Effectiveness of Specialized Palliative Care: A Systematic Review

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There is increasing awareness of the suffering of patients with terminal illnesses, including pain, other physical symptoms, and psychosocial distress, which may arise many months before the patient’s death. Specialized palliative care services have proliferated worldwide, initially focusing on terminal cancer care, but increasingly expanding to include patients with cancer and other terminal diseases who are at earlier stages of their disease trajectory. The objective of such services is to improve the symptom control and quality of life of patients with terminal illnesses and to coordinate care of the patient and support for the family. With the increasing development of such services, it is important to determine their effectiveness compared with other models of care.

There have been previous reviews of the effectiveness of palliative care services, but only 2 of them, both published approximately a decade ago, used detailed quality criteria to assess the validity of randomized controlled trials (RCTs). Until recently, there have not been sufficient RCTs of specialized palliative care to assess studies with this method, and some previous reviews have included both retrospective and prospective studies. Systematic reviews of health care service interventions are more difficult to conduct than those of pharmacological interventions, due to greater heterogeneity of interventions and methods.

In preparing this systematic review, we followed the guidelines outlined by Grimshaw et al, based on the Cochrane Effective Practice and Organization of Care Group standards. The objective of our review was to examine systematically the evidence for specialized palliative care teams are increasingly providing care for the terminally ill. However, the impact of such teams on quality of life, satisfaction with care, and economic cost has not been examined systematically using detailed criteria for study quality.

Objective To systematically review the evidence for effectiveness of specialized palliative care.

Data Sources We performed a keyword search of the following databases from their inception to January 2008: MEDLINE, Ovid Healthstar, CINAHL, EMBASE, and the Cochrane Central Register of Controlled Trials.

Study Selection We included all randomized controlled trials in which specialized palliative care was the intervention and for which outcomes included quality of life, satisfaction with care, or economic cost.

Data Extraction Data on population, intervention, outcome, methods, and methodological quality were extracted by 2 investigators using standardized criteria.

Results Of 396 reports of randomized controlled trials, 22 met our inclusion criteria. There was most consistent evidence for effectiveness of specialized palliative care in improvement of family satisfaction with care (7 of 10 studies favored the intervention). Only 4 of 13 studies assessing quality of life and 1 of 14 assessing symptoms showed a significant benefit of the intervention; however, most studies lacked statistical power to report conclusive results, and quality-of-life measures were not specific for terminally ill patients. There was evidence of significant cost savings of specialized palliative care in only 1 of the 7 studies that assessed this outcome. Methodological limitations were identified in all trials, including contamination of the control group, failure to account for clustering in cluster randomization studies, and substantial problems with recruitment, attrition, and adherence.

Conclusions The evidence for benefit from specialized palliative care is sparse and limited by methodological shortcomings. Carefully planned trials, using a standardized palliative care intervention and measures constructed specifically for this population, are needed.
effectiveness of specialized palliative care in improving quality of life, satisfaction with care, and economic cost.

**METHODS**

**Search Strategy**

Studies were recovered from the following databases from their inception to January 2008: MEDLINE, Ovid Healthstar, CINAHL, EMBASE, and the Cochrane Central Register of Controlled Trials. The keyword groupings used were palliative, terminal, or hospice and quality of life, quality of care, satisfaction, well being, economic, or cost; the search was limited to RCTs. We also hand searched the references of the retrieved articles for further relevant trials.

**Box. Quality Criteria**

**Participants**

Reported
1. Clear description of inclusion and exclusion criteria
   
   Adequate
2. Comprehensive strategy for identification of potential cases
3. Patient recruitment rate >70%12
4. Evaluation of nonparticipants to judge generalizability

**Objectives and Outcome Measures**

Reported
5. Specific objectives and hypotheses
6. Clearly defined primary and secondary outcome measure(s)
   
   Adequate
7. Use of validated outcome measures
8. Blinding to group assignment of those assessing outcome measures

**Baseline Measurement and Homogeneity**

Reported
9. Baseline demographics and clinical characteristics of each group prior to intervention
10. Baseline outcome measures of each group prior to the intervention
   
   Adequate
11. No significant differences present across study groups

**Randomization and Concealment of Allocation**

Reported
12. Study design and method of randomization, including details of any restriction (eg, blocking, stratification, matching)
   
   Adequate
13. Method to generate the randomization sequence explicitly described and adequate
14a. Unit of allocation was by institution, team, or professional, and the number of clusters was adequate (cluster randomization only)
14b. Unit of allocation was by patient and a centralized randomization scheme was implemented by calling a central number, an on-site computer system, or sealed opaque envelopes (individual randomization only)

**Sample Size and Attrition**

Reported
15. How sample size was determined and, when applicable, explanation of interim analyses
16. Flow of participants through each stage
   
   Adequate
17. Intended sample size attained at baseline and based on an adequate sample size calculation
18. Outcome measures obtained for 90% to 100% of participants ("yes") or 70% to 89% ("partial") randomized (stated explicitly)

**Intervention, Control, and Protection Against Contamination**

Reported
19. Precise details of the intervention and how and when it was administered
20. Precise details of the control (contrast between intervention and control clearly defined)
   
   Adequate
21. It is unlikely that control patients received the study intervention or a similar intervention
22. It is documented that intervention patients actually received the intervention

**Analyses**

Reported
23. Statistical methods used to compare groups for primary and secondary outcomes and for subgroup analyses, if relevant
24. For each primary and secondary outcome, a summary of results for each group and estimated effect size and precision (eg, P value or 95% confidence interval)
   
   Adequate
25. Analysis by "intention to treat" (analysis is performed on groups initially produced by the randomization process) and, in cluster trials, accounting for between-cluster variation

*Each of the 25 items is scored 4 (complete marks), 2 (partial marks), or 0.

