EARLY CONTACT WITH PALLIATIVE CARE SERVICES: A randomized trial in patients with newly detected incurable metastatic cancer

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ABSTRACT

Background

It is not known when in the course of incurable cancer referral to a specialist palliative care service should optimally be made.

Methods

We randomly assigned patients with newly detected incurable metastatic cancer with an estimated survival of less than 12 months to receive either (1) standard oncologic care plus contact from a palliative care nurse who served as a link to palliative care services in the hospital and community (PC) or (2) standard oncologic care alone. Quality of life (QoL) measures were assessed at baseline and monthly thereafter. The primary endpoint was quality of life over time measured by the McGill QOL total score.

Findings

120 patients were randomized, 60 to each group. Forty four patients had gastrointestinal cancer, 23 lung cancer, 19 gynaecological cancer and 17 breast cancer. The mean time since initial cancer diagnosis was 34 months in the standard care group and 29 months in the early palliative care contact group. There was no evidence that early PC nurse contact reduced symptoms or improved quality of life. If anything, there was a trend towards the opposite. There were non-significant trends for the place of death of early contact PC patients to be other than in an acute hospital, and for greater PC input during their final acute hospital admission. Early contact with palliative care was not found to influence the number of lines of chemotherapy received.

Interpretation

The study did not demonstrate a QoL benefit for early contact with a PC nurse.

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INTRODUCTION

In cancer patients receiving chemotherapy, 35% experience distress (1) 70% experience nausea (2) while up to 33% experience severe diarrhoea (3). A recent systematic review concluded that over half of people at the end stage of cancer have distress, pain, dyspnoea, and fatigue (4). A large proportion (30-40%) of cancer patients and carers reports significant unmet need for information, symptom relief and support (5, 6).

Health professionals often delay discussion of end of life (EOL) issues until only days before death (7). For example, the US SUPPORT study documenting care for over 9000 seriously ill hospitalised adults (8) reported that only 47% of physicians knew whether their patients preferred to avoid cardiopulmonary resuscitation (CPR), and 46% of do-not-resuscitate (DNR) orders were written within 2 days of death. Wright (9) found that EOL discussions conducted a median of 4.4 months before death were associated with less aggressive medical care near death and earlier hospice referrals. More aggressive medical care has been found to be associated with worse quality of life and no survival benefit.

Early contact with palliative care services has the potential to overcome some of these distressing outcomes. The proportion of terminal cancer patients currently referred to palliative care services varies in Australia, and internationally. Moreover there is wide variation in the time course of advanced cancer when patients are referred to palliative care for the first time. A study from Boston randomised 151 patients with newly diagnosed metastatic non-small cell lung cancer to receive either palliative care integrated with standard oncologic care or standard oncologic care alone (10). Patients assigned to early palliative care had a better quality of life at 12 weeks and fewer depressive symptoms than did patients assigned to standard care

We report the results of a randomised trial of early contact with palliative care services in patients with newly detected incurable metastatic cancer. We hypothesised that early contact with palliative care services would improve patients' EOL experiences through better symptom control and quality of life; addressing patients' supportive care needs; reducing the lines of chemotherapy delivered; and reducing the likelihood of dying in the acute hospital setting. It was anticipated that meeting and talking with a palliative care nurse at the time of recruitment would subsequently provide a pathway for patients to contact the palliative care service independent of the oncologist. It was hoped this facilitated access to the PC service would have the benefit of improved symptom control.

1 METHODS

1.1 Study Design and Intervention

Between April 2003 to January 2005 ambulatory patients with newly detected incurable metastatic cancer attending a medical oncology clinic with a life expectancy of less than12 months were invited to take part in a randomised controlled trial of early contact with a palliative care nurse consultant with ongoing oncologist care or oncologist care alone. For allocation of the participants, a computer-generated list of random numbers was used, and allocation was concealed using sequentially numbered, opaque sealed

envelopes.No stratification was made for oncologist or cancer diagnosis. A sample size of 150 patients was sought to provide over 80% power to detect an effect size of 0.50 (standard deviations) at the two-sided 5% level of significance based on a two-sample t-test; with even greater precision achievable using analyses incorporating the baseline score as a covariate (11).

Patients assigned to the early palliative care group met with a palliative care nurse consultant (PC nurse) member of the hospital palliative care team. She outlined available palliative care services including advice about symptom control, and she offered to arrange review by a palliative care physician, and provided contact details for the palliative care service. The PC nurse offered to telephone the patient monthly to check on their well-being, or, if the patient preferred, provided her contact details. Standard oncologic care was given in line with the oncologist's recommendation. Control patients were referred to the palliative care service when recommended by the oncologist.

