American Journal of Hospice & Palliative Medicine®
Volume 000 Number 00
Month 2009 1-8

10.1177/1049909109331887
http://ajhpm.sagepub.com
hosted at
http://online.sagepub.com

Three Lessons From a Randomized Trial of Massage and Meditation at End of Life: Patient Benefit, Outcome Measure Selection, and Design of Trials With Terminally Ill Patients

Lois Downey, MA, Ruth A. Engelberg, PhD, Leanna J. Standish, ND, PhD, Leila Kozak, PhD, and William E. Lafferty, MD

Improving end-of-life care is a priority in the United States, but assigning priorities for standard care services requires evaluations using appropriate study design and appropriate outcome indicators. A recent randomized controlled trial with terminally ill patients produced no evidence of benefit from massage or guided meditation, when evaluated with measures of global quality of life or pain distress over the course of patient participation. However, reanalysis using a more targeted outcome, surrogates' assessment of patients' benefit from the study intervention, suggested significant gains from massage—the treatment patients gave their highest preassignment preference ratings. The authors conclude that adding a menu of complementary therapies as part of standard end-of-life care may yield significant benefit, that patient preference is an important predictor of outcome, and that modifications in trial design may be appropriate for end-of-life studies.

Keywords: complementary and alternative medicine; end of life; hospice care; palliative care; patient benefit; patient preference; clinical trial design; outcome measure selection

Introduction

> You never ask how important it is to me to receive this service . . . I so much look forward to it . . . I'm amazed you don't ask me this question. It should be the *featured* question.
>
> (Unsolicited comment from a patient in the study)

During the past 2 decades, improving the quality of end-of-life care has become a priority in the United States. Management or elimination of previously fatal acute diseases that brought death to the young, an aging population whose protracted end-of-life period is complicated by comorbidities, and the imminent arrival at old age by the politically powerful "baby boom" generation have brought new urgency to the consideration of palliative care. As in other health care areas, the movement toward evidence-based medicine requires scientific justification for establishing treatment guidelines for care at end of life. In a 1997 report,[1] the Institute of Medicine's Committee on Care at the End of Life called for research to identify methods for improving care of persons approaching death, thus underscoring the importance of evaluating services that might benefit terminally ill patients if added to standard end-of-life care.

From the Department of Health Services, School of Public Health and Community Medicine, University of Washington, Seattle (LD, WEL); Division of Pulmonary and Critical Care Medicine, Department of Medicine, Harborview Medical Center, School of Medicine, University of Washington, Seattle (LD, RAE); Bastyr University Research Center, Kenmore (LJS, LK); and Division of Oncology, Department of Medicine, Seattle Cancer Care Alliance, School of Medicine, University of Washington, Seattle (LK), Washington.

Address correspondence to: Lois Downey, Department of Health Services, School of Public Health and Community Medicine, University of Washington, Seattle, WA 98195; phone: (206) 685-0576; e-mail: ldowney@u.washington.edu.

Among the difficulties encountered in evaluating interventions for improved care, however, is the choice of appropriate outcome indicators. Although this difficulty is not unique to end-of-life trials, measurement is particularly problematic in the study of dying and death, where best measurement practice supports use of patient and family reports of experience, in addition to more objective measures.[2] Researchers have noted the insensitivity of some established measures of this type to interventions of interest,[2-4] calling attention to their failure to permit detection of benefit implied by other outcomes—notably patients' seeking of additional treatment sessions during clinical trials or continuation of treatment after trial conclusion.[3,4]

Following a recent randomized clinical trial with terminally ill patients, we evaluated the impact of 2 complementary and alternative medicine (CAM) therapies (massage and guided meditation/visualization) on patients' end-of-life experience. In analyses using 3 outcome indicators (patients' global quality of life and pain distress ratings collected throughout the service delivery period, and surrogates' ratings of patients' quality of life during the final week before death), we found no significant effects of either CAM treatment, when compared with an attention control condition (friendly visits).[5] However, during surrogate interviews after patients' deaths, we collected information on 2 additional outcomes: the surrogate's assessment of the specific impact of the study treatment on the patient's and their own quality of life. In this article, we report findings related to these additional outcomes and discuss the potential implications for selecting outcome measures and designing trials for future end-of-life research.