**Selection Criteria**

We selected reports of RCTs evaluating intervention of a specialized palliative care service, with at least 1 of the outcomes of quality of life, satisfaction with care, or economic cost. A specialized palliative care service was defined as a service of professionals that provides or coordinates comprehensive care for patients with a terminal illness. Stud-
ies evaluating the impact of only 1 component of comprehensive palliative care on only 1 aspect of quality of life (eg, impact of pain medication on pain; impact of medication or psychotherapy on depression) were excluded.

Evaluation of Studies
Two reviewers (C.Z. and R.R.) independently extracted data from selected studies using a standardized data abstraction form, which was based on the form developed by the Effective Practice and Organization of Care Group. Any differences in opinion were resolved by discussion. Information was extracted on setting; study population; type of intervention and control; end points and outcome measures; methods; results; and study quality. Studies for which there were multiple publications were rated only once, using all information available from the respective publications.

The validity of the selected publications was determined using 25 quality criteria, grouped into 7 categories (Box). These were developed after a comprehensive review of existing criteria and were based on 2 checklists used to rate the quality of reporting of RCTs in general, a checklist used to rate the quality of trials that use interventions to improve professional practice or health service delivery, and 2 checklists designed to rate the quality of trials assessing the effectiveness of palliative care. Three items were modified, added, or both so that they could apply to cluster RCTs. These items included allowing for clustering in the sample-size calculation, including an adequate number of clusters, and accounting for clustering in the analysis. Separate points were assigned for the quality of the methods used and for the quality of reporting them. The criteria were piloted on 5 randomly selected publications and detailed scoring criteria were developed.

Study quality was assessed independently by 2 reviewers (C.Z. and G.R.); discrepancies were resolved by discussion and, if necessary, consensus with a third reviewer (I.T.). Recruitment rate for each study was calculated by dividing the number of patients who completed baseline measures by the number eligible. Loss to follow-up was calculated separately for quality of life and satisfaction outcomes and for economic and health services outcomes, by dividing the number of patients for whom outcome measures were available by the number of patients for whom baseline values were recorded.

We analyzed the studies separately for outcomes of quality of life, patient and family satisfaction with care, and economic cost. The studies were too heterogeneous to permit statistical pooling; therefore, we performed a qualitative synthesis of the studies, taking into account study power and methodological quality in the analysis and reporting of our results.

RESULTS
Study Selection
Our initial search identified 697 individual articles, of which 396 were reports of RCTs (FIGURE). Of these, 128 evaluated chemotherapy or hormonal agents; 81 evaluated cancer-directed procedures or radiation therapy; 64 evaluated pain and symptom medications; 24 evaluated cardiac medications or procedures; 22 evaluated medications or medical procedures for illnesses other than heart disease or cancer; 21 evaluated complementary therapies (eg, massage, hypnosis, spiritual healing, reflexology, aromatherapy); and 27 evaluated health care services interventions (eg, prompt lists, audio-taped interviews, advance directives, interactive computer programs). Twenty-nine articles reported on 23 individual RCTs evaluating specialized palliative care. One was excluded because it was available only in Chinese and another because it included only 9 patients and did not include quantitative data. An additional study was identified by hand searching references of the 27 other articles. Of the 22 individual trials, 13 were not included in any previous reviews, and 1 had previously been reviewed only by its author.

Study Characteristics
The 22 studies spanned the years 1984-2007 and had a median sample size of 60, with a median sample size of 100. The median duration of the intervention was 6 months, and the median duration of follow-up was 6 months. The median number of eligible patients was 100, and the median number of included patients was 25. The median number of deaths was 100, and the median number of observed outcomes was 25. The median number of patients included in the analysis was 25, and the median number of observed outcomes in the analysis was 100. The median number of patients lost to follow-up was 25, and the median number of observed outcomes lost to follow-up was 100.

Figure. Flow Diagram of Study Selection Process
size of 204 (range, 69-4804; Table 1). Three studies were identified from 1980-1989, 6 from 1990-1999, and 13 from 2000-2007. All but 6 studies were based in the United States; 4 were conducted in the United Kingdom,36,37,41,46 and 1 each in Norway38 and Canada.44 Although most studies were individually randomized, 4 used cluster randomization,35,38,43,46 with the number of clusters in each group ranging from 1 to more than 70.46 Eleven trials were conducted in a home setting,28,30,32,39,41,44-46,61 5 at outpatient clinics,30,33,35,36,42 1 each in a nursing home39 and in a combined inpatient and home setting,31 and 4 assessed inpatients.37,40,43,49 Eleven studies included almost exclusively patients with cancer8; 8 assessed patients with cancer as well as other diagnoses, including congestive heart failure(CHF), chronic obstructive pulmonary disease (COPD), motor neuron disease, and AIDS.39,39,31,33,35,39,41,43,48,59 Two studied a geriatric population,34,60 and 1 included only patients with CHF or COPD.32 In 12 studies, the intervention consisted of a multidisciplinary team (= 3 health care disciplines); 4 studies assessed a nursing intervention28,36,43,59; 1 assessed an intervention by a physician and nurse team,40 and 2 studies assessed counseling interventions: one delivered by a social worker42 and the other by a trained facilitator.35 The remaining 3 studies assessed care coordinating services, in 2 of which the coordinator was a nurse or social worker.31,46 The third evaluated a service that assessed patients’ eligibility for hospice and initiated referral as appropriate.39

