

Chapter 3. Results

After a description of the results of the literature search, this chapter first takes up the evidence regarding satisfaction with end-of-life care and the association of satisfaction with other outcomes (Task Order Question 1a). We then address and assess the measures available for the important domains of patient and family experience (Task Order Question 1b). For each of the elements that shape the end-of-life experience and that our work targeted, the ensuing sections take up the topic and address Task Order Questions 2 and 3 around each topic area. Thus, sequential sections of this chapter address symptoms (pain, dyspnea, depression and anxiety, and behavioral symptoms associated with dementia), family caregiver issues, continuity, and advance care planning. Each one generally starts with a summary of the existing systematic reviews, then reviews the interventions that have been studied, and finally reviews the highest-quality observational research. In the sections at the end of Chapter 3, we summarize and synthesize the evidence related to the association of patient, family, and health system factors with those outcomes (2a, 2b, and 2c) and the effectiveness of interventions and population factors related to variation in intervention effectiveness (3a, 3b), so that an overview of the findings related to the questions as asked is readily available.

Results of the Literature Search

The literature search performed by NLM resulted in 16,310 titles. The supplemental library search performed by RAND staff identified an additional 3,748 titles. Library searches performed by NLM focusing on specific clinical conditions of cancer, heart failure, and dementia added 1,187 new titles. In total, the RAND reviewers examined 21,245 titles identified through literature searches, of which 5,563 were considered possibly relevant to our topic areas and continued to abstract review. Out of the 2,493 references used in development of the National Consensus Project clinical practice guideline, our literature searches and title review process had not identified 675. These references were added to the library of abstracts and proceeded on to abstract review. The literature search of the DARE abstracts identified 92 titles, of which 62 were considered potentially relevant to our topic areas and proceeded to abstract review. Another 71 articles were added to the library of abstracts from the NICE guideline, the Health Canada reports, the Toolkit of Measures for End of Life Care, and the files of our content experts. An additional 22 articles were suggested by the TEP and peer reviewers, of which 10 were considered potentially relevant and proceeded to abstract review.

Of the 6,381 titles identified as possibly relevant to our topics, the reviewers screened the abstracts for 5,216 titles; 13 titles were identified as duplicates already abstract screened, and 1,152 titles did not have abstracts to screen. Of the 5,216 abstracts screened, 3040 were excluded for reasons listed as “population, intervention, or outcome exclusion” on the abstract screener: 761 were excluded as not about end-of-life care and outcomes; 26 were excluded as predominately about sudden/violent/ non-chronic death; 148 were excluded as predominately about chemotherapy/surgery/stents/ laser/radiation; 963 were excluded because no outcomes were reported; 620 were excluded because the outcomes were unrelated to patients/families/nonprofessional caregivers; 370 were excluded as primarily useful as background only; 97 were excluded as predominately reporting on prognosis or trajectories; and 55 were excluded because the data were older than 1990. Ten abstracts were excluded because the population discussed was not adults. Thirty-two abstracts were excluded as non-Western in

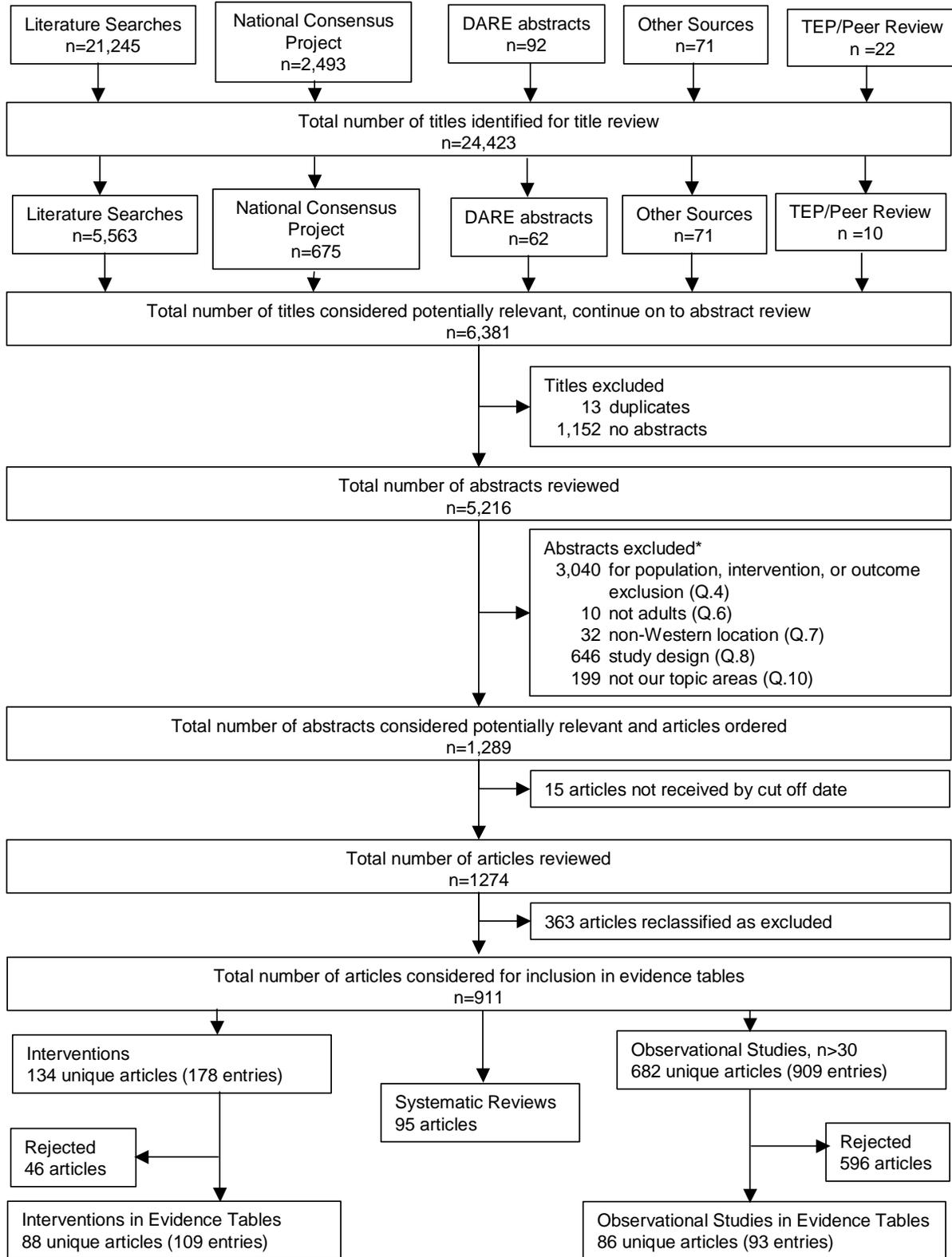
location. Six hundred forty-six studies were excluded due to study design: 239 were qualitative studies; 52 were nonsystematic reviews; 20 were other types of reviews; 138 were observational studies of less than 30 subjects; and 197 had unclear study designs. One hundred ninety-nine abstracts were excluded for topic: 56 as bereavement only; 35 as symptoms other than those included in our scope; 80 as topics other than those included in our scope; and 28 as unclear topic. The remaining 1,289 articles were determined to be potentially relevant to our topic and were ordered.

Of the 1,289 articles ordered, we retrieved 1,274 prior to the cut off date (Sept. 3, 2004). On detailed review of the articles, 363 studies were reclassified as excluded. The remaining articles comprised 134 interventions, 95 systematic reviews, and 682 observational studies of sample larger than 30. These 911 articles were distributed by topic and study design as presented in Table 2. As one article can report on multiple topics the numbers in Table 2 do not add to 911. Figure 1 presents this information pictorially.

Table 2. Study design by Topic Area

Topic Area	Systematic Review	Intervention	Observational
Satisfaction	22	49	203
Measures	10	4	142
Family and caregiver concerns	18	23	134
Advanced care planning	14	25	243
Continuity and coordination of care	15	37	82
Symptoms	55	55	269

Figure 1. Article Flow



* Abstract screener question relating to exclusion reason is in parentheses

A. Key Question 1a. What individual outcome measures are most strongly associated with overall satisfaction with end-of-life care?

Systematic Reviews and Satisfaction with End-of-Life Care

One particularly salient aspect of evaluation of end-of-life care is whether the patients and families are satisfied with care—in other words, how they subjectively perceive the care provided. We included in this literature the range of articles we identified that subjectively rated either global satisfaction or more specific elements of the care provided to patients or in support of caregivers living with serious and eventually fatal illness.

We evaluated ten systematic reviews that potentially dealt with the subject of patient or caregiver satisfaction. Six addressed the project questions and met implicit quality criteria. One of the reviews focused specifically on a cancer population, and the other five did not limit their reviews to one disease cohort. We went beyond the systematic reviews by including other intervention studies addressing the outcome of patient or caregiver satisfaction published after these systematic reviews or published at any time if not already addressed in a systematic review. In total, we reviewed an additional 12 intervention studies. Finally, we explored the observational literature that used a prospective cohort design and that also presented data separately by race, selected disease cohorts, or selected sites of care. In addition, we identified observational studies that addressed the relationship between satisfaction and other outcomes. In total, we reviewed 17 observational studies.

The remainder of this section summarizes the systematic reviews, meta-analyses, intervention, and observational studies relevant to patient and caregiver satisfaction. We also evaluated the qualitative literature in this area to try to better interpret the strength of the literature and meaning of patient satisfaction with end-of-life care. The relationship of satisfaction to other measures is summarized at the end of this section. Summaries of the association of patient, family, and health system factors to satisfaction and the effectiveness of interventions in improving satisfaction are found at the conclusion of Chapter 3.

Table 3. Systematic Reviews for Patient and Family Satisfaction with End-of-Life Care

Study	Relevance	Date Search Concluded	Date of Publication
Wilkinson, 1999 ⁸²	Patient and informal caregiver satisfaction with palliative care	1998	1999
Higginson, 2001 ⁷⁴	Effect of palliative care teams on overall patient and caregiver outcomes including satisfaction	1999	2001
Higginson, 2004 ⁷²	Effect of wide variety of interventions for palliative needs in advanced cancer— including interventions which evaluated satisfaction as an outcome	2003	2004

Wilkinson et al. conducted an extensive search of the English and non-English literature covering the years 1978–1998 including hand searches of major palliative care journals,

reference mining of major citations, consultation with palliative care experts, and a search for gray literature. This review identified 831 documents, of which 688 were retrieved and analyzed. They found 83 papers relevant to patient and caregiver satisfaction with palliative care and were able to retrieve 79 of them. This review described five reports with a randomized controlled design and related to palliative care and satisfaction in the UK and North American literature.