Methods

Study Sample

Outcome data came from 108 "study partners" of terminally ill patients, collected during interviews subsequent to patients' deaths. The patients had participated in a randomized clinical trial testing the efficacy of 2 CAM therapies: massage and guided meditation/visualization.

A detailed description of the larger clinical trial appears elsewhere.[5] However, in brief, patients living in the Seattle, Washington, metropolitan area were eligible for participation if they had been diagnosed with acquired immunodeficiency syndrome (AIDS) or stage IV cancer or were enrolled in a hospice or palliative care program, and if their survival prognosis was between 3 weeks and 6 months. The study protocol excluded patients who were under 18 years of age, did not speak English, would not accept random assignment, or were not capable of providing reliable responses to a 60 to 90 minute baseline interview. Interviews could be continued over a series of shorter sessions if patients' endurance was limited. After the baseline interview, enrollees were randomized to 1 of 3 treatment conditions—massage, guided meditation/visualization, or friendly visits provided by, respectively, licensed massage therapists, licensed naturopathic physicians, or certified hospice volunteers. The assigned practitioner then provided up to 2 treatment visits per week. After every 2 treatment visits, participating patients completed a short follow-up interview, either by telephone or in person, depending upon their preference. Receipt of additional treatment was contingent upon completion of the follow-up interview until the research staff deemed the patient no longer capable of interview. Treatment continued until the patient's death or voluntary withdrawal from the study. All treatment and data-gathering sessions occurred on a schedule of the patient's choice, and both treatment visits and in-person interviews were at locations of the patient's choice—typically at home, but occasionally in hospitals or clinics.

At the time of study enrollment, each patient nominated a study partner who could provide collateral information at baseline and follow-up information after the patient's death. Most study partners were family members or close friends of patients; a few were professional health care providers of socially isolated patients. Many were the patient's primary caregiver.

Measures

Our primary outcome of interest was the perceived effect of the study treatment on the patient's quality of life during study participation. A secondary outcome of interest was the effect of the patient's study-delivered treatment on the responding study partner's quality of life. For both outcomes, the response options ranged from 0 (*the very worst effect I can imagine*) to 10 (*the very best effect I can imagine*).

We considered 2 primary predictors: the patient's randomization group (massage, guided meditation, or

friendly visits), and a dichotomous variable indicating whether the patient was randomized to her or his preferred treatment group. We based the latter variable on ratings patients assigned to the 3 treatment groups prior to randomization. Using a rating scale ranging from 0 (*really disappointed*) to 10 (*really happy*), they indicated their anticipated response in the event that they were assigned to each of the 3 treatment groups. If they were ultimately randomized to the group that received (or tied for) their top rating, we considered them assigned to their preferred treatment; if they gave a higher rating to a treatment other than their randomization group, we considered them assigned to a nonpreferred treatment.

We investigated several additional variables, both as secondary predictors of interest and as potential confounders of associations between the primary predictors and outcomes: from the baseline interviews, the gender, racial-ethnic minority status, age, and educational level of patient and study partner; the relationship between patient and study partner, their length of association, and whether they lived together at the time of the patient's enrollment in the study; the patient's primary life-limiting diagnosis, use of CAM before study enrollment, and enrollment in hospice during the end-of-life period. In addition, we measured the patient's baseline single-item rating of global quality of life (0 = *no quality of life* to 10 = *perfect quality of life*) and the patient's baseline symptom distress score (a composite measure based on the Memorial Symptom Assessment Scale; 0 = *no symptoms* to 4 = *high symptom distress*)[6] as well as the number of days the patient participated in the study between enrollment and death.