**Quality of Life**

Patient quality of life was an outcome in 13 trials and was a specified primary outcome in 4 of them10,16-18 (Table 1). Four studies assessed caregiver quality of life.10,39,42,52 Several instruments were used to assess quality of life: the Multidimensional Quality of Life Scale-Cancer Version52; the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30, used in 3 studies65; the Medical Outcomes Study Short Form (SF-36 or SF-20), used in 3 studies64; the Functional Living Index-Cancer65; the Sickness Impact Profile66; the General Health Rating Index67; the Hospice Quality of Life Index68; the Spitzer Quality of Life Index and Uniscale, each used in 1 study69; and the Caregiver Quality of Life Index-Cancer.70 Only 1 of the studies used a quality-of-life measure that was specific for a palliative care population,69 and 1 study used a cancer-specific measure even though 70% of the patients had advanced COPD or advanced CHF.35

All but 4 of the 13 studies30,32,36,39 reported no significant differences in patient quality of life between randomized groups, and 1 study favored the control.47 However, all except 1 of the studies30 lacked power to detect differences in quality of life, either due to inadequate initial sample size or to high levels of loss to follow-up. Only 3 studies were specifically powered to detect meaningful differences in quality of life,30,36,38 but 1 of them did not adjust the target sample size for cluster randomization,38 and 2 did not adjust for the 70% and 56% loss to follow-up, respectively.36,38 In one of the latter studies missing quality-of-life scores were assigned imputed values,38 but interpretation is difficult with such a large proportion of missing data.

Two studies assessing home palliative care programs using the SF-36 questionnaire reported significant differences in patient quality of life in favor of palliative care. One study found significant differences in 6 of 8 domains using analyses of covariance. The treatment effect coefficients follow: emotional role function, 12.7 (P < .001); social function, 0.6 (P = .03); bodily pain, 2.4 (P = .02); mental health, 3.0 (P = .008); vitality, 1.8 (P = .05); and general health, 0.9 (P = .03).30 The other study reported significant results in only 2 of 8 domains using the difference in the average slope to compare the intervention group with the control group over time: physical functioning, 0.18 vs -1.39 for patients with CHF and 1.00 vs -0.95 for patients with COPD, P < .05; and general health, 0.16 vs -0.17 and 0.54 vs -1.67, P < .05, respectively.32

In a study of nurse-led follow-up of patients with lung cancer using the EORTC QLQ-C30, emotional functioning improved in the intervention group vs the control at 12 months (median score, 91.7 vs 66.7; P = .03); however, 70% of the patients were lost to follow-up.50 This study also measured dyspnea as part of the EORTC QLQ-C30 Lung Module and found a significant benefit for those in the intervention group at 3 months (median, 25.0 vs 33.3; P = .03). A study of a 3-week structured multidisciplinary intervention for radiation therapy outpatients, which assessed patient quality of life using a single-item linear analog scale, found a significantly better score in the intervention group at 4 weeks (mean, 72.8 vs 64.1; P = .047) but not at 8 or 27 weeks.50 Caregiver quality of life was also measured in this study but results were not significant. Two additional studies assessed caregiver quality of life using interventions designed specifically for caregivers.62,64 One of these used random-effects regression models to measure differences in the Caregiver Quality of Life Index-Cancer between groups and found a significant benefit of the intervention at 30 days or 2 weeks after intervention (group × time interaction: estimate 0.096, P = .04)72; however, the attrition at that time was 63%, resulting in possible retention bias.

