavanaugh K, Ryan C, Keenan GI. Conducting research with end-of-life populations: overcoming recruitment challenges when working with clinical agencies. *Appl Nurs Res* 2012;25(4):258-263.
16 Meagher D, Leonard M, Donnelly S, Conroy M, Adamis D, Trzepacz Pl. A longitudinal study of motor subtypes in delirium: relationship with other phenomenology, etiology, medication exposure and prognosis. *J Psychosom Res* 2011;71:395-403.
17 Centeno C, Sanz A, Bruera E. Delirium in advanced cancer patients. *Palliat Med* 2004;18(3):184-194.
18 Hosie A, Davidson P, Agar M, Sanderson C, Phillips J. Delirium prevalence, incidence, and implications for screening in specialist palliative care inpatient settings: A systematic review. *Palliat Med* 2013;27(6):486-498.
19 Kean J, Ryan K. Delirium detection in clinical practice and research: critique of current tools and suggestions for future development. *J Psychosom Res* 2008;65:255-259.
20 Rainsford S, Rosenberg J and Bullen T. Delirium in advanced cancer: screening for the incidence on admission to an inpatient hospice unit. *Journal of Palliat Med.* Accepted for publication 4/2/2014
21 Australian Bureau of Statistics. Australian Demographic Statistics June Quarter 2013. www.abs.gov.au/abs@nsf/mf/3101.0/ Cited 14/2/2014.
22 Trzepacz P, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Validation of the Delirium Rating Scale-Revised-98: comparison with the delirium rating scale and the cognitive test for delirium. *J Neuropsychiatry Clin Neurosci* 2001;13 229-242.
23 Inouye S, van Dyck C, Alessi C, Balkin S, Siegal A, Horwitz R. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990;113:941-948.
24 American Psychiatric Association. *DSM-IV-TR: diagnostic and statistical manual of mental disorders.* 4th edition text revision. Washington, DC: American Psychiatric Association, 2000.

25 Jordhoy M, Kaasa S, Fayers P, Ovreness T, Underland G, Ahlner-Elmqvist. Challenges in palliative care research; recruitment, attrition and compliance: experience from a randomized control trial. *Palliative Med* 1999;13:299-310.
26 Rinck G, van den Bos G, Kleijnen J, de Haes H, Schade E, Veenhof C. Methodological issues in effectiveness research on palliative cancer care: a systematic review. *J Clin Oncol* 1997;15(4): 1697-1707
27 Lynch T, Payne S, Reeve J, Lloyd-Williams M. Learning from challenges in the recruitment of patients with advanced cancer from hospice day care. *Prog Palliat Care 2013;*21(5):265-271.
28 Fick DM, Agostini JV, Inouye SK. Delirium superimposed on dementia: A systematic review. J Am Geriatr Soc 2002;50(10):1723–1732.
29 Sweet L, Adamis D, Meagher D, Davis D, Currow D, Bush S et al. Ethical Challenges and solutions regarding delirium studies in palliative care. *J Pain Symptom Manag.* In press 2014.

FIGURE 1: FLOW CHART OF DELIRIUM SCREENING STUDY

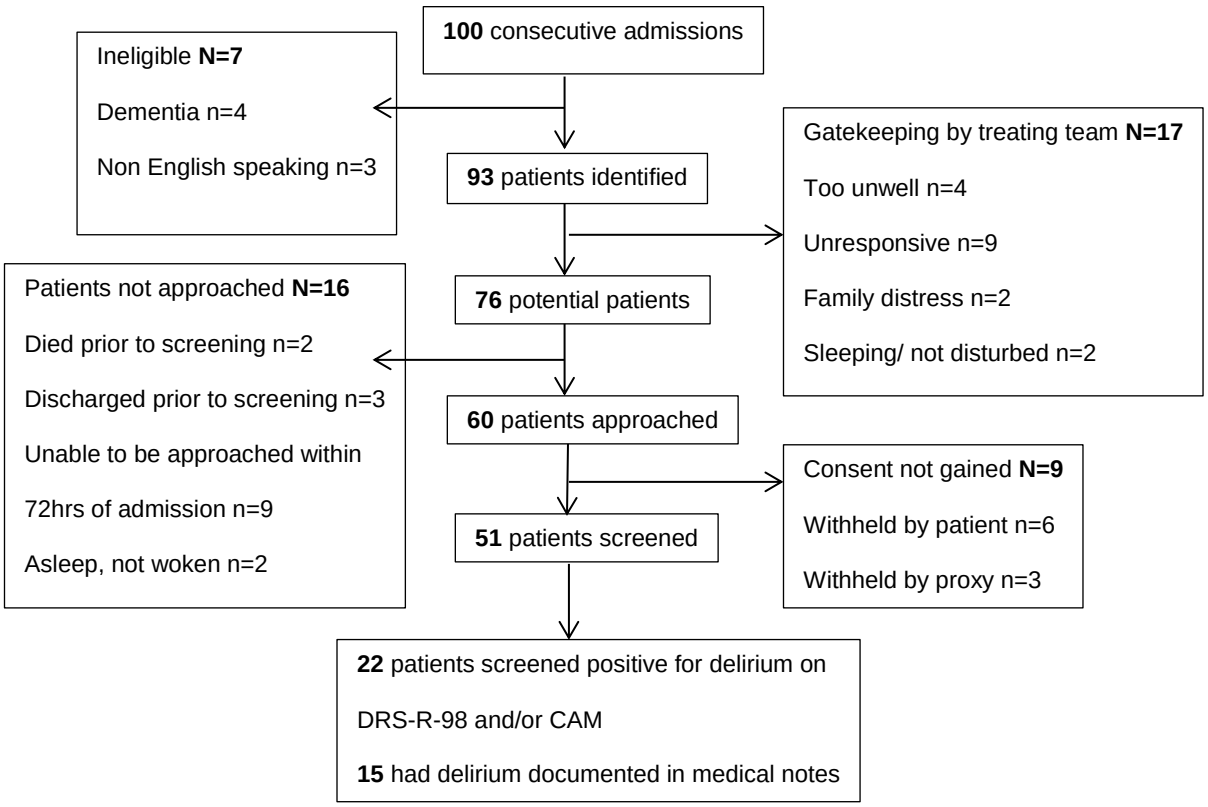

Table 1: Differences between participating and non-participating patients

	Participating Patients.	***Non-participating patients***
N	51	33
Age	Mean= 70.8years	Mean= 65.2years
	(SD 13.7; range 32-92)	(SD 16.9; range 30-95)
Male : Female	19(37%) : 32(63%)	17(52%) : 16(48%)
Reason for admission		
End of life care	19 (37%)	26 (79%)
Symptom management	28 (55%)	7 (21%)
Respite	4 (8%)	-
Death		
Within 24hrs admission	-	6 (18%)
>24-48hrs	1 (2%)	2 (6%)
>48-72hrs	-	2 (6%)
>72hrs- 7days	13 (25%)	12 (36%)
>7days	27 (53%)	6 (18%)
Unknown-Discharged	10 (20%)	5 (16%)