1.2 Assessments and Endpoints

At baseline, oncologists documented their estimate of the patient's life expectancy (12).

Symptom severity, feeling supported and overall QoL were pre-specified as being the key outcome measures. The severity of symptoms and overall quality of life were measured using the McGill quality of life (MQOL) questionnaire (13) and the Rotterdam Symptom Checklist (RSC) (14). Construct validity of the MQOL has been demonstrated through its correlations with the Spitzer Quality of Life scale (15). Cronbach's alpha for subscales was moderate to high (0.462-0.858) and test-retest reliability (Spearman's r(s) ranged from 0.512-0.861 (16). Validity has been demonstrated through correlations with a range of related scales (17).

The degree of perceived support was measured using the Supportive Care Needs – Short Form questionnaire (SCNS-short) (18). Content and face validity has been found to be high and construct validity is supported by a robust factor structure (19). Patients were requested to complete the MQOL and RSC at monthly intervals and the SCNS-short every 4 months.

Other secondary endpoints collected from hospital medical records included end of life experiences, number of lines of chemotherapy, and place of death.

1.3 Analysis Methods

All analyses were performed in accordance with the intention-to-treat principle. Repeated measures analyses were undertaken on the longitudinal RSC, MQOL, and SCNS assessments using a mixed modeling approach with the baseline measure as a covariate and treatment group, assessment time point, and a treatment group-by-time point interaction as factors. The interaction term allowed the model to evaluate the difference between groups at each time point. Imputation of missing data was not required as mixed modeling methods accommodate unbalanced designs. A comparison was also performed between the groups on patients' average scores over the follow-up period, and patients' worst scores over the follow-up period, for the RSC, MQOL, and

SCNS assessments using an analysis of covariance with the baseline score fitted as the covariate. Treatment groups were compared on categorical variables measured at a single time point using a chi-squared test, or Fisher's exact test where appropriate. Survival time in the two groups was compared using a log-rank test and presented graphically using Kaplan-Meier plots. Cox proportional hazards regression models were used to estimate hazard ratios for the treatment effect with and without adjustment for other predictors of survival.

2 RESULTS

2.1 Baseline Characteristics

One hundred and twenty of the 141 patients approached consented to take part and were randomized to either the early referral group (N=60) or standard care (N=60). Recruitment to the study was halted at this point due to resource constraints. Forty four patients had a gastrointestinal primary cancer, 23 lung cancer, 19 gynaecological cancers, 17 breast cancer 2 prostate cancer and 15 other primary sites, or unknown. Most baseline characteristics were adequately balanced across the two study groups (Table 1), however there were differences between the groups in the time since initial cancer diagnosis (mean of 29 versus 34 months in the early referral and standard care groups respectively), and the oncologists' estimate of likely survival (e.g. 11 versus 20 patients with estimates of >12 months likely survival in the early referral and standard care groups respectively). Therefore these variables were controlled for in subsequent analyses. There were no remarkable baseline differences between the groups on the patient reported outcome measures.

2.2 Contact with Palliative Care Services

***Initial contact**:* Patients in the early palliative care contact group had at least one meeting with the PC nurse, with the median time to first contact being 2 weeks after randomisation. Further contact with the PC nurse was more frequent when the initial contact with the PC nurse was face to face. Most patients were happy for the PC nurse to explore the role of palliative care, and for records of their response to be kept. Several patients stated they thought they were not ready for palliative care but were happy to have it explained. Many patients reported feeling better having discussed palliative and end of life care options even though they were receiving anticancer treatments.

Subsequent contact: Many patients preferred to contact the PC nurse when they needed assistance rather than receiving monthly telephone contact, and many made contact during clinic attendance. Twenty eight patients had 1 subsequent telephone contact with the PC nurse, 3 had 2-3 telephone contacts and 5 had more than 3. Two patients preferred to telephone the PC nurse and did so. 20 patients had no subsequent contact with the palliative care nurse. The average number of telephone contacts with the PC nurse in the early contact group was 3.
Fifty one patients in the early palliative care contact group were seen at least once by a palliative care physician consultant compared to 8 patients in the control group. In the intervention group 25 patients were seen by a palliative care physician in the last few weeks of life (16 in the last month of life compared to 6 in the control group)

2.3 Quality of Life and Unmet Needs

Data on patient-reported outcome measures were available on 107 of the 120 patients randomized at baseline (Figure 1). This number declined to 51 of 79 alive at 6 months, 29 of 52 alive at 12 months, and 7 of 36 alive at 18 months. The median duration of follow-up on the self-reported outcome measures was 4.8 versus 8.1 months for the early referral and standard care groups respectively (p-value = 0.13).