Fourteen studies specifically assessed symptoms, some using an overall symptom distress or severity measure,28,30,32,46,47,61 and others using scales for symptoms such as pain,28,33,43,44,47,58 nausea,44 constipation,28 dyspnea,28,35 sleep,35 anxiety,33,35,42,46,71 and depression or morale.30,33,35,42,45,48,73 Only 1 trial demonstrated benefit from the palliative care intervention for any of the individual symptoms measured. This trial assessed effectiveness of an outpatient...
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<th>Studya</th>
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<th>No. of Patients</th>
<th>Intervention</th>
<th>Control</th>
<th>End Points</th>
<th>P Value</th>
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<tr>
<td>McMillan et al,28,52 2007</td>
<td>Hospice: advanced cancer</td>
<td>111 Caregiver coping; 109 Nursing visits</td>
<td>109 Usual hospice homecare</td>
<td>Caregiver QOL&lt;sup&gt;b&lt;/sup&gt; Symptom distress Pain, dyspnea, constipation, and patient QOL</td>
<td>.03 at 30 d .009 (caregiver coping) All NS</td>
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<td>Brumley et al,29 2007</td>
<td>2 HMOs: CHF, COPD, or cancer</td>
<td>≤1 y</td>
<td>155 Interdisciplinary home care</td>
<td>115 Usual Medicare care</td>
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<td>&lt;.05 at 30 and 90 d; &lt;.02 &lt;.001</td>
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<tr>
<td>Rummans et al,30,53 2006</td>
<td>Radiation therapy: advanced cancer</td>
<td>49 Multidisciplinary</td>
<td>54 Usual radiation oncologist care</td>
<td>Patient QOL&lt;sup&gt;c&lt;/sup&gt; Caregiver QOL Symptoms, mood, spiritual well-being</td>
<td>.047 at 4 wk &lt;.05 for 4 of 12 assessments All NS</td>
<td></td>
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<td>Engelhardt et al,31 2006</td>
<td>VA hospitals, 2 HMO: advanced CHF, COPD, or cancer</td>
<td>133 Coordinated care</td>
<td>142 Usual care</td>
<td>Patient satisfaction Advance directive Treatment planning attitude and cost</td>
<td>&lt;.03 .006 (completed ≥1) Both NS</td>
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<td>Miller et al,33 2005</td>
<td>Internal medicine Oncology outpatients</td>
<td>&gt;6 mo</td>
<td>37 Group education/support</td>
<td>32 Mailed self-help materials</td>
<td>Depression, anxiety, spiritual well-being, and death-related distress</td>
<td>All NS</td>
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<td>Casarett et al,34 2005</td>
<td>3 Nursing homes</td>
<td>107 Interviewed and faxed hospice authorization request</td>
<td>98 Interviewed and hospice description</td>
<td>Hospice referral&lt;sup&gt;c&lt;/sup&gt; Caregiver quality of care&lt;sup&gt;c&lt;/sup&gt; Acute care admissions and days in acute care</td>
<td>&lt;.001 .04 (n = 17)</td>
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<td>Rabow et al,35 2004</td>
<td>Outpatient: Cancer, COPD, or CHF</td>
<td>1-5 y</td>
<td>50 Palliative care team</td>
<td>40 Usual care</td>
<td>Patient pain, dyspnea, sleep, depression, anxiety, QOL spiritual well-being, satisfaction, and advance care planning, and satisfaction</td>
<td>.01 Dyspnea .03 Anxiety .007 Spiritual well-being NS all the rest</td>
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<td>Hughes et al,36 2000</td>
<td>16 VA Hospital: Terminal, severe disability, or homebound CHF or COPD</td>
<td>981 home-based primary care team</td>
<td>985 Usual care, Medicare homecare, and hospice</td>
<td>Patient and caregiver QOL</td>
<td>.05 for 6 of 8 SF-36 subscales (terminal patients and caregivers) Patients: NS, Caregiver: &lt;.005, 5 of 6 subscales (terminal subgroup) .006 Higher for intervention at 12 mo</td>
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<td>Ahronheim et al,40 2000</td>
<td>Teaching hospital: dementia</td>
<td>&lt;6 mo</td>
<td>48 Palliative care physician/ nurse</td>
<td>51 Usual care</td>
<td>Admissions, length of stay, procedures, interventions, and care plans</td>
<td>.03 Intravenous hydration .008 for palliative care plan NS for the rest</td>
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<td>Toseland et al,42 1995</td>
<td>Cancer center: ECOG 0 or 4 excluded</td>
<td>38 Caregiver counseling</td>
<td>40 Usual care</td>
<td>Patient and caregiver depression, caregiver anxiety and QOL</td>
<td>All NS</td>
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<td>SUPPORT,43,54,55 1998</td>
<td>5 Teaching hospitals: life-threatening diagnoses</td>
<td>2652 Nurse led</td>
<td>2152 Usual hospital care</td>
<td>Caregiver satisfaction Timing of DNR order, patient-physician CPR choice, days in aggressive treatment, pain, and hospital resource use&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.04 (for discharged patients who died) All NS</td>
<td></td>
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<tr>
<td>Study</td>
<td>Population</td>
<td>Prognosis</td>
<td>Intervention</td>
<td>Control</td>
<td>End Points</td>
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<td>Hughes et al,45,56 1992</td>
<td>VA hospital: 89% cancer</td>
<td>&lt;6 mo</td>
<td>86 VA hospital-based home care</td>
<td>85 Usual Medicare home or hospice care</td>
<td>Patient and caregiver satisfaction Cost&lt;sup&gt;b&lt;/sup&gt; Health service use, cognitive functioning, morale</td>
<td>≤.02 Patients and caregivers at 1 mo, NS patients and caregivers at 6 mo NS for the rest</td>
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<tr>
<td>McCorkle et al,47 1989c</td>
<td>20 Health Care Centers: 166 &gt;stage 2 lung cancer, homebound</td>
<td>Oncology home care; Standard home care</td>
<td>Office care</td>
<td>Pain, symptom distress, distress, mood, and health services use</td>
<td>.03 Symptom distress, NS for the rest</td>
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<td>Zimmer et al,48 1984</td>
<td>Urban community: Seriously ill homebound</td>
<td>82 Home care team</td>
<td>76 Usual care</td>
<td>Health service use satisfaction Health and morale</td>
<td>Less out-of-home services but more ED use (P not reported) &lt;.001 caregiver, NS patients at 3 and 6 mo NS</td>
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<tr>
<td>Kane et al,49,57,58 1984</td>
<td>VA hospital inpatients</td>
<td>2 wk-6 mo</td>
<td>137 Hospice homecare team and inpatient unit</td>
<td>110 Usual care</td>
<td>Pain, symptoms, activity, anxiety, depression, hospital d, cost Patient and caregiver satisfaction</td>
<td>All NS</td>
</tr>
<tr>
<td>Moore et al,36 2002</td>
<td>Lung cancer outpatients</td>
<td>&gt;3 mo</td>
<td>100 Nurse-led follow up</td>
<td>103 Usual medical outpatient care</td>
<td>Patient QOL at 3 mo&lt;sup&gt;b&lt;/sup&gt; Patient satisfaction&lt;sup&gt;b&lt;/sup&gt; Health services use, death at home Overall cost</td>
<td>.03 Dyspnea at 3 mo; NS other QOL subscales &lt;.01 at 3 mo &lt;.05 Medical consultations, radiographs, death at home NS</td>
</tr>
<tr>
<td>Hanks et al,37 2002</td>
<td>Teaching hospital: inpatients, 90% cancer</td>
<td>&gt;24 h</td>
<td>175 Palliative care physician and nurse</td>
<td>88 Telephone consultation</td>
<td>Symptom control, QOL, length of stay, readmission&lt;sup&gt;b&lt;/sup&gt; Patient and caregiver satisfaction, and hospital resource use</td>
<td>All NS</td>
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<td>Grande et al,41,59 1999</td>
<td>Urban: cancer, motor neuron disease, or AIDS</td>
<td>&lt;2 wk</td>
<td>186 Hospital at home</td>
<td>43 Standard hospital, hospice, or home care</td>
<td>Place of death&lt;sup&gt;b&lt;/sup&gt; Support, symptoms, time at home, physician home visits</td>
<td>All NS</td>
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<tr>
<td>Addington-Hall et al,46 1992</td>
<td>Urban: cancer</td>
<td>&lt;1 y</td>
<td>153 Nurse coordinators</td>
<td>128 Usual care</td>
<td>Symptoms, satisfaction, distress, social support, patient QOL</td>
<td>All NS</td>
</tr>
<tr>
<td>Jochay et al,38,80,81 2001</td>
<td>8 Health care districts: cancer</td>
<td>2-9 mo</td>
<td>235 Multidisciplinary palliative care team</td>
<td>199 Usual care by home care team</td>
<td>Death at home&lt;sup&gt;b&lt;/sup&gt; Patient QOL&lt;sup&gt;b&lt;/sup&gt; Caregiver satisfaction</td>
<td>.02 NS at 4 mo &lt;.01</td>
</tr>
<tr>
<td>McWhinney et al,44 1994</td>
<td>Urban: 146 Metastatic cancer patients</td>
<td>&gt;2 mo</td>
<td>Palliative care team</td>
<td>4wk waiting list</td>
<td>Pain and nausea&lt;sup&gt;b&lt;/sup&gt; Patient QOL, caregiver health</td>
<td>All NS, 1 mo</td>
</tr>
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</table>

Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CPR, cardio-pulmonary resuscitation; DNR, do not resuscitate; ECOG, Eastern Cooperative Oncology Group; Ed, emergency department; EORTC, European Organisation for Research and Treatment of Cancer; HADS, Hospital Anxiety and Depression Scale; HMO, health maintenance organization; NCI, National Cancer Institute; NS, not statistically significant; QOL, quality of life; VA, Veterans Affairs.<br><br>The year represents the article from which the majority of data were abstracted.<br><br>The number of patients in each group was not reported.<br><br>The number of patients in each group was not reported.

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palliative care consultation service for patients with cancer, COPD, and CHF using analyses of covariance with 9 outcome measures, including those for dyspnea, pain, sleep, anxiety, and depression. There was an improvement in the intervention group compared with controls only for the frequency that dyspnea limits activities (group × time interaction, \( F=6.83, P=.01 \)) with borderline results for anxiety (\( F=4.09, P=.05 \)). This study had methodological deficiencies including failure to define a primary measure, use of cluster randomization with only 2 clusters, and imbalance of men and women in the comparator groups.

In 3 studies, results favored the intervention for symptom distress but not for symptom severity. One study of patients with lung cancer assessed symptom distress, health perceptions, mood, and pain. Although the office care group (control group) experienced elevated mean Symptom Distress Scores 6 weeks earlier than what the combined oncology home care and standard home care groups experienced (\( F=5.01, P=.03 \)), health perceptions improved paradoxically in the control group over time and declined in the combined intervention groups (\( F=4.06, P=.05 \)). The second study measured symptom control using items from the Memorial Symptom Assessment Scale to assess the effectiveness of a home palliative care team for patients with CHF and COPD. At 3 months, patients with COPD who were receiving the interdisciplinary team intervention had lower symptom distress scores (mean score, 3.4 vs 4.29, \( P<.05 \)) and tended to have lower scores at 6 months (mean score, 2.85 vs 3.80, \( P<.07 \)). However, patients with CHF had equivalent or higher scores in the intervention and control groups at both time points (mean score, 3.72 vs 3.32; \( P=NS \) at 3 months; 4.03 vs 3.30; \( P<.05 \) at 6 months). A third study assessed the effect on patients of a coping intervention for their caregivers. Symptom severity and quality of life did not improve, but symptom distress significantly decreased over time in the intervention group compared with the control (hospice care) group (random-effects regression model, group × time interaction, \(-0.101; P=.009\)).

### Satisfaction With Care

Patients’ satisfaction with care was assessed in 10 studies, which were conducted in home, hospital, and outpatient settings in the United States and in the United Kingdom (Table 1). Four studies showed significantly increased satisfaction in the intervention groups compared with the control groups. One study—the first RCT to examine the effectiveness of hospice care in the United States—used repeated-measures analyses with 5 cohorts of patients defined according to the minimum numbers of interviews completed (3-7 interviews over 18 weeks); there was statistically significant increased satisfaction with interpersonal care (adapted Ware scale) in the intervention group for all cohorts. Two studies using ad hoc measures found increased satisfaction with care at 3 months in the intervention group compared with the control.