These five reports were from four RCTs and included a study of an inpatient hospice for veterans that found a positive effect on patient and caregiver satisfaction, a study of case management for terminally ill cancer patients in a London health district that had no effect on satisfaction, a study of home-based primary care that included non-terminal and terminally ill veterans (all of whom had advanced illness), and a study of multidisciplinary home care including 24-hour telephone availability for homebound chronically or terminally ill persons. The two RCTs describing home-based services both demonstrated effects on patient and caregiver satisfaction, and these are described below in the Higginson review from 2001, as is the study of inpatient hospice for veterans.

Many of the studies described by Wilkinson et al. related to comparative, often retrospective or cross-sectional assessments of specific inpatient or outpatient supportive services for patients near the end of life. The review described research reports that were heterogeneous in their comparisons and methods, although they generally described hospital care unfavorably compared with alternatives that included a variety of home care and hospice models. The nature of the research designs and heterogeneity of service models did not suggest the superiority of one form of palliative care delivery over another. This review highlighted a number of important methodological issues in end-of-life research in satisfaction including

- lack of *a priori* definitions of satisfaction
- ceiling effects of specific items or measures of satisfaction
- lack of well-validated measures for assessing satisfaction with end-of-life care
- the difficulty of assessing association between respondent reports of satisfaction in non-randomized designs because of large observed differences in samples
- unresolved methodological issues in end-of-life care satisfaction assessment including timing of patient assessment due to frail health states, use of proxies, and questions related to retrospective assessment.

In addition, this review identified a large descriptive study that found differences between cancer and dementia patients' caregivers satisfaction related to differential satisfaction with information and the physical attributes of the hospital environment.

Higginson et al. undertook a systematic review and meta-analysis of the effectiveness of palliative care teams in 2001, which examined satisfaction⁷⁴ as one of the outcomes. Using a robust search strategy to identify studies of palliative care services and their effects on patients, caregivers, and economic outcomes, the review searched ten databases from 1977 to 1999. The review identified 25 experimental and observational studies with outcomes that could be synthesized. Five studies included satisfaction as a measure and the pooled weighted mean was 0.24 (–0.04–0.52) favoring the intervention. Although not analyzed separately as an outcome, satisfaction was combined with pain, other symptoms, quality of life, referral to other services, and therapeutic interventions. This aggregate variable demonstrated a small effect (weighted

mean 0.32 [0.15–0.49]), excluding one outlier) of palliative care services on overall outcomes, although sample sizes of the studies were very small.

Among these studies, one study evaluated the effect of an inpatient hospice on veterans and their caregivers and reported a positive effect of a multidisciplinary team on both patient and caregiver satisfaction, associated with improved ratings of interpersonal care. Several interventional studies described outcomes of home-based services with generally positive effects on satisfaction. One Australian RCT of home-based hospice care compared with regular home care reported greater dissatisfaction among non-hospice patients. The only other difference noted was higher pain duration among non-hospice patients. An RCT of home-based primary care for veterans reported significant improvements in health-related quality of life (HRQOL) among terminal patients but no significant improvement in satisfaction (the effect was positive and moderately large, but not statistically significant). In the larger group of nonterminal but very ill patients who were homebound with CHF and COPD, HRQOL did not improve, but satisfaction showed roughly the same difference between those with and without home-based primary care as was in evidence for “terminal” patients, though the differences were not statistically significant at the $p < 0.05$ level. Caregivers in both groups receiving home-based primary care experienced improvements in HRQOL and satisfaction. A quasi-experimental study of home-based hospice found improvements in pain processes and overall symptoms in hospice but high satisfaction in both hospice and conventional care groups. An RCT of home-based multidisciplinary care for patients with terminal and advanced chronic illness reduced hospitalization, nursing home admission, and outpatient visits and increased home death. In addition, home-based care was associated with greater patient and caregiver satisfaction.

Gysels and Higginson’s systematic review of supportive and palliative care for adults with cancer⁷² identified studies published up to 2003 and was organized around a wide variety of supportive interventions in oncology including coordination of care, patient activation, communication, information provision, psychological support, social support, spiritual support, palliative care services, rehabilitation, complementary therapies, and family/caregiver support. Of 5263 studies reviewed and 443 potentially eligible studies accepted after abstract review, 40 papers describing heterogeneous interventions that measured satisfaction as an outcome were accepted into the review. Of these 40 papers, seventeen RCTs examined effects of an intervention on the satisfaction of either patients or caregivers. This systematic review did not report summary conclusions of the evidence.

Gysels and Higginson’s review described randomized controlled trials in the area of care coordination, advance care planning, and information provision to patients. Several of the RCTs identified by this review were described in the context of previous reviews. Among those that were not, one improved the coordination of end-of-life care by using a Patient Care Traveling Record (PCTR). It did not report an effect on satisfaction, but dropout due to patient frailty was quite extensive. Another RCT of a patient held record (PHR) reported no improvement in satisfaction with information—although perception of communication was relatively high in this sample, which included both oncology outpatients and patients who were already enrolled in a home hospice service. An RCT that involved randomizing patients followed by hospital-based specialists to early follow-up that included their primary care physician, and the intervention group reported higher satisfaction. A small CCT ($n=24$) implemented a “coaching” intervention intended to improve patient interaction in oncology consultations, and it did not result in higher satisfaction, although it did achieve improved patient perception of decision quality and MD-

patient agreement. In an intervention that involved a patient-nurse meeting for counseling and education of newly diagnosed cancer patients, both improved information and satisfaction with the consultation were reported by patients and their spouses. A similar RCT that simply involved an informational pamphlet without the personal involvement did not affect either information or satisfaction.

Additional Interventional Studies and Satisfaction with End-of-Life Care

Our review identified a number of additional interventional trials in palliative care that included as an outcome a measure of patient or caregiver satisfaction with care. Several of these addressed comprehensive or coordinated services for chronically ill patients. The following text summarizes these studies, first the studies of comprehensive or coordinated services and then the studies of communication or advance care planning. Within each section, we first discuss RCTs and then articles with other study designs.

Grande et al. conducted a randomized controlled trial of a hospital-at-home service in the UK for the terminally ill.⁸³ This intervention provided in-home nursing support up to 24 hours daily for up to two weeks, predominantly used for terminal care during the final weeks of life. Referrals came from general practitioners and one-third from inpatient discharges. All patients were eligible to receive other care concurrently, including a variety of home services and hospice. Of the 262 referrals, 43 were randomized to control (C) and 186 to intervention (I). The majority of intervention and control patients had cancer. The study incorporated questionnaires that assessed general assessment of care and symptom management. Informal caregivers noted no difference in any supportive services, caregiver support, or symptoms with the exception of pain, which the control group rated as a relatively unmet need (3.00 vs. 2.52). The Jadad score for this study was 3.

Ringdal et al. conducted a cluster randomized trial which involved six Norwegian health districts randomized to an intervention that included a community education and close integration of hospital-based palliative care with local provider activities.⁸⁴ Within health districts designated for intervention, adult cancer patients with a life expectancy between two and nine months were eligible. Researchers measured caregiver satisfaction using the 20-item FAMCARE scale, which was developed specifically to measure satisfaction with advanced cancer care. A large proportion of caregivers refused to participate in completing surveys (114 / 426). Of those who completed the study, caregiver satisfaction scores favored the intervention with regard to specific items related to pain management, communication with the family about prognosis, treatments, and involvement of caregivers. Ringdal et al. examined the association of overall satisfaction with caregiver gender, age, education, relationship to the deceased; gender, age, and cancer type of the deceased; and place of death. Satisfaction was higher among spouses than children, higher if the deceased individual was a man, and higher among family of patients who died at home. In a fully adjusted model, in addition to the main intervention effect, only relationship to the deceased was significantly related to overall satisfaction. Spouses scored on average 12.5 points higher on the 0–100 FAMCARE scale than children. The Jadad score for this study was 2.

Hanks et al. conducted a randomized controlled trial of the effectiveness of a UK hospital Palliative Care Team on symptoms, quality of life, and patient, caregiver, and provider satisfaction.⁸⁵ All non-emergent inpatient referrals of persons who were not immediately likely

to die were randomized to either physician-to-physician telephone consultation or in-person interdisciplinary palliative care team consultation. Satisfaction was evaluated with four items from MacAdam's Assessment of Suffering Questionnaire. Caregiver satisfaction was assessed using FAMCARE, Hospital Anxiety and Depression Scale (HADS), and additional items about hospital communication. A more detailed interview was also conducted with caregivers of all discharged patients. The satisfaction of community physicians and nurses of all discharged patients was assessed related to the appropriateness of care and support arrangements and communication with the hospital. Component and overall measures of satisfaction were high in both groups (3.5–3.6 / 4 where 4 is “very satisfied” on all patient measures; 1.9–2.5 / 5 where 1 is “very satisfied” on all caregiver measures) and did not differ at either time point. The Jadad score for this study was 2.

Rabow et al. conducted a controlled trial of an interdisciplinary team that targeted physical, emotional, and spiritual care for 90 patients in two university outpatient general medicine clinics randomly assigned as intervention or control clinics.⁸⁶ Patients with cancer, advanced COPD, or CHF with a life expectancy of 1–5 years were eligible. The intervention improved dyspnea and sleep quality but not pain. Intervention patients reported higher spiritual well-being overall and in religious activities, and completed more advance directives. However, satisfaction as measured by 25 items (0–100 scale) from the Group Health Association of America Consumer Satisfaction Survey (satisfaction with care, attitude toward care) was high in both groups at baseline (satisfaction 73.7–I, 77.0–C; attitude 13.4–I, 14.0–C) and did not change. The Jadad score for this study was 3.

Brumley et al. conducted a pre-post test at Kaiser Permanente of a palliative care program and compared patients enrolled in that program (n=210) to a group of somewhat comparable patients (n=348) concurrently referred for home care.⁸⁷ The Reid-Gundlach Satisfaction with Services 13-item instrument (0–48) measures overall ratings, perceptions of providers, and likelihood of recommendation. This analysis reported the change score in patient satisfaction 60 days after baseline in a subset of the original participants who died during the course of the study and completed the interviews (I =161 C = 139). At baseline, both groups reported a mean satisfaction of 40/48 and at follow-up satisfaction improved in both groups. Satisfaction did not differ significantly at either time.