There was no evidence that early PC intervention was superior to the control on patient reported measures. Figures 2 and 3 summarize the estimates for the two groups over the first 12 months of follow-up on the MQOL total score, the RSCL physical symptom scale and the RSCL psychological distress scale. Across these measures there were consistent post baseline trends of modest magnitude favouring the control arm with differences that occasionally reached statistical significance. These results were not materially changed when adjusted for the oncologist's baseline estimate of likely survival, diagnosis, months since diagnosis, and gender were included as covariates (results presented in e-supplement).

Table 2 presents a summary of the symptoms ever reported on the MQoL as severe (i.e. assigned a score > 5) by the 47 patients who completed an assessment within the three months prior to death. Unexpectedly, somewhat more patients in the early PC intervention group than in the control group had severe scores for pain and poor appetite.

2.4 Cancer treatment and PC input during the final acute hospital

Patients from both groups received an average of 1.8 lines of chemotherapy. Forty-two patients (42/49 86%) randomized to the early referral group received palliative care contact during the last acute hospital admission compared to 29 patients (29/37 78%) in the control group (p=0.37).

2.5 Survival

The median survival of the early PC contact group was 7.0 months (95% CI: 5.2-9.8) compared to 11.7 months (95% CI: 9.8-18.8) for the standard care group (log rank p=0.014) (Fig 3). The estimated hazard ratio was 1.6 (95%CI: 1.1 to 2.3; p=0.015). This estimate changed to 1.5 (95%CI 0.99 to 2.2; p=0.06) when adjusted for the oncologist's baseline estimate of likely survival, diagnosis, months since diagnosis, and gender.

3.6 Place of death

There was little evidence of a difference between randomization groups in terms of place of death (Table 3). Only 2 patients (both early palliative care contact group) were admitted to ICU during their final acute hospital admission. One patient had attempted cardiopulmonary resuscitation (early palliative care contact group), and 2 had mechanical ventilation (1 in each group)

3 DISCUSSION

This trial provides no evidence that early PC contact with a specialist PC nurse – who

outlined available palliative care services, and offered to arrange review by a palliative care physician ultimately improved patient symptoms or quality of life. If anything, there was a trend towards the opposite. There were non-significant trends for the place of death of early contact PC patients to be other than in an acute hospital, and for greater PC input during their final acute hospital admission.

There was a trend for control patients' scores for overall QoL, pain and appetite to be better than the early intervention group. The trend might simply be due to chance imbalances between the treatment groups. Early PC contact patients may have felt more comfortable reporting symptoms because of PC contact – less trying to "please the doctor". These factors also may have contributed to the greater mean scores in the early PC contact group in the RSCL physical symptoms and psychological distress scales, and the pattern of scores in the MQOL. Alternatively patients in the standard care group may have experienced a protective effect of denial. Lung cancer patients who displayed a moderate or increasing level of denial over time reported better quality of life compared with those who displayed low levels of denial ($p<0.0001$) (20).

There was a statistically significant difference in survival time favouring the control arm. The estimated effect was smaller and of marginal statistical significance when adjusted for gender, diagnosis, months since initial diagnosis and the oncologist's baseline estimate of likely survival time. The observed survival differences are likely due to chance imbalances between the groups.

Our results differ from those reported by others (10). Differences in the eligibility of patients may have played a role in that our trial included patients with a range of cancer types, most of whom had recurrent cancer. The Boston trial recruited advanced lung cancer patients within 8 weeks of first cancer diagnosis. The nature and 'dose' of the palliative care intervention also differed between our study and that reported from Boston. In Boston, PC contact involved the patient meeting with a member of the PC team which consisted of 5 palliative care physicians and one advanced practice nurse, and 55% of the consultations were conducted by physicians, and 44% by the advanced practice nurse. The median time for the first palliative care outpatient visit was 55 minutes (21). Subsequent contact in Boston was at least monthly in the outpatient setting.

Our results also differ from those obtained in Project Enable (Educate, Nurture, Advise, Before Life Ends) (22), where the intervention involved not only specialist palliative care nurse educators, but also nurse practitioners, and palliative care physicians. It used a case management, educational approach with monthly shared medical appointments to encourage patient activation, empowerment, and self-management. There was higher quality of life ($P < 0.02$), lower symptom intensity ($P < 0.06$), and lower depressed mood ($P < 0.02$) in Project Enable patients.

Several strengths and limitations of our study deserve mention. In spite of randomization, there were differences between the groups in the numbers of patients with breast cancer, the time since initial cancer diagnosis, and the treating oncologist's prediction of expected survival. Findings from a single institution and palliative care nurse consultant may not be generalizable. A larger, stratified multicentre trial is needed to reduce the likelihood of important imbalances, and to improve the generalisability of the results.