A study of interdisciplinary home-based health care for homebound patients showed increased satisfaction in the intervention group at 30 days (odds ratio [OR], 3.37; 95% confidence interval [CI], 1.42-8.10; \( P=.006 \)) and 90 days (OR, 3.37; 95% CI, 0.65-4.96; \( P=.03 \)), but not at 60 days (OR, 1.79; 95% CI, 0.65-4.96; \( P=.26 \)). However, baseline measures were not balanced, with significantly higher satisfaction with care at baseline for the intervention group (measured after results of randomization were disclosed). In all of the remaining studies, the results were not statistically significant. However, all of these studies were affected by substantial loss to follow-up and diminished statistical power.

Assessments of caregiver satisfaction showed a statistically significant benefit for caregivers in the intervention group in 7 of the 10 studies but not in 3 studies. Three of 5 studies that evaluated caregiver satisfaction longitudinally during the course of the study reported greater satisfaction among those in the intervention group. One study that assessed satisfaction both longitudinally and after death did not show significant differences.

### Economic Cost and Use of Health Care Services

Economic cost was measured in only 7 studies, whereas all except 6 of the 22 studies evaluated use of health care services (Table 1). Outcome measures for use (or avoidance) of health care services included the number of emergency visits, number and/or length of hospitalizations, use of hospital resources, advance care planning, referral to hospice, death at home, and time spent at home.

All but 1 of the studies directly measuring cost of care were based in the United States. The single study conducted in the United Kingdom found no significant differences in overall costs of care for nurse-led follow-up compared with standard medical follow-up for patients with lung cancer (median cost per patient at 12 months, $696.50 vs $744.50; \( P=.66 \)). The only US study with significant findings for cost was a recent trial of in-home palliative care set in 2 health maintenance organizations in 2 states. Overall costs were significantly lower for intervention patients than for patients in the usual care group (average cost per day, $95.30 vs $212.80; \( P=.02 \)) even after adjusting for the significantly shorter survival of the intervention group (196 days vs 242 days). Two other studies, one assessing Veterans Affairs (VA) hospital–based home care services, used repeated-measures analyses with 5 cohorts of patients defined according to the minimum numbers of interviews completed (3-7 interviews over 18 weeks); there was statistically significant increased satisfaction with interpersonal care (adapted Ware scale) in the intervention group for all cohorts. Two studies using ad hoc measures found increased satisfaction with care at 3 months in the intervention group compared with the control.

A study of interdisciplinary home-based health care for homebound patients showed increased satisfaction in the intervention group at 30 days (odds ratio [OR], 3.37; 95% confidence interval [CI], 1.42-8.10; \( P=.006 \)) and 90 days (OR, 3.37; 95% CI, 0.65-4.96; \( P=.03 \)), but not at 60 days (OR, 1.79; 95% CI, 0.65-4.96; \( P=.26 \)). However, baseline measures were not balanced, with significantly higher satisfaction with care at baseline for the intervention group (measured after results of randomization were disclosed). In all of the remaining studies, the results were not statistically significant. However, all of these studies were affected by substantial loss to follow-up and diminished statistical power.

Assessments of caregiver satisfaction showed a statistically significant benefit for caregivers in the intervention group in 7 of the 10 studies but not in 3 studies. Three of 5 studies that evaluated caregiver satisfaction longitudinally during the course of the study reported greater satisfaction among those in the intervention group. One study that assessed satisfaction both longitudinally and after death did not show significant differences.

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care and the other a home health care team, found that total hospital costs were greater in the control group while total home care costs were greater for the intervention group. In both of these studies, as in a more recent study assessing economic outcomes for patients at 3 VA medical centers, overall per capita costs were lower in the intervention group, but the results did not reach statistical significance.

Contradictory results were found in an early study of VA hospice care, which measured only the cost of hospital inpatient days and therapeutic procedures. Even though this study excluded the cost of home care, average expenditures for the intervention group were at least as high as those for the control group ($15,263 vs $15,493, if it is assumed that the cost of a hospice day is equivalent with that of a day in an intermediate care ward, or $17,770 vs $15,493, if a hospice day is equivalent to a day in a general medical ward). Another study assessing the effectiveness of VA team–managed home-based primary care found that total costs were 12.1% higher in the intervention group than in the usual VA care group at 12 months (mean, $31,401 vs $28,008; P = .005).

Only 1 of the studies assessing utilization of health care services found consistently significant differences in favor of the intervention group. In this study, 205 nursing home residents were randomly assigned to receive (or not) a structured interview identifying those who were hospice-eligible, followed by a request to the resident's physician for authorization of an informational visit to a hospice. Those in the intervention group had higher hospice enrollment (25% vs 6%; P < .001), fewer acute care admissions (mean, 0.28 vs 0.49; P = .04), and spent fewer days in an acute care setting (mean, 1.2 vs 3.0; P = .03). Another study reported reduced length of stay in an acute care center for the intervention group (mean inpatient days, 9.94 vs 15.86; P = .03).

Of 9 other studies measuring number of hospital admissions, only 1 had significant results favoring the intervention group (36% vs 59% patients hospitalized, P = .001). Results for number of emergency visits were mixed. A study assessing a home care team found patients in the intervention group had mean utilization per patient per month for days at risk in first 6 months of 0.26 emergency department visits vs 0.05 in the control group (P < .05). A second study found fewer emergency room visits in the intervention group (difference of 35%, P = .02). Two other studies reported no significant differences between the randomized groups.