Analysis Methods

The distributions of both outcomes showed significant departure from the normal distribution (*P* values for both the Kolmogorov-Smirnov and Shapiro-Wilk tests = 0.000). Therefore, we based findings on ordinal logistic regression models. We considered any variable that altered the odds ratio (OR) for the primary predictor by 15% or more in either direction, when added to the bivariate model, to be a confounder, and re-evaluated the association between the primary predictor and outcome after adjustment for confounders. We used Microsoft Access 2002 for data management, SPSS 14.0.0 for descriptive and simple nonparametric statistics[7] (Pearson χ^2, Fisher exact, Mann-Whitney, Kruskal-Wallis, and Friedman tests), and Mplus 5.1 for regression modeling.[8]

Results

Completion Rates

We randomized 167 patients to the 3 treatment groups: 56 (33.5%) to massage, 56 (33.5%) to meditation, and 55 (32.9%) to friendly visits. Of these, 28 patients (16.8%) withdrew from the study before death, with the remaining 139 completing the study. Although patient withdrawal was considerably higher from the meditation and friendly visit groups than from the massage group, attrition rates between groups did not differ significantly: 6 (10.7%) from the massage group, 12 (21.4%) from the meditation group, and 10 (18.2%) from the friendly visit group ($\chi^2 = 2.421$, $df = 2$, $P = .298$). Withdrawal was significantly higher among patients assigned to a nonpreferred treatment than among those assigned to a preferred treatment (22.2% vs 9.6%, Fisher exact test = 0.035).

Of the 139 patients who completed the study, 117 died during study participation, with the remaining 22 surviving to the end of the study. The decedents included 40 patients assigned to massage, 38 to meditation, and 39 to friendly visits. Study partners of 108 (92.3%) of the 117 decedents completed follow-up interviews: 37 (92.5%) from the massage group, 34 (89.5%) from meditation, and 37 (94.9%) from friendly visits. Follow-up rates for study partners did not differ significantly between treatment groups ($\chi^2 = 0.793$, $df = 2$, $P = .673$) but were higher for nonpreferred than for preferred treatments (98.3% vs 87.0%; Fisher exact test = 0.026).

Characteristics of the Responding Study Partners and the Decedents They Represented

Study partners and decedents were predominantly white non-Hispanic women, study partners averaging about 54 years of age and decedents about 20 years older. The median length of association between study partners and decedents was 41 years. More than half of the study partners and over 40% of the decedents had college or advanced degrees. Most study partners were either spouses or children of

decedents, and almost half lived with the decedent at the time of enrollment in the study. Almost one third of the patients had used some form of CAM (broadly defined) during the year before study enrollment, over 90% were enrolled in hospice at the time of death, and over 70% died with cancer. At the time of study enrollment, most patients rated their quality of life as reasonably high (median = 7 on a 0-10 scale) and their symptom distress relatively low (1 on a 0-4 scale). Overall, patients gave high preassignment ratings to the treatment to which they were ultimately assigned (median = 8 on a 0-10 scale), and over 44% were assigned to a preferred treatment (Table 1).

Patients' preassignment ratings differed significantly for the 3 potential treatment assignments, with median ratings for massage highest (8), followed in order by friendly visits (7) and meditation (6). Preassignment ratings of the treatment actually assigned were, similarly, significantly different by treatment group (with median ratings of 10, 8, and 6, respectively, for massage, friendly visits, and meditation) and by whether the patient was assigned to a preferred or nonpreferred treatment (median ratings of 10 and 5, respectively; Table 2).

Association of Predictors of Interest With Benefit From Study Treatment Sessions

Study partners' ratings of the impact of the study treatment sessions on patients' quality of life showed considerable variability and—before adjustment for confounders—were significantly associated with patients' baseline quality of life, length of time in the study, assignment to the massage group, and assignment to a preferred treatment (Table 3).

However, several variables acted as confounders. First, patients who were assigned to their preferred treatment reported slightly higher symptom distress at baseline than did their counterparts. Adjustment for this confounder increased the OR for assignment to preferred treatment, revealing an even stronger benefit for treatment matching.