Weisbord et al. conducted a pre-post uncontrolled study of a palliative care consultation in 39 poor prognosis hemodialysis patients.⁸⁸ Nineteen of them evaluated the program, both before and then again two weeks after their consultation and a follow-up visit. Nine (47%) patients “strongly agreed” and four (21%) “somewhat agreed” that the meetings were useful. A similar proportion of patients also agreed that follow-up by the palliative care team would be useful. This intervention also assessed nephrologist satisfaction for 14 patients, and they also “strongly agreed” or “agreed” that the consultation was useful for symptoms. Nephrologists agreed that palliative care consultation had provided useful information to 11 of the patients. Nephrologists asked palliative care providers to follow 12 of their patients at the conclusion of the study.

In other studies, Riegel et al. examined satisfaction with care as an outcome of a case management program using a standardized protocol and software support program for CHF.⁸⁹ In this randomized controlled trial, telephone case management was provided to hospitalized patients with moderate to advanced heart failure (57% of sample were NYHA Class III and 15% Class IV at time of entry/hospitalization). The case manager also coordinated information with the patient's physician. Over the six-month trial, intervention patients received an average of 17

calls. Satisfaction with treatment, convenience, patient education, medication schedule, and MD care was evaluated. Of 358 patients randomized, survey data were obtained on 242, and only 184/242 patients completed a satisfaction survey. The difference demonstrated slightly higher overall satisfaction among the intervention group (22.88–I, 21.66–C), and both groups reported high satisfaction. The Jadad score for this study was 3.

We identified three RCTs that assessed satisfaction as part of a communication or advance care planning intervention. Bruera et al. studied 60 patients with cancer who were randomized to standard care (which included a written summary) or to receive a multidisciplinary outpatient cancer consultation with audiotaped recording to take home.⁹⁰ Patients returned for follow-up on day 8 and responded then to questions about global satisfaction with the clinic's care, understanding and recall of the original consultation, and ability to discuss their illness with family and friends. Intervention patients compared to controls (31–I, 29–C) reported higher "usefulness" of the clinic (8.7/10 vs. 7.7/10, $p = 0.04$), but did not describe a significant difference in their perceived understanding and recall of recommendations, or in their perceived ability to discuss their illness with family and friends. The Jadad score for this study was 5.

Schneiderman et al. assessed perceptions using a structured interview as the outcome of a randomized controlled trial of an intensive care unit (ICU) communication intervention by an ethics team.⁹¹ The trial enrolled patients in whom treatment conflicts were imminent or already present (considering conflicts within or between the healthcare team and/or family). The study randomized 546 patients (276 – I, 270 – C) and conducted interviews with 108 intervention surrogates and 272 professional providers involved in 152 patients' care. Both surrogates and providers rated the consultation highly on a number of general attributes (helpful, informative, supportive, fair, respectful of values) and in facilitating specific processes (identifying, analyzing, resolving, educating, and presenting views). Both groups rated the consultation as moderately stressful. The Jadad score for this study was 3.

Molloy et al. conducted a trial of advance care planning in nursing homes using an educational program for staff, residents, and families combined with a validated advance care planning tool (Let Me Decide) that offered choices for life-threatening illness, cardiac arrest, and nutrition.⁹² Three pairs of randomly selected nursing homes were matched for hospitalization and case-mix, and site of death. This multifaceted intervention succeeded in increasing advance directive completion rates from 57% in control homes to 70% in the intervention homes, where most care plans used the more flexible Let Me Decide directive. Satisfaction was measured using two previously validated 23- and 29-item measures that assess satisfaction with involvement in care.⁹³ Pre-post satisfaction (1–7) was 4.77 and 5.07 in the intervention and 5.09 and 5.10 in controls, and adjusted mean difference (–0.16, 95% CI, –0.41–0.10) was not significant. The Jadad score for this study was 1.

Bookbinder et al. conducted an uncontrolled pre-post study of a continuous quality improvement (CQI) intervention to reduce pain.⁹⁴ The intervention consisted of intensive staff education and problem-solving targeted specifically at improving pain documentation, nursing pain knowledge, and patient satisfaction. Six hundred ninety-six patients who experienced pain during hospitalization were interviewed (398 pre-intervention and 298 post-intervention) about their overall satisfaction as well as satisfaction with their nurse and physician care. Patients reported a high level of satisfaction in both periods: 71% after intervention, contrasted with 61% before intervention, reported satisfaction with nursing care; 67% after vs. 63% before reported satisfaction with MD care; and 62% after vs. 54% before reported overall satisfaction.

Satisfaction correlated with longest time to wait for medication ($r=0.335$), extent of pain relief ($r=-0.304$), and time to change medication ($r=0.457$).

Pietersma et al., in a study in which patients served as their own controls, evaluated patient satisfaction with a food cart on a palliative care service compared with standard food service (e.g., food trays). During a ten-day cart trial, 27 patients consented and participated, and patients were generally more satisfied with the food cart, which allowed them to choose their own items and portion sizes.⁹⁵

Observational Studies Evaluating Satisfaction in Palliative Care

Of studies that examined racial/ethnic differences, several looked at white/nonwhite differences⁹⁶⁻⁹⁸ and two studies included African-American and Hispanics as separate categories.^{27, 99} The majority of this literature did not examine racial differences at all—many probably because they were small studies or performed in settings in which there were insufficient numbers of minorities. Of studies that examined racial/ethnic differences, some did not describe any differences,^{96, 97} although in several studies race/ethnicity was considered an exploratory variable⁹⁸ or control that was not presented in available published comparisons.²⁷ One study that did report racial differences noted that African-Americans (OR 3.3) and other non-whites (OR 2.5) compared with Whites were more likely to agree with the importance of using all available treatments no matter what the chance of recovery.⁹⁹

We identified a number of observational studies that addressed end-of-life care within particular settings. A number of studies have addressed end-of-life care for hospitalized adults,^{27, 96, 98, 100} or more specifically end-of-life care in the ICU.^{97, 101} We also identified studies describing satisfaction in home care^{102, 103} or hospice/palliative care services.¹⁰⁴⁻¹⁰⁶ Other studies have assessed end-of-life care in general and in doing so, compared satisfaction with care across settings typically including home/hospice, hospital, and nursing homes.^{27, 107-112} These comparative studies highlight important differences with hospice users or caregivers of patients who died at home generally reporting higher satisfaction with many attributes of care^{27, 107, 108, 110} than those who died or were cared for in other settings at the end of life.

With regard to disease, we found little evidence that satisfaction differs by disease.^{96, 98, 99, 104} At the same time, few studies have examined specific diseases or employed measures that are disease-specific.^{100, 113} To the extent that a particular disease is well represented by the literature, the experience of cancer patients and their caregivers is best characterized because many of the studies have either focused on cancer or have been conducted in palliative care settings where cancer predominates.

Several studies have evaluated satisfaction with aspects of end-of-life care in the context of large or particularly notable cohort studies. Teno et al.²⁷ evaluated the U.S. dying experience through interviews with surviving family members representing 1,578 decedents from the mortality follow-back survey regarding patient and family centered end-of-life care. Sixty-seven percent of decedents died in an institutional setting while 33% died at home. Of those dying at home, 38% did not receive nursing services, 13% used home nursing services, and 49% had home hospice services. About 25% of all patients with pain or dyspnea at the end of life did not receive adequate treatment and one-quarter reported concerns with physician communication. More than one-third of respondents cared for by a home health agency, nursing home, or hospital reported insufficient emotional support for the patient and/or one or more concerns with family emotional support, compared with about one-fifth of those receiving home hospice services.

Nursing home residents were less likely than those cared for in a hospital or by home hospice services always to have been treated with respect at the end of life (68% vs. 77% and 96% respectively). Family members of patients receiving hospice services were more satisfied with overall quality of care: 71% rated care as “excellent” compared with less than 50% of those dying in an institutional setting or with home health services. These data suggest that those dying in institutions have unmet needs for symptom management, physician communication, emotional support, and being treated with respect. Family members of decedents who died with home hospice services were more likely to report a favorable dying experience.

Tilden et al. (2004)¹¹⁴ examined the end-of-life experiences of elderly decedents dying out of the hospital in Oregon through a telephone survey of 1,189 family caregivers of decedents aged 65 and older who died of natural causes in community settings between 2000 and 2002. Outcome variables included advance directives, hospice enrollment, use of life-sustaining treatments, perceived decedent symptom distress, financial hardship, out-of-pocket costs, and family caregiver strain. Results showed that most decedents had an advance directive (78.3%) and were enrolled in hospice (62.4%). Although perceived decedent symptom distress was low overall, certain symptoms (e.g., pain, dyspnea, constipation) were distressing for approximately half of decedents experiencing them. Financial hardship, out-of-pocket expenses, and caregiver strain were frequently reported. American Indian race and younger age were associated with decedent symptom distress. Greater perceived decedent symptom distress, hospice enrollment, more caregiver involvement, and more financial burden were associated with greater caregiver strain. Thus, despite high rates of advance directives and hospice enrollment, perceived symptom distress was high for a subset of decedents, and caregiver strain was common.

Steinhauser et al.⁹⁹ conducted a cross-sectional, stratified random national survey of 340 seriously ill patients, 332 recently bereaved family members, 361 physicians, and 429 other healthcare providers (nurses, social workers, chaplains, and hospice volunteers) to determine the factors considered important at the end of life. Twenty-six items consistently were rated as being important by greater than 70% of respondents, including pain and symptom management, preparation for death, achieving a sense of completion, decisions about treatment preferences, and being treated as a “whole person.” Results also highlighted differences among the respondent groups. Eight items received strong endorsement from patients but less from physicians ($p < .001$), including being mentally aware, having funeral arrangements planned, not being a burden, helping others, and coming to peace with God. Ten items had broad variation within as well as among the four groups, including decisions about life-sustaining treatments, dying at home, and talking about the meaning of death. Participants ranked freedom from pain most important and dying at home least important among nine major attributes. The findings from this study suggest that quality end-of-life care is a dynamic process that is negotiated and renegotiated among patients, family and healthcare professionals, a process moderated by individual values, knowledge, and preferences for care.

Fisher et al. conducted a retrospective cohort study using Medicare data including the Medicare Current Beneficiary Study (MCBS) to measure satisfaction.¹¹⁵ They constructed retrospective cohorts of patients hospitalized with hip fracture, colorectal cancer, and acute myocardial infarction. As the main regressor of interest, they considered the End of Life Expenditure Index (EOL-EI) to evaluate whether higher resource utilization at the end of life was associated with beneficial patient outcomes. This study found no association between higher

expenditures for end-of-life care in these chronically ill Medicare beneficiaries and satisfaction as determined by 20 items from the MCBS.