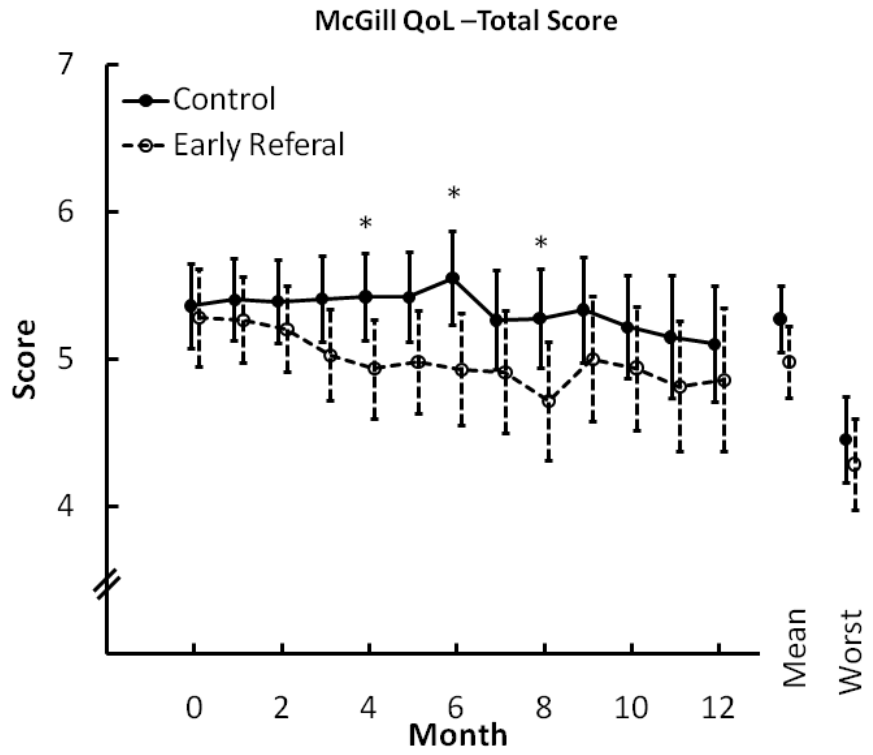
A strong case can be made for further, rigorously-designed, large randomized trials in

differing health care settings of better-defined ‘early’ PC intervention in cancer patients with limited survival expectations, to determine effects on quality of life, quality of death, and survival. Future studies should specify the issues that were addressed during the PC “consultation” such as pain management, symptom control, psychosocial and spiritual issues, prognosis, burdens and benefits of different treatment options, advanced care planning, and preferences for place of care. Similarly the endpoints of new trials should include repeated measures of quality of life, and measures of hope and denial. Studies also need to distinguish between patients whose palliative care needs are straightforward and manageable by the oncologist versus more complex presentations (23).

Figure 1:

Trial profile: Qs = number of patients who undertook the assigned questionnaire battery. Following baseline, the MQOL and RSC were to be completed monthly whilst the SCNS was to be completed every 4 months. Completion rates at months 1, 3, 6, 9 and 12 are shown. All patients with a baseline and at least one post-baseline assessment were included in the repeated measures analyses.

(a)


McGill QoL –Total Score
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(b)