Three variables (baseline quality of life, prior use of CAM, and assignment to preferred treatment) confounded the association between massage and treatment benefit. The strongest of these was assignment to preferred treatment. Patients assigned to the massage group were significantly more likely than their counterparts to have been assigned to their preferred treatment (68.6% of the massage group, 29.4% of the meditation group, and 35.1% of the friendly visit group having given their top rating to the assigned group; $\chi^2 = 12.667$, $df = 2$, $P = .002$). Addition of the preferred treatment predictor to the regression model reduced the OR for massage to 2.037 and rendered it statistically nonsignificant ($P = .108$). Although massage offered some benefit to patients in this sample, over and above benefit derived from being assigned to their treatment of choice, the effect was not strong enough to be generalizable beyond the sample.

A multivariate model of patients' benefit from study treatment sessions retained 3 significant predictors of benefit from treatment (Table 4). Based on study partners' ratings, patients received significantly greater benefit if they were assigned to their preferred treatment, reported higher quality of life at the time of study enrollment, and participated longer in the study.

In addition to benefit gained by patients, study partners indicated that they, themselves, benefited more when their patient was assigned to their preferred treatment. The median ratings of treatment benefit to study partners of patients assigned to preferred versus nonpreferred treatments were 6 and 5, respectively (Mann-Whitney Z-approximation = -2.277, $P = .023$).

Discussion

Our analysis of study partners' perceptions of patient benefit from 3 treatments offered in a clinical trial suggests that therapeutic massage over an extended end-of-life period may offer enhanced benefit to terminally ill patients, when compared with either guided meditation/visualization or friendly visits. Of even greater potential benefit, however, is the matching of available treatments to those actively preferred and requested by patients. In fact, much of the apparent benefit of massage over the other 2 therapies resulted from patients' prior preference for massage. These findings were counter to results obtained in earlier analyses of patients' global quality of life and pain distress, rated by both patients and their study partners, which did not vary significantly by treatment assignment or treatment matching.[5] Our current analyses also showed evidence of benefit to patients' significant others when patients received their preferred treatment.

Table 1. Characteristics of Study Partners and Deceased Patients

	Study Partner[a]	Deceased Patient[b]
Female (%)	74.0	61.1
Racial-ethnic minority (%)	6.7	8.3
Median (range) age	54 (22-87)	74 (36-98)
Education		
High school or less (%)	9.7	21.3
Post high school without college degree (%)	26.0	36.1
Four-year college degree (%)	33.7	20.4
Post college education (%)	30.8	22.2
Respondent's relationship to patient		
Spouse/partner (%)	26.0	–
Child of patient (%)	36.5	–
Parent of patient (%)	1.9	–
Sibling (%)	5.8	–
Other relative (%)	6.7	–
Friend (%)	16.3	–
Professional caregiver (%)	6.7	–
Lived with patient (%)	46.2	–
Median (range) years of association	41 (<1-75)	–
Patient's primary diagnosis		
Cancer (%)	–	71.3
Cardiovascular disease (%)	–	13.9
Pulmonary disease (%)	–	5.6
Neurological disease (%)	–	5.6
Other conditions (%)	–	3.7
Used CAM in year before study enrollment (%)	–	31.5
Received hospice care (%)	–	90.7
Median (range) patient baseline quality of life[c]	–	7 (0-10)
Median (range) patient baseline symptom distress[d]	–	1.08 (0.05-2.58)
Median (range) days from patient baseline interview to death	–	106 (6-693)
Perceived effects of study treatment		
Median (range) effect on patient quality of life[e]	6 (0-8)	–
Median (range) effect on respondent's quality of life[e]	6 (0-7)	–
Treatment groups		
Assigned to massage (%)	–	34.3
Assigned to meditation (%)	–	31.5
Assigned to friendly visits (%)	–	34.3
Assigned to preferred treatment (%)	–	44.3
Median (range) rating of assigned treatment	–	8 (0-10)

Abbreviation: CAM, complementary and alternative medicine.