Qualitative Studies Evaluating Satisfaction with Palliative Care

We identified 32 qualitative studies that specifically reported satisfaction related to care of the patient at the end of life.^{23, 24, 116-145} All of these studies reported the importance of health care in relationship to aspects of quality of life, quality of the dying experience, or satisfaction with care. The majority (20/31) examined the experience of patients, but 11/31 examined the experience of caregivers, and 6/31 examined perceptions of end-of-life care from the providers' perspective. Even among studies that incorporated multiple viewpoints, few explicitly compared patient, caregiver, and professional providers' perspectives.¹³³ Most qualitative analyses employed either focus groups or unstructured interviews. With regard to settings, the most frequently studied settings was at home, whether in formal home care or not. We noted relatively few studies that incorporated participants or examined the end-of-life experience in nursing homes.^{24, 119} or that were relevant to satisfaction with end-of-life care in ICUs,¹²³ although this may be related to our initial exclusion criteria (e.g., excluding cases of sudden, traumatic death). Most studies did not focus on specific diseases, and the majority of studies with a disease-specific focus examined aspects of cancer care rather than patients with other conditions.^{24, 125, 133, 137, 139, 146}

One study that compared CHF with cancer¹²⁵ noted important differences in the experience of medical care between these conditions. This study suggested the particular importance of information provision in CHF because patients are not ordinarily "expected to die." Thus, prognosis is not discussed, and providers have little stimulus to acknowledge that advanced CHF will be fatal. CHF patients' care arose almost entirely from a medical model focused on treatment. Patients with cancer receiving treatment experience a rapidly changing clinical condition emphasizing a high need for coordination, and the value of being closely connected to supportive resources. CHF patients experience relatively stable but prolonged functional disability generating a need for support, but such services were infrequently available, at least compared to their availability for patients with cancer. Patients described the relative importance of various symptoms (a feeling of "drowning" in CHF vs. pain in cancer). Vig et al. also examined the quality of life and death for heart disease and cancer patients in an ambulatory setting.¹³⁷ This study did not find differences in themes, but these interviews were less about the experience of health care than about overall aspects of living and dying.

In the aggregate, this group of qualitative studies shares a strong and striking sense of common themes related to important aspects of health care for people living with serious, eventually fatal conditions. These themes were repetitive across all the studies that examined the experience of patients and caregivers broadly and emphasized

- professional competence in symptom management
- continuity and coordination of multiple providers and across settings
- responsive, flexible care that is available and adaptable to changing clinical needs
- adequate provision of information about disease course, prognosis, and treatments

- care from all providers that is empathic and that respects the individual as a person
- spiritually supportive care and environments
- adequate practical support for patients and caregivers in the home environment and informational support for practical planning in hospital and institutional settings.

Summary of the Relationship of Satisfaction to Other Measures of Process and Outcome

Several studies described in the context of our systematic reviews noted the association between satisfaction and interventions that improved communication or addressed other interpersonal aspects of care.^{90,82, 84, 91} Other important processes or attributes of care that were highlighted by the interventional literature include the relationship of pain management, practical support, enhanced caregiving, and provider accessibility to satisfaction.^{83, 84, 147} The observational literature was similarly supportive of the importance of these indicators and their relationship to satisfaction. The observational literature adds to our understanding of these relationships by illustrating how these specific processes or attributes of care are helpful in distinguishing healthcare performance in different settings.^{72, 74}

The qualitative literature suggests some important insights related to patient perception of care at the end of life. To the extent that satisfaction measurement reflects subjective perception of care, these qualitative data endorse the fact that patients and caregivers positively regard many of the attributes typified by palliative care (e.g., underscoring the importance of pain and symptom management, continuity, responsiveness, adequate information, respectful empathic, spiritually supportive care, and practical support). To the extent that interventions successfully target them and satisfaction measures embody these domains, they are likely to detect positive effects. In fact, this seems often, but not uniformly, to be the case in the interventional literature. In addition to measurement, as our findings suggest, the qualitative literature also supports the idea that this relationship between interventions and satisfaction could be confounded by other factors including differences in patient, caregiver, or healthcare settings.

B. Key Question 1b. What is the reliability and validity of specific instruments for measuring quality of life or quality of care at end of life?

Measurement of Patient and Family Outcomes

Our literature search identified one comprehensive systematic review of measures relevant to end-of-life care that Teno has published on the World Wide Web.³⁰ The Toolkit of Instruments to Measure End of Life Care (TIME) project, last updated with a literature review current through 2000, created a web-based resource of patient-focused, family-centered instruments that address the needs and concerns of patients and their families at the end of life (see Methods). The Toolkit is a comprehensive list of the highest quality measurement tools for evaluating end-of-life care from the perspective of patient-focused, family-centered evaluation. The Toolkit organizes measures into 11 domains:

- Pain and other symptoms
- Emotional and cognitive symptoms
- Functional status
- Survival time and aggressiveness of care
- Advance care planning
- Continuity of care
- Spirituality
- Grief and bereavement
- Patient-centered reports and rankings (i.e., satisfaction) with the quality of care
- Caregiver well-being
- Quality of life.

The Toolkit website, www.chcr.brown.edu/pcoc/bibliographies.htm, gives an extensive summary of the 35 recommended instruments,³⁰ including reports of reliability and validity. Measures that the review process labeled as being only potentially relevant are listed on the web site with a one-sentence summary and corresponding reference. The Toolkit has a number of limitations. Its search terms were limited and inclusion criteria focused on measures that were accessible and easy to use. These criteria suggest that the Toolkit could have missed some important measurement tools for research. The Toolkit omitted clinician/provider focused issues and evaluation of quality end-of-life care from perspectives other than patient and family, even though those perspectives might also inform evaluations of the quality of end-of-life care. Nevertheless, the Toolkit is a remarkable and widely used working document, and wide use is likely to have led to reasonably broad coverage of measurement instruments.

Literature Review of Measures

Given the availability and quality of the Toolkit, our review focused on the literature after 2000 or on reports that were not identified in the Toolkit search. We searched especially for the development of new measures and for reports that describe reliability and validity data on specific instruments. We identified 48 new measures that supplement the Toolkit. Appendix H2 provides detailed validity and reliability data for measures we identified that supplement the 35 recommended Toolkit measures (the extensive data on reliability and validity testing summarized in the Toolkit website was not reproduced in this report). Our discussion below is organized in a similar fashion to the Toolkit. We highlight measures that fit best within the discreet domains as used in the Toolkit, but we grouped together multidimensional measures of quality of life, quality of care, and satisfaction with care. We report on measures to evaluate both overall quality of life and quality of care as well as specific domains relevant to both.

In the course of identifying all citations relevant to measurement, we also identified a number of citations that are important to understanding the application of measurement tools. This literature is not strictly within the scope of the RFTO, which focused on the reliability and validity of measurement tools themselves, but reports of the use of the measurement tools are important to understanding the application of the measures we identified and to assessing the implications for research and research priorities in the field. For that reason, we have included an accounting of these citations as a separate Appendix H1. A summary of the literature describing the properties and psychometric evaluation of measures is provided at the end of this section.

Multidimensional Measures: Quality of Life, Quality of Care and Satisfaction

Measures of Quality of Life

The Toolkit³⁰ reviewed 41 measures of quality of life and recommended four that have detailed data on validity and reliability: McGill QOL Questionnaire (MQOL),¹⁴⁸ Missoula-VITAS QOL Index (MVQOLI),¹⁴⁹ European Organization for Research and Treatment Core Quality of Life Questionnaire version 3.0 (EORTC QLQ C-30), and the Functional Assessment of Cancer Therapy (FACT)/Functional Assessment of Chronic Illness Therapy (FACIT Fact-G).

The EORTC QLQ-C30, extensively described in the Toolkit, was evaluated in a palliative care population. Validity testing included generally moderate, statistically significant interscale correlations; discrimination by functional status; responsiveness to changes in health status over time and to palliative treatment. Factor analysis showed six factors, and Cronbach's alpha ranged from 0.56 to 0.79.¹⁵⁰ A second article reported psychometric data in lung cancer for the EORTC QLQ-C30 demonstrating Cronbach's alpha overall = 0.93, subscales = 0.69 to 0.89 (7 of 12 subscales > 0.80).¹⁵¹ This same longitudinal study reported supplementary data on the Duke-UNC Social Support Scale in this population; Cronbach's alpha overall = 0.94, subscales = 0.88 to 0.92.¹⁵¹

The Brief Hospice Inventory, developed for use in hospice patients, showed two factors in factor analysis; Cronbach's alpha ranged from 0.84 to 0.94.¹⁵²

The Hebrew Rehabilitation Center for the Aged index (HRCA-QL) index is a version of the Spitzer Quality of Life Index adapted for patients with advanced cancer. For criterion validity, it

showed correlations with the Karnofsky Performance Scale and an Instrumental Activities of Daily Living index. Cronbach's alpha was 0.7, and test-retest and inter-rater reliability were good. Scores declined as patients became closer to death or health status changed.¹⁵³

The McMaster Quality of Life Scale was designed for use by proxies or patients. Concurrent (correlation with Spitzer Quality of Life and construct (those able to rate it themselves scored higher than those who could not) validity were tested. Intra-observer and inter-rater reliability were high, and the measure was responsive to perceptions of change in clinical status.¹⁵⁴

The Palliative Care Quality of Life Instrument includes 28 items in six scales. Validity testing included face, construct (correlation with AQEL), criterion (ability to predict independent criterion variables, convergent and discriminative. Patients with better and worse Eastern Cooperative Oncology Group (ECOG) status showed significant differences, as did patients before and after treatment. Internal consistency and test-retest reliability were also high.¹⁵⁵

Giorgi et al. describe comparisons between a linear analogue scale (LAS) for measuring quality of life in cancer patients and results with categorical unvalidated assessment that was not included in the Toolkit.¹⁵⁶ Correlation between the LAS and a performance status measure is 0.46 and the questionnaire and performance status correlation is 0.38. Internal consistency testing for LAS reveals a poor Cronbach alpha for the LAS.

Green et al. proposed a chronic heart disease specific tool to measure physical limitation, symptoms, QOL, social interference, and self-efficacy.¹⁵⁷ The Kansas City Cardiomyopathy Questionnaire is a self-administered, 23-item tool that was compared to the SF-36 and Minnesota Living with Heart Failure Questionnaire (LiHFe). Convergent validity was 0.46–0.74 across seven domains. Physical limitation subscale was correlated to the six-minute walk ($r=0.48$), SF-36 ($r=0.84$), and LiHFe (0.65). Reliability testing demonstrated Cronbach's alpha of 0.62–0.95 across seven domains; test-retest at three months for patients without exacerbations changed only 0.8 to 4 points on the 1–100-point scale.