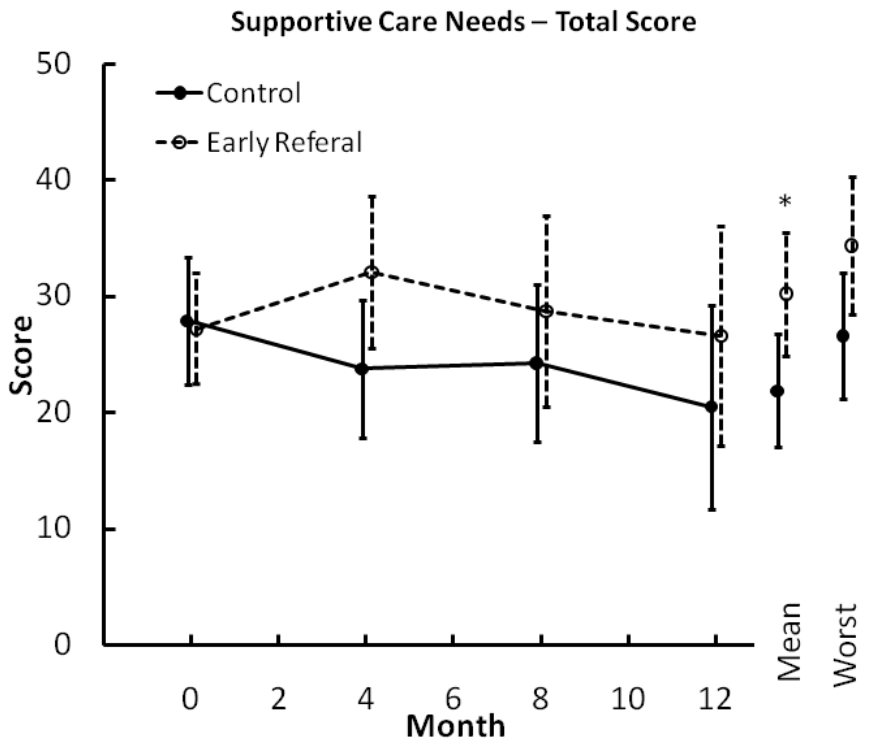
Supportive Care Needs – Total Score
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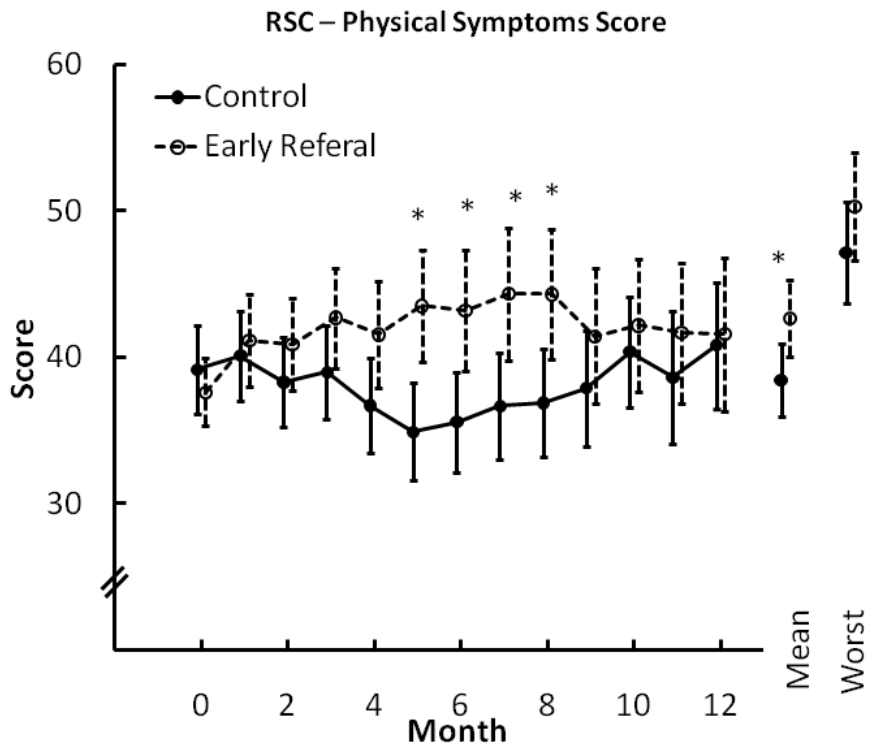
Figure 2

(a)


RSC – Physical Symptoms Score
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(b)