[a] Effects of study treatment based on 108 respondents. Other items based on baseline interviews of 104 respondents; the remaining 4 respondents were replacements for study partners who became unavailable between the baseline and follow-up interviews.

[b] Only 106 of the 108 patients whose study partners completed follow-up interviews provided ratings of the treatment arm to which they were ultimately assigned. Percentage assigned to preferred treatment arm and median rating of assigned treatment are based on baseline interviews with those 106 patients; all other patient statistics are based on 108 baseline interviews.

[c] Patient's single-item rating of overall quality of life at baseline interview: 0 = *no quality of life* to 10 = *almost perfect quality of life*.

[d] Composite measure based on 32-item short-form Memorial Symptom Assessment Scale at baseline: 0 = *no symptoms* to 4 = *high symptom distress*.

[e] Single-item rating at follow-up interview: 0 = *extremely negative effect* to 10 = *extremely positive effect*.

Other researchers studying palliative care have noted problems related to selection of outcome measures and have suggested the importance of developing and testing measures optimal for the specific research context, rather than relying exclusively on already existing standard measures.[9] The outcomes selected must be sensitive to potential effects of the intervention,[10,11] and measures of global quality of life and pain distress may be too broad to allow detection of effects by interventions of the type we studied. Moreover, such outcomes may be affected by disease-related factors and personal

Table 2. Patients' Preassignment Ratings of the Study Treatments

	Median (Range) Rating	*P*
Preassignment Rating of Potential Treatment Assignment		.000[a]
What if you were assigned to massage?	8 (2-10)	
What if you were assigned to meditation?	6 (0-10)	
What if you were assigned to friendly visits?	7 (0-10)	
Preassignment rating of actual treatment assignment		
Treatment group assigned		.001[b]
Massage	10 (4-10)	
Meditation	6 (0-10)	
Friendly visits	8 (2-10)	
Assigned to preferred treatment?		.000[c]
Yes	10 (5-10)	
No	5 (0-9)	

[a] Based on Friedman test applied to preassignment ratings by 104 patients who rated all 3 treatment types.
[b] Based on Kruskal-Wallis test applied to preassignment ratings of the treatment group to which they were ultimately assigned by 106 patients (2 patients assigned to the massage group had not rated that treatment type).
[c] Based on Mann-Whitney test applied to 106 patients.

Table 3. Unadjusted Associations between Predictors/Covariates and Patient Benefit from Study Treatment[a]

	n	Odds Ratio	*P*
Patient Characteristics			
Female	104	0.991	.980
Racial-ethnic minority	104	1.227	.764
Age	104	1.003	.798
Education	104	0.822	.253
Cancer diagnosis	104	1.140	.764
Prior CAM use	104	0.501	.059
Received hospice care	104	0.797	.704
Baseline quality of life[b]	104	1.233	.011
Baseline symptom distress[c]	104	0.584	.063
# Days in study[d]	104	1.003	.004
Respondent characteristics			
Female	100	0.605	.166
Racial-ethnic minority	100	1.536	.469
Age	99	1.001	.956
Education	100	0.924	.689
Relationship to patient	104		
Other relationship		1.000	–
Spouse/partner of patient		1.732	.189
Child/parent of patient		1.504	.338
Lived with patient	100	1.029	.934
Years of association	100	1.008	.381
Treatment assignment			
Friendly visit	104	1.000	–
Massage		2.617	.027
Meditation		1.066	.900
Assigned to preferred treatment[e]	102	3.736	.000

Abbreviation: CAM, complementary and alternative medicine.
[a] Benefit from treatment was based on surrogate's single-item rating at follow-up interview: 0 = *extremely negative effect* to 10 = *extremely positive effect*. Analyses were based on ordinal logistic regression models.
[b] Patient's single-item rating at baseline interview: 0 = *no quality of life* to 10 = *almost perfect quality of life*.
[c] Composite measure based on 32-item short-form Memorial Symptom Assessment Scale at baseline: 0 = *no symptoms* to 4 = *high symptom distress*.
[d] Elapsed time between baseline interview and death.
[e] Dichotomous measure: 0 = patient was assigned to a treatment condition to which she or he gave a lower rating (0-10) than at least 1 other treatment condition, 1 = patient was assigned to a treatment condition that received (or tied for) the patient's highest rating.