Higginson et al. is cited in the Toolkit reporting validity testing of the Support Team Assessment Schedule (STAS) for seven of STAS's 17 items.¹⁵⁸ The measures have items scaled 0–4 and use ten items to rate patient and family status and seven items to rate services delivered. Agreement on the seven items for patient and staff ($n=62-78$) ranged from kappa 0.12 to 0.78, total score Spearman rho 0.66; kappa for family and staff ($n=58-67$) ranged from $-0.06-0.51$, total score Spearman rho 0.44. Carson et al. report validity and reliability testing of the STAS in Canada in an acute care oncology unit and a palliative care unit.¹⁵⁹ Validity data by comparison to patient ratings resulted in an overall $r=-0.09$ for the palliative care team and $r=0.28$ for the oncology team; comparison to family ratings resulted in overall $r=0.38$ and $r=0.37$, respectively (all $p>0.05$). Inter-observer correlations ranged from 0.27 to 1.0 and intra-observer correlations from -0.33 to 0.88. Test-retest correlations were 0.50 for palliative care team and 0.71 for oncology team.

Steinhauser et al. describe the Quality of Life at End of Life (QUAL-E) instrument that consists of 24 items.¹⁶⁰ Factor analysis revealed five domains: life completion, relationships with the healthcare system, preparation/anticipatory concerns, symptom impact, connectedness and affective social support; Cronbach's alpha ranged from 0.6 to 0.84 for the subscales.

The Life Evaluation Questionnaire (LEQ) was described in 1996 but was not reviewed in the Toolkit.¹⁶¹ The LEQ is a self-administered, 121-item measure across five subscales (freedom,

appreciation of life, contentment, resentment, social integration) that was developed in incurable cancer patients in both outpatient and inpatient care settings. Salmon et al. report convergent validity to the RSCL that ranged from 0.01 to 0.62 (sufficient only for freedom, resentment, and social integration); convergent validity to MacAdam and Smith Support scale that ranged from 0.02 to 0.62; Cronbach's alpha for freedom = 0.70, appreciation of life = 0.76, contentment = 0.76, resentment = 0.85, social integration = 0.78); test-retest in 40 individuals at two to three days were freedom $r=0.80$, appreciation of life $r=0.91$, contentment $r=0.77$, resentment $r=0.92$, social integration $r=0.84$).¹⁶¹

Measures of Quality of Care and Satisfaction

The Toolkit³⁰ reviewed 20 measures and recommended the Medical Outcome Study Satisfaction Survey, Toolkit of Instruments to Measure End of Life Care Bereaved Family Member Interview, Picker-Commonwealth Survey, and FAMCARE. Our literature search identified six additional measures in the domain of satisfaction or quality of care that also had available psychometric information. We identified one additional validation study for the FAMCARE scale¹⁰⁹ that added data to the Toolkit citation.^{30, 162} Kristjanson et al. report an inter-item correlation criterion (minimum 50% with $r = 0.3$ to 0.7) for 18 of 20 items, item correlation to total score of 0.4 to 0.76 for 15 of 20 items, and a Cronbach's alpha = 0.90.¹⁰⁹ The authors also reported on two additional measures evaluated concomitantly, the Family Assessment Device (FAD) and the F-Care Expectations & Perceptions Scales. The FAD is a 12-item scale assessing family functioning; inter-item correlations met criterion (minimum 50% with $r = 0.3$ to 0.7) for 12 of 12 items; item correlation to total score was 0.4 to 0.75 for 12 of 12 items; Cronbach's alpha = 0.93.¹⁰⁹ The F-Care Expectations Scale assesses family members' care expectations and was reported to have inter-item correlations at criterion for 13 of 16 items; item correlation to total score of 0.4 to 0.72 for 12 of 16 items, and Cronbach's alpha = 0.88.¹⁰⁹ The F-Care Perceptions Scale assesses family members' care perceptions; inter-item correlations met criterion for 18 of 21 items; item correlation to total score was 0.4 to 0.72 for 13 of 21 items; Cronbach's alpha = 0.86.¹⁰⁹

The Toolkit After-Death Bereaved Family Member Interview^{30, 31} is a telephone survey for family members and has versions for hospice, nursing homes, and hospital deaths; U.S. norms are available. There are eight domains. Scales were moderately correlated with overall satisfaction and with the corresponding individual rating question for the construct. Cronbach's alpha was greater than 0.7 for scales with more than three items, and test-retest reliability was high. Families of those who died in hospice reported better care than families of those who did not.³¹

The Quality of Dying and Death (QODD) instrument is a 31-item family after-death interview across six domains;¹⁶³ it includes an assessment of frequency and a linked quality ratings; construct validity $r=-0.52$ against the Memorial Symptom Assessment Scale (MSAS), $r=-0.47$ MSAS psychological subscore, $r=-0.42$ MSAS physical subscore; discriminative study with independent symptom questionnaire significant at $p<0.01$, preferences at $p<0.01$, and communication $p<0.001$; correlation to global rating of last seven days of life $r=0.55$, moment of death $r=0.51$ (two factors explaining 38% of QODD variance); overall 31-item QODD Cronbach alpha = 0.89.¹⁶⁴ A separate report demonstrated Cronbach alpha = 0.96 for a 14-item nurse version of the QODD.¹⁶⁵ A study in the of the after-death QODD adapted for the intensive care unit demonstrated interobserver reliability 0.44 for the overall ICU-QODD score (23 item ICU

version); components ranged from an intra-class correlation (ICC) of 0.15 to 1.0 for frequency components (mean 0.54), and ICC 0.16 to 0.59 for quality rating component (mean 0.32).¹⁶⁶

The QUEST includes four scales for evaluating quality of end-of-life care and satisfaction with treatment: MD care, MD satisfaction, RN care, and RN satisfaction. Face (expert review), construct (moderate correlation with Patient Satisfaction Index), and correlation between subscales and with unrelated constructs were all tested. Test-retest kappas were 0.43–0.86, and Cronbach’s alpha was 0.83–0.95. Scores were negatively correlated with symptoms and lower for those with “do not resuscitate” (DNR) orders.¹⁶⁷

A four-item measure of patients’ assessment of the quality of communication about end-of-life care was highly correlated with overall satisfaction with care. Those with higher-rated communication had clinicians more likely to know if the patient had a durable power of attorney, and Cronbach’s alpha was 0.81.¹⁶⁸

The WALT measures Willingness to Accept Life-sustaining Treatment. It was reviewed for face validity by patients and experts, and showed correlation with a simple measure of preference. Inter-rater and test-retest reliability were good, and scores were associated with age, ethnicity, and functional impairment in a moderately ill population.¹⁶⁹

A relatives’ patient management questionnaire was developed to assess families’ attitudes, perceptions, and patterns of choice in the management of terminal cancer patients. It includes 21 items and five scales. Construct and discriminant validity were demonstrated through interscale and interitem correlations, and Cronbach’s alphas were 0.5–0.69.¹⁷⁰

Volicer et al. report the evaluation of three scales for dementia patients including a caregiver satisfaction scale, the Satisfaction With Care at the End of Life in Dementia (SWC-EOLD).¹¹³ The ten-item scale was shown to have one factor; item-total correlations range 0.33 to 0.79; Cronbach’s alpha = 0.90.

A postal questionnaire to examine caregiver satisfaction with palliative care was described by Jacoby et al.¹¹² This 89-question after-death postal survey of caregivers demonstrated discriminant validity tested with 36 attitudinal questions when health problems identified—only four were significant by Chi square; convergent testing was reported in tabular form in the reference; Cronbach’s alpha = 0.68 to 0.84 across seven subsets.

We also identified several needs assessment tools, a domain that measures an element of patient-centered care but was not addressed in the Toolkit. The Cancer Patient Needs Survey has 51 items in five categories, including coping, help, information, work, and cancer shock. Different scores were found for hospice and clinic patients, and Cronbach’s alpha was 0.91; this questionnaire was developed for the general cancer population.¹⁷¹

The Concept of a Good Death measure includes 17 descriptive statements of relevant concepts in three subscales: closure, personal control, and clinical criteria. Factor analysis showed three subscales, there was small-to-moderate association with other measures, and test-retest reliability was high. Scores were related to age, gender, and ethnicity.¹⁷²

Emanuel et al. report the rigorous development of a 13-question clinical screening instrument for terminal care needs, the Needs at the End-of-Life Screening Tool (NEST).¹⁷³ This multidimensional screening tool was developed from factor analysis of a 135-item survey administered to 988 dying patients. The measure requires further validation and reliability testing.

Finally, we identified two tools for evaluating the quality of palliative care, one for use by both patients and staff and one for use by staff only. Hearn et al. reported development and testing of the Palliative Care Outcome scale (POS).¹⁷⁴ The measure was developed by systematic literature review and underwent refinement by a multidisciplinary advisory group over several iterations of pilot testing. The measure was specifically developed as an outcome measure for the quality of end-of-life and palliative care for use in hospice patients. The measure includes 12 items, most using a 0–4 scale and consists of two parts, one patient self-administered questionnaire and one palliative care staff responses. Validity testing was performed across eight sites in England and Scotland with 148 patients completing evaluation. On average, the measure was completed in less than ten minutes for each type of respondent. Reliability testing included test-retest, internal consistency (Cronbach alpha for patient = 0.65, staff = 0.70), and a comparison of staff to patient responses. Validity testing included assessments of face validity and change over time; construct validity achieved a Spearman's rho 0.43–0.80 against ETORTC QLC-C30 and Support Team Assessment Schedule (STAS). The Resident Assessment Instrument for Palliative Care was designed for clinician assessment in nursing homes. It builds on the standard RAI, and includes nine domains. Intra-observer kappas were 0.77–0.9.¹⁷⁵

Measures Related to Other Specific Domains

Measures of Pain and Other Symptoms

Sixty-four measures were reviewed in the Toolkit³⁰ and five measures were recommended for assessing either pain or overall symptoms: McGill Pain Questionnaire (MPQ),¹⁷⁶ Wisconsin Brief Pain Questionnaire, Memorial Pain Assessment Card, Edmonton Symptom Assessment System (ESAS),¹⁷⁷ and Memorial Symptom Assessment Scale (MSAS).¹⁷⁸

With regard to the MSAS, we identified a validation trial for the MSAS in non cancer patients where convergent validity to the Piper Fatigue Scale ranged from $r=0.15$ to 0.56 for cancer patients and 0.29 to 0.61 for non-cancer patients (best for behavioral and sensory subscales of the PFS); factor analysis yielded one psychological factor and one physical symptom with three subgroups; Cronbach's alpha = 0.85 in cancer patients ($n=66$) and 0.77 in non-cancer end-stage group ($n=69$).¹⁷⁹ Also, Chang et al. report univariate correlations for the MSAS to RAND Mental Health Inventory (MHI) well-being scale -0.60 (-0.53 to 0.66 for three subscales), MHI distress 0.65 (0.48 to 0.80), Functional Living Index-Cancer (FLIC) -0.78 (-0.61 to -0.78 , subscales of FLIC range -0.45 to -0.73), SDS 0.79 (0.57 to 0.81), and Karnofsky -0.58 (-0.31 to -0.65); the physical and global distress index subscales performed better than the psychological symptom subscale.¹⁸⁰

More recent studies of the ESAS have shown that telephone administration was possible in 62% of palliative care patients.¹⁸¹ correlation to MSAS Global Distress $r=0.73$; concurrent validity ESAS summary distress score to MSAS demonstrated: TMSAS scale (0.72), Global Distress Index (GDI) (0.73), physical symptom subscale (0.74), and psychological symptom subscale (0.56); ESAS summary distress score to FACT demonstrated: physical well-being subscale (-0.75), sum QOL (-0.69), functional well-being (-0.63), emotional well-being (-0.52) and social/family well-being (-0.25); all item correlations reported as significant; calibration studies showed overlap for median values within scales for all items; Cronbach alpha 0.79 ; test-retest Spearman correlation 0.86 at two days and 0.45 at one week; all items significantly correlated at two days ($r = 0.43$ to 0.86) but at one week only pain (0.75), activity (0.65),

depression (0.54), shortness of breath (0.53) and distress (0.45) were significantly correlated.¹⁸² We identified seven additional measures with descriptions of psychometric properties in the current effort.