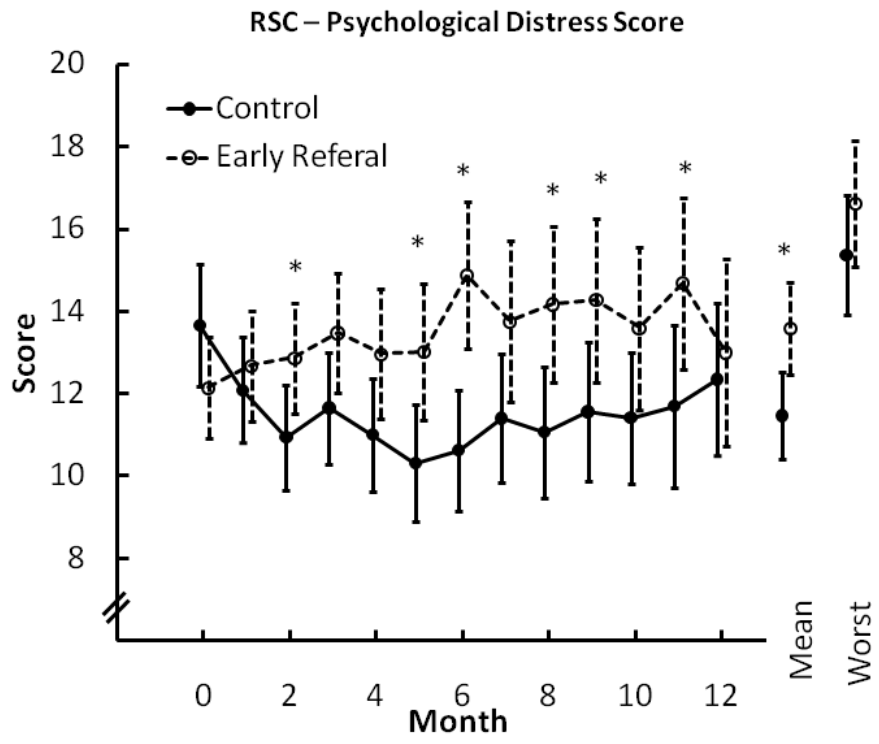
RSC – Psychological Distress Score
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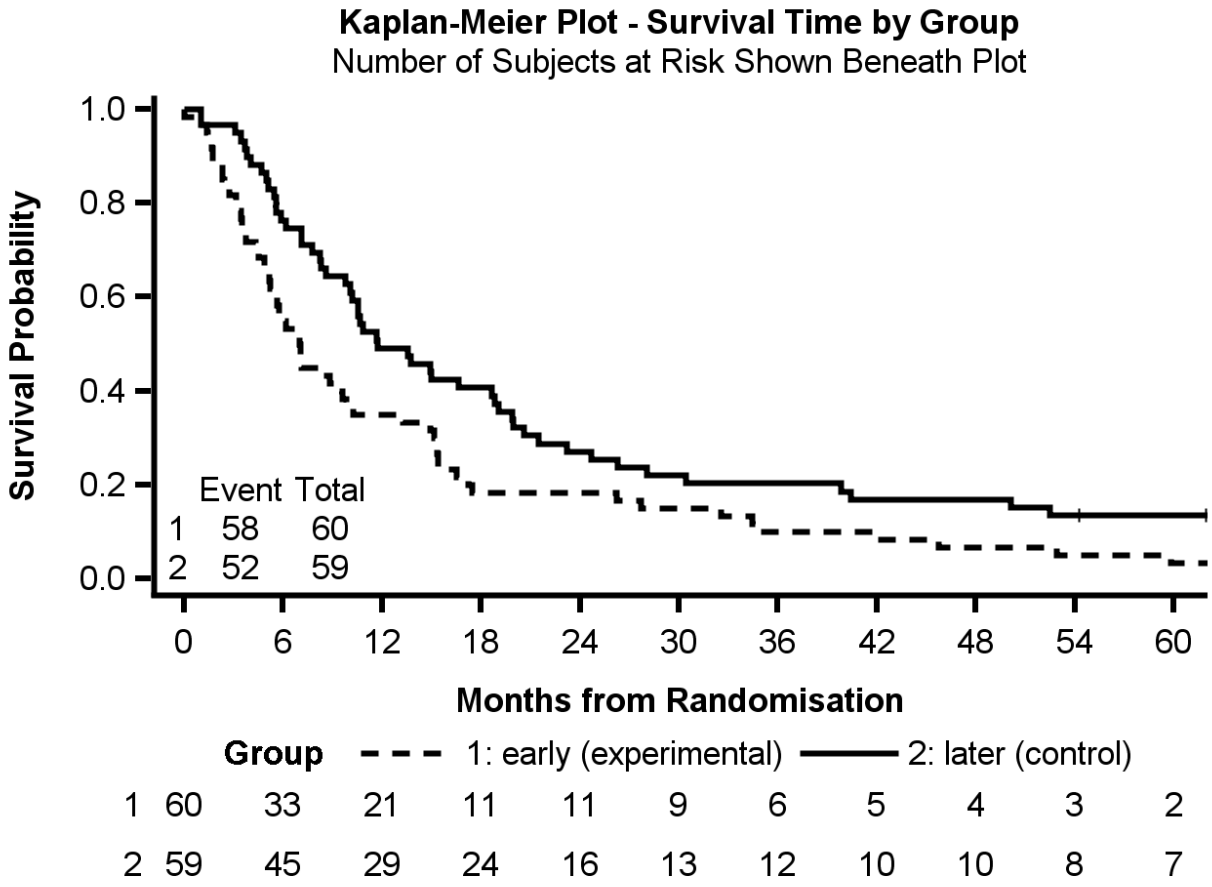
Figure 3

Legend for Figures 2 and 3: Estimates are presented with 95% confidence intervals. An asterisk indicates a statistically significant difference at $p<0.05$. A larger score on the MQOL reflects a more favorable outcome, whilst a larger score on the SCNS and the RSC scales reflects a less favorable outcome. The baseline (i.e. month 0) estimate is the (unadjusted) mean score. The estimates for the mean post-baseline score to 12 months, and the worst post-baseline score to 12 months, are from the ANCOVA models. The estimates at months 1 through 12 are from the MMRM analysis fitted to all available data from patients with a baseline and a least one post-baseline assessment (i.e. 86 patients for MQOL total score, 64 patients for SCNS total score, 86 patients for RSC Psychological Distress score, and 86 patients for RSC Physical Symptoms score).