Table 4. Multivariate Model: Patient Benefit From Study Treatment[a]

	Odds Ratio	*P*
Assignment to preferred treatment group[b]	3.825	.001
Baseline quality-of-life rating[c]	1.183	.047
# Days of participation in study[d]	1.003	.018

[a] Based on 102 respondents with valid responses to all 3 predictors. Study benefit measured by the respondent's single-item rating at follow-up interview: 0 = *extremely negative effect* to 10 = *extremely positive effect*. Analyses were based on ordinal logistic regression models.
[b] Dichotomous measure: 0 = patient was assigned to a treatment condition to which she or he gave a lower rating (0-10) than at least 1 other treatment condition, 1 = patient was assigned to a treatment condition that received (or tied for) the patient's highest rating.
[c] Patient's rating at baseline interview of overall quality of life: 0 = *no quality of life* to 10 = *almost perfect quality of life*.
[d] Elapsed time between baseline interview and death.

circumstances, in addition to factors related to care.[12] Our patients evaluated global quality of life and pain distress at follow-up interviews, occurring at least 1 calendar day following treatment, with over 28% of the interviews occurring 3 or more days after treatment. Similarly, surrogate respondents rated the quality of patients' last week of life, a period that was sometimes substantially removed from their final treatment visit (about 15% of patients had their final treatment 3 weeks or more before death). These patient and study partner ratings were potentially influenced by numerous factors subsequent to intervention delivery.

The outcome we used for the current article—surrogate respondents' perceptions of the specific effects of the study treatment on quality of life—was a late addition to the study partner follow-up interview, and we failed to add a comparable question to interviews with patients during their study participation. The unsolicited comment from one of our clinical trial participants, presented as an epigraph to this article, suggests that patients might have welcomed such an addition. Although the growing emphasis on family-centered care underscores the importance of soliciting evaluations from patients' intimate associates, collecting this information directly from patients, as well, would have strengthened our investigation. Researchers considering clinical trial outcome measures have noted not only that omission of important outcomes may waste resources and produce misleading results that miss potential benefits of an intervention, but that investigators would do well to involve consumers (ie, the affected populations) in both clinical trial design and the selection of measures.[13] In the words of 1 health care researcher, "Clinical trials are only as credible as their endpoints."[14] Selection of credible endpoints remains a worthy goal for investigators.

Additionally, our finding that study partners' assessments of study benefit were significantly associated with patients' assignment to a preferred treatment has implications for design of intervention studies at end of life. Randomization of terminally ill patients to nonpreferred treatments, particularly if there is no opportunity for later receipt of a preferred treatment, presents an ethically questionable use of patients' limited time and energy. Almost 20 years ago, 2 British researchers recommended that studies randomize only those patients who have no treatment preference and assign all other participants to their treatment of choice—allowing tests of both treatment efficacy and participant motivation.[15] This recommendation has received little notice to date in the design of intervention evaluations and is nowhere more relevant than in end-of-life studies.

Limitations

Our study is based on a small number of participants from a single geographic area and may not reflect patterns that exist in more inclusive samples. Moreover, because the outcomes we investigated were perceptions of decedents' surrogates, rather than those of the patients who actually received the study treatments, findings may not match those that would have obtained had we questioned patients directly.