The Cambridge Palliative Assessment Schedule (CAMPAS-R) was developed for palliative care in primary care. Patients rate physical and psychological symptoms and their caregiver's psychological symptoms on a visual analog scale. Face and content validity was tested with patients, physicians, and nurses; criterion validity showed correlation with the EORTC and HADS for some items but not for others; and discriminant validity was shown through significant differences between patients who did and who did not survive. Cronbach's alpha for correlation between symptoms was 0.77–0.8.¹⁸³

The Symptom Monitor is a ten-item diary for physical symptoms, developed for feasibility in patients with advanced illness. Inter-rater intra-cluster correlations were >0.75 .¹⁸⁴

Two validation reports were identified for the Lung Cancer Symptom Scale (LCCS).^{185, 186} The measure uses nine patient-scored visual analogue scales and six observer-scored four-point scaled items to measure symptoms prevalent in lung cancer. Construct validity against Karnofsky was 0.15–0.63 across items (symptomatic distress 0.49, effect on activities 0.63, QOL 0.43).¹⁸⁵ Criterion validity was reported (patient scale and observer scale, respectively) relative to the Karnofsky ($r=0.63$, NA), Sickness Impact Profile (SIP) (0.40, 0.56), Profile of Mood States (POMS) (0.67, 0.54), American Thoracic Society Questionnaire (ATS 29) cough (0.56, 0.65) and dyspnea (0.46, 0.64), and McGill Pain Questionnaire-short form (SF-MPQ) (items range 0.51–0.67). Internal consistency was done to Brief Symptom Inventory (BSI) ($r=0.93$), SIP ($r=0.94$), POMS ($r=0.94$), SF-MPQ ($r=0.91$, $r=0.64$ –0.74 for three components). Hollen, et al. describe normative data and trends for QOL in stage III and IV lung cancer using the LCCS.¹⁸⁷

Sarna et al. applied the Symptom Distress Scale (SDS) to female lung cancer patients.¹⁸⁸ The 13-item, self-report scale was developed and modified in the 1970s to 1980s. In this study, factor analysis with principal components and varimax rotation resulted in a five-factor model explaining 65% variance. The study provides only limited validity data beyond factor analysis but notes negative correlations of certain items to parts of Karnofsky Performance Status ($r= -0.27$ to -0.48) and an overall $r=-0.58$.

Warden et al. reports psychometric testing for a novel, disease-specific measure, Pain Assessment in Advanced Dementia (PAINAD).¹⁸⁹ The five-item, observer assessment demonstrated convergent validity to Discomfort Scale—Dementia Alzheimer's Type (DS-DAT) and Discomfort Scale—Visual Analogue Scale (DS-VAS) ($r=0.76$, $n=19$) and PAIN-VAS ($r=0.75$, $n=18$). Factor analysis was noted and also done in different conditions ($r>=0.82$ for pain with activity). Cronbach's alpha ranged from 0.57 to 0.83 in multiple phases of the study.

Volicer et al. reports the evaluation of two symptom scales for dementia patients: the Symptom Management at the End of Life in Dementia (SM-EOLD) and the Comfort Assessment in Dying With Dementia (CAD-EOLD).¹¹³ The SM-EOLD is a nine-item scale shown to comprise two factors; item-total correlations range 0.18 to 0.66; correlation for symptom items on CAD-EOLD $r = 0.475$ to 0.559; Cronbach's alpha = 0.78. The CAD-EOLD is a 14-item scale with four subscales (physical distress, dying symptoms, emotional distress, well-being); item-total correlations range 0.39 to 0.79; correlation for symptom items on SM-EOLD $r = 0.475$ to 0.559; Cronbach's alpha = 0.85 overall; subscales (physical distress $r=0.74$, dying symptoms $r=0.70$, emotional distress $r=0.82$, well-being $r=0.80$).

Measures of Emotional and Cognitive Symptoms

The Toolkit³⁰ reviewed 41 measures and recommended five: Profile of Mood States, Memorial Symptom Assessment Scale, Center for Epidemiologic Studies Depression Scale (CES-D), and RAND Mental Health Inventory (MHI-5). Our literature search identified six reports describing measures in the domain of emotional symptoms. A single-item screening for depression, “Are you depressed?” correctly identified depression in all 24 terminally ill patients evaluated.¹⁹⁰

The communication capacity scale is a five-item clinician rating scale developed for palliative care populations. Principal components analysis demonstrated only one component, and the scale was highly associated with cognitive items on the MDAS and DRS (delirium rating scale) and not with irrelevant items. Cronbach’s alpha was 0.96 and inter-rater kappa was excellent.¹⁹¹

The agitation distress scale is a six-item clinician rating scale. Principal components analysis demonstrated only one component, and the scale was highly associated with agitation items on the Memorial Delirium Assessment Scale (MDAS) and DRS and not with irrelevant items. Cronbach’s alpha was 0.91 and inter-rater kappa was excellent.¹⁹¹

Kurlowicz et al. evaluated the 19-item clinician interview Cornell Scale for Depression in Dementia (CSDD) in a study of 642 nursing home patients.¹⁹² Oblique rotation four-factor matrix and inter-factor correlation analysis resulted in a 16-item, four-domain measure. Criterion validity was performed and reported. Internal consistency revealed a Cronbach alpha of 0.76.

Hopwood et al. applied two previously developed measures to a sample of 204 patients with breast cancer.¹⁹³ Only weak validity metrics are reported for the Hospital Anxiety and Depression Scale (HADS) and the Rotterdam Symptom Checklist (RSCL).

Measures of Functional Status

The Toolkit³⁰ reviewed 15 measures and recommended six within this domain: Index of Independence in ADLs, Barthel Index, Physical Self-Maintenance Scale, Rapid Disability Rating Scale, Stanford Health Assessment Questionnaire, and FIM™ Instrument. Our literature search identified four reports describing measures in the domain of functional status with specific psychometric descriptions of measures. Two reports were refinements to the Edmonton Functional Assessment Tool (EFAT); the original measure was evaluated in the Toolkit and not recommended; however, the revision, EFAT-2, was not available at the time of the last Toolkit update.^{194, 195} EFAT-2 is a ten-item rating assigned by a professional grading symptoms and functions and assigns a summary functional assessment. The Cronbach’s alpha was 0.86 and inter-rater correlation was 0.97 for self trained clinicians (n=2) and 0.95 for formal trained (n=2).^{194, 195} The measure was not correlated with pain but demonstrated discriminant validity in different groups based on discharge location.

Gerety et al. report on a 54-item measure to evaluate frail elderly individuals that requires calibrated specialized performance measuring equipment, the Physical Disability Index (PDI).¹⁹⁶ They report discriminate validity against Folstein Mini-Mental State Exam ($r=0.11$) and convergent validity to the Physical Self-Maintenance Scale ($r=-0.71$) and Sickness Impact Profile ($r=-0.59$). Test-retest correlation in 36 patients at two to five days was $r=0.97$ overall, four subscales 0.92–0.96; inter-rater reliability coefficients ranged from $r=0.81$ to 0.99 except for the mobility scale which was $r=-0.02$ to 0.70.

Gloth et al. report on the Frail Elderly Functional Assessment Questionnaire (FEFA), which is a 19-item, interviewer administered tool for the elderly at very low activity levels.¹⁹⁷ They report correlation to direct observation ($r=0.90$), Katz's ADL index ($r=0.86$), Barthel index ($r=0.91$), and Lawton's IADL index ($r=0.67$). Test-retest in 29 patients at a two-week interval revealed a kappa 0.82 overall; all items had kappas greater than 0.40 (0.45–0.91).

Measures of Survival Time and Aggressiveness of Care

The Toolkit³⁰ reviewed four chart-based instruments and three prognostic tools. Several individual questions are recommended, but validity/reliability information on tools is not available. As described in the methods section, a review of prognostication and prognostic indices relevant to the definition of the end of life is included in Appendix A.

Measures of Advance Care Planning

The Toolkit³⁰ reviewed and recommended the Toolkit of Instruments to Measure End of Life Care Bereaved Family Member Interview. Our literature search identified one additional report describing measures in the domain of advance care planning with specific descriptions of the psychometric properties of measures.

Koedoot et al. (2001) describe a measure not captured in the Toolkit that has applicability to advance care planning.¹⁹⁸ The decisional conflict scale (DCS) is tested in a Dutch translation version for psychometric properties in a cancer patient group. The measure consists of 16 items, each scored on a five-point Likert scale, across three subscales (uncertainty, factors contributing, and effective decision-making). Construct validity among subscales was measured at $r=0.58$ to 0.76 . Criterion validity on the uncertainty subscale was described as significant between certain versus uncertain group. Prior reliability testing was noted in the report demonstrating internal consistency (Cronbach alpha = 0.78–0.89) and test-retest reliability ($r>0.80$).

Measures of Continuity of Care

The Toolkit³⁰ reviewed four measures and recommended the Picker-Commonwealth Single Item, Smith-Falvo Patient-Doctor Interaction Scale, McCusker Scale, and Chao Patient Perception measures. Our literature search identified no additional reports describing measures in the domain of continuity of care with descriptions of specific psychometric properties of measures.