Figure 4



Log-rank test p-value = 0.014

Table 1. Baseline Demographics and Clinical Characteristics of Study Patients

	Early Palliative Care Contact group N=60	Standard care group N=60
Age in years: Mean (SD)	63 (11.2)	64 (11.1)
Female sex: N (%)	28 (47%)	34 (57%)
Partner: N (%)	40 (67%)	41 (68%)
Education Year 10 or less: N (%)	23 (38%)	32 (53%)
Australian born: N (%)	29 (48%)	36 (60%)
Months since initial cancer diagnosis Mean (SD) (5 missing values)	29 (40.0)	34 (53.0)
Cancer diagnosis: N (%)		
Gastrointestinal	20 (33%)	24 (40%)
Lung	12 (20%)	11 (18%)
Prostate	0 (0%)	2 (3%)
Breast	5 (8%)	12 (20%)
Gynaecologic	11 (18%)	8 (13%)
Other/Unknown primary	12 (20%)	3 (5%)
Oncologist estimate of patient's likely survival time: N (%)		
4-12 weeks	1 (2%)	0 (0%)
3-6 months	9 (15%)	6 (10%)
6-12 months	33 (55%)	30 (50%)
>12 months	11 (18%)	20 (33%)
Not stated	6 (10%)	4 (7%)

Table 2: Severe symptoms (i.e. ever assigned a score > 5) reported on the MQoL within the three months prior to death

Troublesome Symptom*	Randomisation Group				p-value**	Total	
	Intervention N=24		Control N=23				
Pain	12	(50%)	8	(35%)	0.38	20	(43%)
Tired	8	(33%)	7	(30%)	1.00	15	(32%)
Appetite	9	(38%)	2	(9%)	0.04	11	(23%)
Other	8	(33%)	3	(13%)	0.17	11	(23%)
Weakness	8	(33%)	3	(13%)	0.17	11	(23%)
Breathing	5	(21%)	3	(13%)	0.70	8	(17%)
Sleep	3	(13%)	4	(17%)	0.70	7	(15%)
Constipation	4	(17%)	2	(9%)	0.67	6	(13%)
Nausea	2	(8%)	2	(9%)	1.00	4	(9%)
Diarrhoea	1	(4%)	1	(4%)	1.00	2	(4%)

* Symptoms reported by subjects on multiple occasions appear only once in this table. Infrequently reported symptoms have been coded to other category

** Fisher's Exact Test

Table 3 Place of death, and palliative care contact during last admission

	Early Palliative Care Contact group	Standard care group	P-value
Place of death			0.46
Home	13 (22%)	8 (15%)	
Hospice/Nursing Home	11 (19%)	8 (15%)	
Acute Hospital	34 (59%)	37(70%)	
Total	58	53	
Palliative care contact at last admission			0.37
Yes	42 (86%)	29 (78%)	
No	7 (14%)	8 (22%)	
Total	49	37	