Five studies assessed death at home, which was the primary outcome for 2 of these. Three studies reported that more patients in the intervention group died at home than patients in the control group (United States, 71% vs 51%; P < .001, United Kingdom, 40% vs 23%; P = .04, Norway, 25% vs 15%; P < .05). The Norwegian study also measured time spent at home, which was not significantly increased. A US study of VA hospice care found no significant difference in death at home between the intervention (3%) and control groups (7%). In a UK study assessing effectiveness of “hospital at home,” 58% of control patients died at home vs 67% in the intervention group. This difference was not significant, but the study was underpowered, and 39% of the patients randomized to “hospital at home” were not admitted to the service, resulting in dilution of any effects in the intention-to-treat analyses.

Assessment of Quality of Studies

The RCTs were of variable quality, with 11 (50%) scoring 60 points or more out of 100. All 11 were published since 1994, and the 8 studies scoring 70 or higher were published since 2000. The greatest difficulties were with recruitment, attrition, and documentation regarding generation and implementation of the randomization sequence. Further details are given below (Table 2).

Patients and Recruitment. Many studies relied on referrals, rather than systematic screening potentially eligible cases. The median recruitment rate was 60% (range, 18%-94%; n = 17 studies). For 5 studies the recruitment rate was impossible to determine because the number of eligible patients was not given.

Only 4 studies evaluated nonparticipants to judge generalizability of their findings or compared the baseline demographics of their patients to published statistics for the general population that they were investigating. In one study, the recruited patients were younger than the general population of lung cancer patients; in another, participants were less likely to have Medicaid (24% vs 55%) or a “do not resuscitate” order (37% vs 53%); yet another showed that nonrandomized patients were less well and had a shorter survival time. Thus, there was a tendency to exclude patients who might benefit most from a palliative care intervention.

Objectives, Outcomes, and Homogeneity. Validated outcome measures were used in almost all of the studies, but there was a tendency to assign the research staff that interviewed patients in only 9 studies. In 2 of these specified more than 3 primary outcomes.

Randomization, Sample Size, and Attrition. The method to generate the randomization sequence was adequately described in only 8 of 18 individually randomized studies and the method to implement it in only 7 studies. In 2 of 4 cluster randomization studies, the number of clusters was not adequate (6 and 2 total clusters, respectively). Of the 11 studies referenced, 3 were published since 2000.
ies using individual randomization, only 5 described a formal sample size calculation,\textsuperscript{34,37,41,44,49} and of these only 3 attained their intended sample size.\textsuperscript{34,37,49} Although all 4 cluster randomization trials reported such a calculation, there was no mention of the intracluster correlation coefficient or cluster size in 3 of them.\textsuperscript{35,43,46} The remaining cluster randomization study acknowledged that cluster size and within-cluster correlation should be accounted for, but nevertheless based the planned sample size on practical and economical considerations.\textsuperscript{38}

Loss to follow-up was much greater for outcomes of quality of life and satisfaction (median, 40%; range, 3%-92%; n = 20 studies) than for economic outcomes and use of health care services (median, 14%; range, 0%-53%; n = 16 studies). This was to be expected, given the possibility of objective assessment of the latter outcomes compared with the former, which need to be completed by the patient or caregiver.

**Contamination and Analyses.** In many individually randomized trials, there was the potential for contamination in the control group because the same group of physicians cared for both intervention and control patients,\textsuperscript{30,33,34,36,40} because care similar to the intervention could be obtained elsewhere,\textsuperscript{29,32,39,45,47,59} or because of explicit crossover from control to intervention group.\textsuperscript{31,37,44} Of the 4 cluster randomization studies, 2 studies included control and intervention clusters at the same hospital,\textsuperscript{35,43} and in 1 study, some control groups were transferred to the intervention group during the course of the trial.\textsuperscript{46} Most studies used intention-to-treat analyses, but between-cluster variation was accounted for in the analysis of only 1 of the 4 cluster randomization studies.\textsuperscript{38}

**COMMENT**

There is scant evidence to support the effectiveness of specialized palliative care for patients with terminal illnesses in terms of quality of life, patient and caregiver satisfaction, or economic cost. Of these outcomes, there is consistent evidence only for better caregiver satisfaction. However, the evidence base is sparse, and we were unable to use formal meta-analytic pooling methods due to the heterogeneity of the studies, interventions, and outcomes. Given the number of statistical comparisons described in our review, some of the results that are of borderline significance might have occurred by chance. Furthermore, the studies have been hindered by methodologi-

### Table 2. Quality Scores of Trials Assessing the Effectiveness of Specialized Palliative Care Services Study\textsuperscript{a}

<table>
<thead>
<tr>
<th>Study\textsuperscript{b}</th>
<th>Participants/Generalizability (16)</th>
<th>Objectives/Outcomes (16)</th>
<th>Measures/Homogeneity (12)</th>
<th>Randomization (12)</th>
<th>Sample size/Attrition (16)</th>
<th>Intervention/Contamination (16)</th>
<th>Analyses (12)</th>
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Abbreviation: NA, not available.
\textsuperscript{a}Each of the 25 items is scored 4 (complete marks), 2 (partial marks), or 0 for a maximum of 100 points.
\textsuperscript{b}The year represents the article from which the majority of data were analyzed.
cal challenges, which limit the quality of the evidence and the conclusions that can be drawn.