Measures of Spirituality

The Toolkit³⁰ reviewed 25 measures and recommended the Meaning in Life Scale, Spiritual Well-Being Scale, Spiritual Perspective Scale, Death Transcendence Scale, Death Attitude Profile, and Herth Hope Index. Our literature search identified one additional report describing measures in the domain of spirituality with descriptions of specific psychometric properties of measures.

The Santa Clara Strength of Religious Faith Questionnaire (SCSORF)¹⁹⁹ is a 10-item scale with good internal consistency (Cronbach's alpha = 0.95) and test-retest reliability (0.82) in a population with mainly early-stage breast cancer. Convergent validity was demonstrated through a strong correlation with intrinsic religiosity and moderate correlations with religious practice, perception of self as spiritual, and comfort derived from religion.

The 45-item Life Closure Scale was developed to measure psychological adaptation in the dying and tested in hospice patients. The content validity index, as assessed by experts, was 0.83, and Cronbach's alpha was 0.80.²⁰⁰

Measures of Grief and Bereavement

The Toolkit³⁰ reviewed 24 measures and recommended the Grief Resolution Index and Anticipatory Grief Scale. Our literature search identified four additional reports describing measures in the domain of grief and bereavement that provided specific psychometric properties of measures.

The CBI (Core Bereavement Items) includes 17 items in three subscales. The measure was developed from the bereavement phenomenology questionnaire. Testing included face validity, factor analysis, and discriminant validity for time and group effects; Cronbach's alpha was 0.91.²⁰¹

The Hogan Grief Reaction Checklist (HGRC)²⁰² is a 61-item measure across six constructs (despair, panic behavior, blame and anger, disorganization, detachment, and personal growth) that was developed in grieving adults from mixed sources. Hogan et al. reported convergent validity to earlier measures in general grief that ranged from $r=0.20$ to 0.78 with significant correlations across subscales; discriminant validity in subset of mothers who experienced death of a child by different mechanisms and by timing of death; Cronbach's alpha overall was 0.90.

An eight-item adaptation of the Bereavement Risk Index showed significant differences in the Brief Symptom Inventory between low- and high-risk group, which were maintained for 25 months after death.²⁰³

Feldstein et al (1995) used the Grief Experience Inventory (GEI) measure in a study of oncology nurse grief and summarized the original validation data reported in 1985.²⁰⁴ The measure uses 102 yes/no statements in a self-administered inventory that is further scored into nine composite scales. Data reported includes discriminant validity between bereaved versus nonbereaved individuals at the significance level 0.001 on all subscales, test-retest coefficients 0.53–0.87, and internal consistency Cronbach's alpha = 0.52–0.84 on bereavement scales.

Measures of Caregiver Well-being

The Toolkit³⁰ reviewed 53 measures and recommended the Caregiver Strain Index and Caregiver Reaction Assessment. Our literature search identified two additional reports describing measures in the domain of caregiver well-being with specific psychometric descriptions of measures.

Travis et al. describe the development of the Family Caregiver Medication Administration Hassles Scale designed to capture problems caregivers experience with assisting elderly with medications.²⁰⁵ The 24-item paper survey is designed to capture four subscales (information, safety issues, scheduling, and polypharmacy). Principal components and factor analysis was done (66.5% cumulative variance). Construct validity against the Medication Complexity Index ($r=0.19$) and modified Caregiver Strain Index ($r=0.44$) were reported. Test-retest at two weeks ($n=53$) correlated at $r=0.84$. Internal consistency was reported at 0.95 (0.800.92 across subscales).

The Cost and Reciprocity Index (CRI) (modified) includes 25 items in four subscales and was modified for use with hospice caregivers. Concepts include social support and conflict.

Extensive testing was done with the original instrument in healthy populations; in this study, relations between subscales were consistent with the theoretical framework and Cronbach's alpha was 0.68–0.83.²⁰⁶

Other Measures

A number of measures were identified in our endeavor that did not specifically fit into any domains established by the Toolkit but may have applicability to end-of-life care research. Our literature search identified three reports describing measures in outside of the Toolkit domains with descriptions of specific psychometric properties of measures.

Kristjansson, et al. report on an index of social support developed from data gathered in the Canadian Study of Health and Aging (CSHA).²⁰⁷ The six-item measure was developed from factor analysis (item correlations 0.26 to 0.83) and item response theory (IRT) analysis for half the study population. External (construct and predictive validity on second half of study population), and IRT ($r=0.53$ to network size)/classical ($r=0.61$) comparison was done. Cronbach alpha = 0.76; IRT marginal reliability was 0.85.

We identified a number of clinical scoring tools. The Hospice Pressure Ulcer Risk Assessment Scale (HoRT) measures physical activity, age, and mobility. PPV was 50%, NPV 100%.²⁰⁸ The Clinical Dementia Rating Scale looked only at demographic, clinical, and prognosis to death correlation to CDR scores CDR correlates to death during follow up $r=0.36$.²⁰⁹

Fowell et al. report a novel application of an integrated care pathway (ICP) to gain quality of end-of-life care data.²¹⁰ The investigators developed and employed the ICP across the healthcare system in Wales and captured data about the end-of-life care experience from variance sheets that were required when the care provided deviated from the expected course of care delineated in the ICP guideline. Although not a validated measure, this quality improvement method provided significant evaluative data about the care of the dying across the healthcare system in Wales.

Summary of Measures

Many new instruments have been developed or have undergone further evaluation in end-of-life settings since the last Toolkit update in 2000, particularly in the domains of quality of life, quality of care and satisfaction, and pain and physical symptoms. However, many articles did not report a theoretical framework or a careful development process, and reliability and validity testing was often limited in scope. Since patients at the end of life often receive care in multiple settings, instruments that are useful longitudinally and in hospitals, intensive care, outpatient settings, nursing homes, and at home are essential for comprehensive evaluations, but most instrument evaluations were limited to a single setting. End-of-life issues and symptoms often also vary substantially with cultural backgrounds. However, development, reliability, and validity studies addressing different populations were also very uncommon. Finally, although end-of-life care varies substantially among different regions of the United States, most studies were conducted in a single center, often in tertiary care settings.

Many commonly used instruments have not been evaluated in end-of-life populations, where psychometrics, burden, or applicability may be very different. Few instruments were developed for or tested specifically in non-cancer populations. In certain areas, particularly continuity, advance care planning, and aggressiveness of care, we found few instruments tested in the end-

of-life population. In other areas, such as quality of life or satisfaction, lack of theoretical frameworks, limited evaluations, and lack of consensus often make it difficult for researchers to choose appropriate instruments. Finally, few instruments have been developed or evaluated for the purpose of clinical practice, evaluation studies, or quality assessment or improvement interventions. Improving the quality of the intervention literature requires further evaluation of carefully developed instruments and development or testing of continuity, advanced care planning, and aggressiveness of care specifically for the purpose of evaluating interventions.

C. Key Questions 2 and 3:

2. What patient, family, and healthcare system factors are associated with better or worse outcomes at end of life?

3. What processes and interventions are associated with improved or worsened outcomes?

Elements associated with patient experience: symptoms of pain, dyspnea, depression and anxiety, and behavioral issues in dementia

We reviewed 27 systematic reviews or meta-analyses because they addressed selected symptoms of a palliative care population. Of those considered, we identified 12 that addressed the project questions and met implicit quality criteria. Two of the reviews included here focused specifically on a cancer population, one on patients with COPD, three on patients with dementia, and another six did not limit their reviews to only one disease cohort. In our review, we went beyond the systematic reviews by including intervention studies addressing our chosen symptom topics if those studies were not included in the systematic reviews. In total, we identified an additional 18 intervention studies. Finally, we explored the observational literature that addressed selected topics. Specifically, we identified prospective, observational cohort studies addressing any of our selected symptom topics and that also presented data separately by race, selected disease cohorts, or selected sites of care. In total, we reviewed 14 observational studies.

The remainder of this section summarizes the systematic reviews, meta-analyses, and intervention studies for each of the symptom groups separately: pain, dyspnea, depression and anxiety, and behavioral issues for dementia patients. A discussion of all the observational studies is presented at the end of the whole section. Summaries of the association of patient, family, and health system factors to symptoms and the effectiveness of interventions in improving symptoms are found at the conclusion of Chapter 3.

Table 4. Systematic Reviews for Symptoms: Pain, Dyspnea, Depression/Anxiety, Behavior in Dementia

Study	Symptoms Addressed	Date Search Concluded	Date of Publication
Higginson, Draft ⁷²	Pain, dyspnea, depression, anxiety	March 2003	Unpublished
Wilson, 2004 ²¹¹	Pain	Mid-2003	Draft in press
Booth, 2004 ²¹²	Dyspnea	2002	2004
Salman, 2003 ²¹³	Dyspnea	September 2000	2003
Higginson, 2003 ²¹⁴	Pain	2000	2003
Carr, 2002 ³⁴	Pain, depression	June 2001	2002
Jennings, 2002 ²¹⁵	Dyspnea	May 1999	2002
Higginson, 2001 ⁷⁴	Pain	1999	2001
Pan, 2000 ²¹⁶	Pain, Dyspnea	September 1998	2000
Finnema, 1999 ²¹⁷	Aggression, agitation, wandering	1999	2000
Opie, 1999 ²¹⁸	Aggression, agitation, wandering	1998	1999
Forbes, 1998 ²¹⁹	Aggression, agitation, wandering	May 1997	1998

Pain

Systematic Reviews and Pain

Six systematic review publications reflecting five separate reviews were identified that addressed the topic of pain.^{34, 72, 74, 211, 214, 216} The systematic reviews by Higginson et al.^{74, 214} include the original report and a peer-reviewed publication from that report and are treated as one review. Two of the systematic reviews addressed pain specifically in cancer populations,^{34, 72} one included a meta-analysis of the literature on the effects of palliative care teams on pain,^{74, 214} and two reviews examined the literature on complementary and alternative medicine (CAM) or otherwise deemed “non-pharmacologic” interventions to address pain and other symptoms.^{211, 216}

One of the more recent reviews, conducted by Gysels and Higginson,⁷² examined the literature on improving support for and palliative care of cancer patients. This review considered studies published before March 2003, including randomized or quasi-randomized controlled studies, non-randomized controlled studies, observational studies and systematic reviews. This review was not organized specifically around pain or other symptoms; however, many symptom-related studies were reviewed in the context of other topic areas, including “coordination of care,” “user involvement in planning, delivering, and evaluating services,” “psychological support services,” “general palliative care services,” “specialist palliative care services,” “rehabilitation services,” and “complementary therapy services.” In total, 44 symptom-related studies were identified, 27 of which addressed pain. Among the studies reviewed was the systematic review by Pan et al.²¹⁶ on complementary and alternative medicine (CAM), a study separately identified during our search of the literature and which will be described below. Of the 27 studies identified on pain, nine were randomized or quasi-randomized controlled trials and 12 were observational studies. The remainder were qualitative studies (2), a systematic review, and

three studies with unclear study designs. Sample sizes in these studies ranged from 9 to 695. Interventions to address pain symptoms included clinical pathways and special clinical teams, education, hospice (either inpatient or outpatient), palliative care teams, specialized home care teams, and massage. Overall, the studies identified in this review reported beneficial positive results in which pain symptoms experienced by cancer patients were alleviated by the interventions. Of the 19 studies reporting beneficial results, 11 were observational studies. One of the qualitative studies identified substantial unrelieved pain in the sample included in its study. There were six studies that reported no significant difference in pain symptoms between the intervention and control groups or between baseline and follow-up. Five of these studies were randomized or quasi-randomized controlled studies and one was a prospective observational study.