References

1. Zabora J, BrintzenhofeSzoc K, Curbow B, Hooker C, Piantadosi S. The prevalence of psychological distress by cancer site. *Psycho Oncology.* 2001;10(1):19-28.
2. Booth CM, Clemons M, Dranitsaris G, et al. Chemotherapy-induced nausea and vomiting in breast cancer patients: a prospective observational study.*J Support Oncol.*2007;5(8):374-80.
3. Maroun J, Anthony L, Blais N, et al. Prevention and management of chemotherapy-induced diarrhea in patients with colorectal cancer: a consensus statement by the Canadian Working Group on Chemotherapy-Induced Diarrhea. *Curr Oncol.* 2007 14(1):13-20.
4. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. *J Pain Symptom Manage.* 2006;31(1):58-69.
5. Sanson-Fisher R, Girgis A, Boyes A, et al. The unmet supportive care needs of patients with cancer. Supportive Care Review Group. *Cancer.* 2000;88(1):226-237.
6. Cancer Institute NSW. *NSW Cancer Patient Satisfaction Survey. Catalogue number: CF-2010-01 SHPN: (CI) 100028*2010.
7. Koedoot CG, Oort FJ, de Haan RJ, et al. The content and amount of information given by medical oncologists when telling patients with advanced cancer what their treatment options are. palliative chemotherapy and watchful-waiting.Europ J Cancer. 2004; 40: 225-35.
8. The SUPPORT Principal Investigators. A controlled trial to improve care for seriously ill hospitalized patients. The study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). *JAMA.1995. 274: 1591-1598*
9. Wright AA, Zhang B, Ray A, Mack JW, Trice E, Balboni T, Mitchell SL, Jackson VA, Block SD, Maciejewski PK, Prigerson HG. Associations between end of life discussions, patient mental health, medical care near end of life, and caregiver bereavement adjustment. JAMA 2008; 300: 1665-73
10. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, Dahlin CM, Blinderman CD, Jacobsen J, Pirl WF, Billings JA, Lynch TJ. Early palliative care for patients with metastatic non-small lung cancer. New Eng J Med 2010; 363: 733-742.
11. Borm GF, Fransen J, Lemmens WAJG. A simple sample size formula for analysis of covariance in randomized clinical trials. J Clin Epidemiol 2007;60:1234-817.
12. Stockler MR, Tattersall MHN, Boyer MJ, Clarke SJ, Beale PJ, Simes RJ. Disarming the guarded prognosis: predicting survival in newly referred patients with incurable cancer. Brit J Cancer 2006, 94: 2006.
13. Cohen SR, Mount BM, Bruera E, Rowe J, Tong K.Validity of the McGill Quality of Life Questionnaire in the palliative care setting. A multi-center Canadian study demonstrating the importance of the existential domain. Palliative Medicine 1997, 11: 3-20.
14. Haes JCJM, van Knippenberg FCE, Neijt JP. Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom checklist. Br J Cancer 1990, 62: 1034-38
15. Cohen SR, Mount BM, Strobel MG, Bui F. The McGill Quality of Life Questionnaire: a measure of quality of life appropriate for people with advanced disease. A preliminary study of validity and acceptability. Palliat.Med 1995;

9(3):207-19.
16. Lua PL, Salek S, Finlay I, Lloyd-Richards C The feasibility, reliability and validity of the McGill Quality of Life Questionnaire-Cardiff Short Form (MQOL-CSF) in palliative care population. Qual Life Res. 2005 Sep;14(7):1669-81.
17. De Haes JCJM, Olschewski M, Fayers P, Visser MRM, Cull A, Hopwood P, Sanderman R. Measuring the quality of life of cancer patients with the Rotterdam Symptom Checklist. A manual. 1996, University of Groningen, Northern Centre for Healthcare Research (NCH).
18. Boyes Alison, Girgis A, Lecathelinais C. Brief assessment of adult cancerpatientsperceived needs: development and validation of the 34 item Supportive Care Needs Survey (SCNS-SF34) Journal of Evaluation in Clinical Practice 2009, 15: 602-606.
19. Bonevski B, Sanson-Fisher R, Girgis A, Burton L,Cook P, Boyes A. Evaluation of an instrument to assess the needs of patients with cancer. Supportive Care Review Group. Cancer 2000; 88:217–225.
20. Vos MS, Putter H, van Houwelingen HC, de Haes HCJM. Denial and social and emotional outcomes in lung cancer patients: the protective effect of denial. Lung cancer 2011, 72: 119-24.
21. Jacobsen J, Jackson V, Dahlin C, Greer J, Perez-Cruz P, Billings JA, Piri W, Temel J. Components of early outpatient palliative care consultation in patients with metastatic nonsmall cell lung cancer. J Pall Med 2011, 14: 459-64.
22. Bakitas M, Lyons KD, Hegel MT, Balan S, Brokaw FC, Seville J, Hull JG, Li Z, Tosteson TD, Byock IR, Ahles TA. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer. The project ENABLE 11 randomized controlled trial. JAMA 2009; 302: 741-9.

Author contribution:
Martin Tattersall (MHNT), Michael Boyer (MB), Paul Glare (PG), Martin Stockler (MS) and Phyllis Butow (PB) developed the research proposal and conducted the trial. MHNT and PG performed the literature search.
Rhonda Devine (RD) & Joan Ryan (JR) recruited patients, and assisted with gathering base line information & QoL measures. JR was the Palliative Care (PC) nurse involved in the early PC contact intervention. Lucy Hastings (LH) reviewed the patients' medical records to identify patients' end of life experiences. Andrew Martin (AM), Jesse Jansen (JJ) and PB performed the data analysis, and all authors were involved in data interpretation.
MHNT & AM wrote the first draft of the manuscript, and all authors had input in preparing the final version.

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MHNT had full access to all the data in the study and had final responsibility for the decision to submit for publication.

All authors have completed the Unified Competing Interest form at www.icmje.org.coi.pdf (available on request from the corresponding author)