An appropriate sample-size calculation was not performed for many studies, resulting in studies that were underpowered. Such a calculation should take into account attrition, lack of completion of questionnaires, potential limited penetration of the intervention, and contamination of the control group in individually randomized studies or intracluster correlation if cluster randomization is used. In many studies patients were randomized after referral to a palliative care service. This recruitment method engenders difficulties with attrition and compliance in a frail population with a typical prognosis of 2 months or less.75,76 Moreover, once patients are referred to palliative care, it is generally expected that they will be seen immediately. This perceived lack of equipoise may cause contamination or concomitant therapy due to transfer from the control to the intervention group or to a similar service. Conversely, there may be patients who are not referred who could also benefit from palliative care. Future studies should use eligibility criteria of prognosis and performance status and identify potential participants using active screening by research personnel.77

Several studies used cluster randomization to avoid contamination of controls. However, such trials require particular care in their design and analysis in order to produce valid results. None of the cluster RCTs reviewed accounted for clustering in the sample-size calculation, resulting in underestimation of the sample size, loss of power, and type 2 error.19 Three of 4 cluster RCTs failed to account for clustering in the analyses. Although this may cause type 1 error, the results for these trials were not statistically significant. Such errors in the design of cluster randomized studies are common and have led to the construction of amended CONSORT guidelines for their reporting.22

Only half of the studies identified a primary outcome measure; this can lead to invalid conclusions because of multiple significance testing. Quality of life was frequently selected as an outcome measure for the evaluation of effectiveness of palliative care, which is appropriate given its emphasis in the mission statements of national and international palliative care organizations.82-84 However, the existing validated and widely used quality-of-life measures were not developed for terminally ill patients.85,82,83 For such individuals, there should probably be greater emphasis on existential and spiritual concerns, effective communication, and planning and preparing for the end of life.84-86 Although quality-of-life questionnaires have been developed for terminally ill patients,87-89 their responsiveness to change and minimal clinically important difference are as yet unknown and further research is needed.11,90 Specific measures that evaluate symptoms have been recommended as alternate outcome measures to multidimensional quality-of-life scales.90 However, the outcomes should be chosen to reflect the care that is given by the intervention and the assessment of specific symptoms may not reflect the broad mandate of specialized palliative care services for increasing quality of life for patients with terminal illnesses.

Satisfaction of patients and caregivers is an important indicator of quality of care.91-93 However, assessment of satisfaction with care can be problematic, in view of the ceiling effect of generally high satisfaction ratings, the subjective variability in defining satisfactory care, and the possibility of satisfaction with care that is suboptimal according to established standards.93,94 We found that caregiver satisfaction was the one outcome showing consistent improvement in the studies that we reviewed. At baseline, caregivers tend to rate care less favorably than patients, which may reflect a difference in aspects of care considered to be important or a reluctance of patients to criticize their care providers.94,95 Hence, there may be greater opportunity for improvement of caregiver scores, with less tendency for a ceiling effect. It may also be preferable to measure satisfaction in an ongoing manner throughout the study, as after-death interviews may be subject to recall bias92 and grieving families may be difficult to contact.

The perceived high costs of care at the end of life in developed countries have led to a desire to increase the efficiency and cost-effectiveness of end-of-life care.96 Six of 7 RCTs directly measuring cost were conducted in the United States and showed that hospital costs generally decreased, while home care and hospice costs increased, when patients were referred to a palliative care program. Although there was minimal evidence to demonstrate an overall cost savings of palliative care programs, the studies did not define or quantify cost-effectiveness. Moreover, traditional cost analyses measured in quality-adjusted life-years may not be appropriate for programs providing end-of-life care, given the short duration of care provided and the considerable societal and personal value placed on its quality.97 In addition, the studies did not assess the large personal costs that may be incurred by patients and their family members, including expenses for medications, transportation, homemaking, personal care, and lost income.98 Caregivers can also experience substantial physical and psychological morbidity or even mortality as a consequence of caregiver burden.99,100 With its emphasis on holistic care, specialized palliative care has the potential to lessen such costs for the patient and family, and consideration should be given to measuring such outcomes in future RCTs.

Although access to specialized palliative care programs has expanded rapidly throughout the developed world, the rigorous evaluation of such programs is challenging and is a recent phenomenon. The existing studies do not provide conclusive evidence, and carefully planned trials, using a standardized palliative care intervention and measures constructed specifically for this population, are needed.
Assessment of specific treatments given in palliative care, such as opioids or nonsteroids for pain control, or psychotherapy for depression, were outside the scope of this study, but have recently been reviewed.101 Recent pilot studies evaluating early palliative care for patients with terminal cancer are encouraging.102,103 Further research is necessary to substantiate these findings for patients with other illnesses and in larger randomized trials.

Author Contributions: Dr Zimmermann had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Zimmermann, Riechelmann, Krzyzanowska, Rodin, Tannock. Acquisition of data: Zimmermann, Riechelmann, Rodin. Analysis and interpretation of data: Zimmermann, Riechelmann, Krzyzanowska, Rodin, Tannock. Drafting of the manuscript: Zimmermann. Critical revision of the manuscript for important intellectual content: Zimmermann, Riechelmann, Krzyzanowska, Rodin, Tannock. Statistical analysis: Zimmermann. Obtained funding: Zimmermann. Administrative, technical, or material support: Riechelmann. Study supervision: Zimmermann, Rodin, Tannock.

Financial Disclosures: None reported.

Funding/Support: This review was made possible through grant 017257 from the National Cancer Institute of Canada, with funds from the Canadian Cancer Society (Dr Zimmermann).

Role of the Sponsor: The funding agency had no role in the design or conduct of the study; the collection, analysis or interpretation of the data, or the preparation, review, or approval of the manuscript.

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1708 JAMA, April 9, 2008—Vol 299, No. 14 (Reprinted) ©2008 American Medical Association. All rights reserved.