Conclusions

The explicit purpose of our clinical trial was to test whether either of the 2 nontraditional therapies—massage or guided meditation—might provide quality-of-life improvements sufficient to warrant their integration into standard end-of-life care. The outcomes on which we based our primary analysis—traditional measures of global quality of life and pain distress—clearly provided important information in the evaluation of treatment efficacy. However, more tightly focused questions regarding surrogates' perceptions of benefit from the interventions led to different conclusions, and these findings also merit consideration. Results of the present analyses suggest 3 lessons. First, targeted questions about treatment benefit are worth including in *patient* assessment

batteries used in future trials. Our failure to elicit this information directly from patients required that we infer benefit from 1 step removed. Inasmuch as patients' perceptions are the most germane to assessment of benefit, they will be essential for making informed decisions regarding potential changes in standard care protocols. Second, the strong and significant association between perceived benefit and patients' assignment to a preferred treatment underscores the importance of re-evaluating the appropriateness of randomized controlled trials for end-of-life research. Finally, making massage, as well as other coveted CAM therapies, available as regularly offered options to enrollees in hospice and palliative care programs may offer significant benefit, particularly if provided over an extended period. Determining the appropriate payment mechanisms for such services will require further research.

Acknowledgments

The National Institutes of Health / National Cancer Institute (grant #5R01-CA106204) and the Lotte & John Hecht Memorial Foundation provided funding for this study. The authors are grateful for the time, energy, and goodwill provided by the participating patients, their family and friends, and their hospice and palliative care providers.

References

1. Field MJ, Cassel CK, eds. *Approaching Death: Improving Care at the End of Life*. Committee on Care at the End of Life, Division of Health Care Services, Institute of Medicine. Washington, DC: National Academy Press; 1997.
2. Engelberg RA. Measuring the quality of dying and death: methodological considerations and recent findings. *Curr Opin Crit Care*. 2006;12:381-387.
3. Wilkie DJ, Kampbell J, Cutshall S, et al. Effects of massage on pain intensity, analgesics and quality of life in patients with cancer pain: a pilot study of a randomized clinical trial conducted within hospice care delivery. *Hospice J*. 2000;15:31-53.
4. Wilcock A, Manderson C, Weller R, et al. Does aromatherapy massage benefit patients with cancer attending a specialist palliative care day centre? *Palliat Med*. 2004;18:287-290.
5. Downey L, Diehr P, Standish LJ, et al. Might massage or guided meditation provide "means to a better end"? primary outcomes from an efficacy trial with patients at the end of life. Under review at *J Palliat Care*. 2009; 25(2). In press.
6. Chang VT, Hwang SS, Feuerman M, Kasimis BS, Thaler HT. The Memorial Symptom Assessment Scale Short Form (MSAS-SF). *Cancer*. 2000;89: 1162-1171.
7. SPSS, Inc. *SPSS for Windows, Release 14.0.0*. Chicago: SPSS Inc; 2005.
8. Muthén LK, Muthén BO. *Mplus User's Guide*. 4th ed. Los Angeles, CA: Muthén & Muthén; 1998-2006.
9. Mitchell GK, Abernethy AP. Investigators of the Queensland Case Conferences Trial; Palliative Care Trial. A comparison of methodologies from two longitudinal community-based randomized controlled trials of similar interventions in palliative care: what worked and what did not? *J Palliat Med*. 2005;8: 1226-1237.
10. McWhinney IR, Bass MJ, Donner A. Evaluation of a palliative care service: problems and pitfalls. *Br Med J*. 1994;309:1340-1342.
11. Grande GE, Todd CJ. Why are trials in palliative care so difficult? *Palliat Med*. 2000;14:69-74.
12. Rinck GC, van den Bos GAM, Kleijnen J, Haes HJCJM, Schadé E, Veenhof CHN. Methodologic issues in effectiveness research on palliative cancer care: a systematic review. *J Clin Oncol*. 1997;15:1697-1707.
13. Sinha I, Sinha I, Jones L, Smyth RL, Williamson PR. A systematic review of studies that aim to determine which outcomes to measure in clinical trials in children. *PLoS Med*. 2008; 5:e96.
14. Tugwell P, Boers M. OMERACT conference on outcome measures in rheumatoid arthritis clinical trials: introduction. *J Rheumatol*. 1993;20:528-530.
15. Brewin CR, Bradley C. Patient preferences and randomized clinical trials. *Br Med J*. 1989;299:313-315.