A systematic review of the management of cancer symptoms, including pain, was conducted by the New England Medical Center Evidence-Based Practice Center for the Agency for Healthcare Research and Quality.³⁴ This review considered the literature published in or before September 2001 that addressed the prevalence, assessment, or treatment of the selected symptoms. The report considered the full trajectory of disease rather than focusing on end-of-life care specifically. Given the focus of our review, we will only report on the findings from the review of studies related to treatment of pain. Only randomized controlled trials were accepted for this portion of the review. The authors of this report summarized the literature on the treatment of cancer pain published following the publication of a systematic review on cancer pain by Goudas et al.²²⁰ A total of 24 studies were identified; one addressed the relative efficacy of particular nonsteroidal anti-inflammatory drugs (NSAIDs) in comparison to other NSAIDs or placebo; six were identified that evaluated adjuvant analgesics in cancer pain management; six compared one opioid with another; five considered bisphosphonates in treating metastatic bone pain (comparing different doses or comparing to placebo) and six studies considered CAM treatments for managing cancer pain. Of these 24 studies, 14 interventions reported beneficial results. The six studies comparing different types of opioids, different dosages of the same opioid, or different means of opioid delivery did not report statistically significant results.

In an extensive review conducted by Higginson et al.,^{74, 214} the authors explored the role that palliative care teams play in affecting a number of symptoms in end-of-life care populations. The authors searched ten databases, the gray literature, journals, and the references of included studies. The most recent study was published in 2000. A total of 54 studies were identified after excluding case reports. The palliative care interventions identified in these studies included a number of settings: home care, hospital-based, combined home/hospital-based, inpatient unit, and integrated teams. A meta-analysis was conducted with a subset of 19 studies. The study designs included in this review were primarily prospective or retrospective/observational/cross-sectional. A meta-analysis of palliative care versus conventional care based on 13 studies reported an overall beneficial effect of palliative care teams on pain outcomes (OR: 0.38, 95% CI: 0.23, 0.64; odds ratio less than 1 means less pain). When the studies were stratified by study design, a significant effect on pain was only seen among the studies with non-randomized and observational/retrospective designs; there were three RCTs in this review (OR: 0.82, 95% CI: 0.52, 1.28), three non-randomized controlled trials (OR: 0.41, 95% CI: 0.30, 0.57) and seven observational/retrospective studies (OR: 0.30, 95% CI: 0.12, 0.74).

One systematic review produced by Health Canada addressed the symptoms of populations nearing the end of life.²¹¹ In this review, the authors focused on managing end-of-life pain and

other symptoms through non-pharmacological means. The search incorporated the literature published through mid-2003 in nine databases, the gray literature, monographs, and policy statements. A total of 21 research articles were identified (6 individual studies and 15 reviews). Non-pharmacological treatments of pain were the subject of 17 out of 21 of the research studies reviewed. Topics included acupuncture, hypnosis, music therapy, relaxation, massage, imagery, therapeutic touch, magnets, transcutaneous electrical nerve stimulation (TENS), microcurrent electrical neuromuscular stimulator (MENS), radiation therapy, and pediatric palliative care; however, only a subset of these were the subject of intervention. Where an intervention was conducted, results were generally beneficial, but most studies were observational in design.

One study by Pan et al²¹⁶ explored the role that complementary and alternative medicine (CAM) interventions might have in reducing or eliminating pain among palliative care populations. The authors searched six databases for CAM interventions, focusing on the following interventions: acupuncture, TENS, massage therapy, behavioral/relaxation therapy, music therapy, and psychological therapy. A total of 21 studies were identified in this review; eleven of these studies were RCTs, two were non-randomized trials, and eight were case studies. The most recent of the studies identified was published in 1998. A total of 14 studies addressed pain as the primary outcome of interest. Although the search criteria did not limit the review to cancer populations only, of the 14 studies, 12 included patients with cancer diagnoses only. One other study examined CAM interventions for pain in an HIV-positive population and another focused on a patient population that had received bone marrow transplantation. We summarize the findings from this review by type of intervention below, and further details regarding these citations can be found in the systematic review by Pan et al.²¹⁶

TENS: In a double blind RCT of 15 hospice cancer patients, the authors of one study did not have enough power to detect differences on pain measurement between the intervention and control groups, however, overall quality of life improved among intervention patients. A prospective pre/post intervention study of 60 patients with cancer pain included a 2-week intervention with TENS and resulted in 28% of patients reporting an excellent response that decreased to 15% after three months. A case study of nine patients with advanced cancer identified improvement in pain for 66% of them and partial relief in 22% of patients. Another case study including 29 frail cancer patients evaluated the joint intervention of TENS with acupuncture and found that 62% of patients had pain relief and 27% had pain reduction.

Acupuncture: In one study of 92 cancer patients, an intervention of acupuncture for one to two weeks achieved pain relief for one month in all patients with mild to moderate pain and 72% with severe pain. Among 183 cancer patients in another study, 48% had pain relief for three days or more or experienced an increase in mobility after a treatment of acupuncture one to four times weekly. In the only RCT involving acupuncture, 239 HIV-positive patients were randomized to real or sham acupuncture twice weekly for six weeks followed by once weekly for another eight weeks. The study found no statistically significant differences in pain reporting between groups.

Massage: There was one RCT and two case studies that explored the role massage might play in reducing pain symptoms. In an unblinded RCT of 28 cancer patients, men had immediate pain relief lasting for one hour while women experienced no significant improvement in pain symptoms. In a case series of nine cancer patients, patients reported a reduction in pain symptoms following two consecutive 30-minute massages. In another case series of 103 cancer patients, massage plus aromatherapy promoted pain relief in 33% of participants.

Behavioral and Relaxation Therapy: In a case series of 58 hospice cancer patients, participants were referred to relaxation therapy. Approximately 38% of study participants reported reduced pain symptoms following the intervention. An RCT of 94 bone marrow transplant patients with oral mucositis reported pain improvement by relaxation and imagery.

Music Therapy: In an RCT of nine terminally ill cancer patients, no significant difference was reported among groups in pain relief following an intervention of music therapy, although the review authors suggest that there was not sufficient power to detect small differences in the outcome.

Psychological Therapies: An RCT of therapy with or without self-hypnosis was conducted among 58 women with advanced breast cancer. The authors of this study reported that therapy reduced pain sensation and suffering and self-hypnosis provided further relief.

Additional Interventional Studies of Pain

We identified an additional ten randomized clinical trial or controlled clinical trial intervention studies addressing pain in end-of-life or palliative care populations. Six of the studies were focused specifically on cancer pain. Due to the recent publication of systematic reviews addressing cancer pain specifically, we selected those studies for review here that were published between 2002 and 2004,²²¹⁻²²⁶ with the exception of one study published in 1998 but not otherwise addressed by the reviews we identified.²²³ Of these six studies, one examined the role of hospital-based palliative care teams in improving symptoms of cancer patients, one included an aromatherapy massage intervention, two examined pain relief through medication (one with NSAIDs, one comparing opioids, and one comparing delivery method), and two examined the role of structured assessment on pain and other symptoms. An additional four studies focused on the treatment of pain in palliative care for non-cancer or mixed diagnosis populations. Three of these studies were published between 2002 and 2004.^{86, 227, 228} Another study, published in 1998, was not previously reported on in any of the systematic reviews we considered and is described here.²²⁹ One intervention compared different doses of the same opioid on pain, one looked at the role exercise plays in reducing pain among nursing home residents, one examined the influence of a more comprehensive and coordinated medical record on pain and other symptoms, and one explored the role of an outpatient palliative medicine consultation on various symptoms including pain. These ten studies have been organized into four categories loosely based on the intervention types, rather than by disease cohort. The categories are pharmaceutical interventions, system/institutional interventions, CAM, and exercise.

Pharmaceutical Interventions: In one study, Smith and colleagues²²⁵ conducted a randomized controlled trial of an implantable drug delivery system (IDDS) and comprehensive medical management versus medical management alone (control) in 200 outpatients with cancer (101 in intervention group; 99 in control group). While the IDDS and control groups had the same results in terms of pain reduction ($\geq 20\%$ reduction in pain as measured by a 100-point VAS) and six-month survival, this finding is limited by a baseline pain assessment for both groups, which ensured some therapy for the control group. Also, the findings are confounded by the longer survival of the intervention group. There was a 50% reduction in toxicity scores for the intervention group as compared to 17% reduction in the control group ($p=0.004$). The Jadad score for this study was 3.

Buprenorphine is an opioid analgesic that has been mostly available in sublingual and parenteral formulations. In the study by Sittl and colleagues,²²⁸ the authors examine the efficacy and tolerability of transdermal buprenorphine. A randomized, double blind controlled trial of 157 patients with cancer- and non-cancer-related pain compared the efficacy and tolerability of transdermal buprenorphine in three doses (35.0, 52.5, and 70.0 µg/h) plus placebo. Patients received a new patch every 72 hours for up to 15 days and were allowed to use sublingual buprenorphine tablets for rescue analgesia. The lower doses of transdermal buprenorphine produced higher response rates (measured as needing ≤ 1 rescue analgesia pill per day) than placebo at 35.0 and 52.5 µg/h (p=0.032 and p=0.003, respectively). There were no significant differences between the largest dose and the placebo. The Jadad score for this study was 3.

In a third drug study, Mercadante and colleagues²²⁶ examined the effect of ketorolac, a non-steroidal anti-inflammatory drug (NSAID) on morphine escalation in a randomized controlled trial. Patients with cancer-related pain (n=47) were randomized into two groups: the intervention group received ketorolac (60 mg/daily p.o.) in three doses with opioid escalation as needed and the control group were treated with opioid escalation only. Those in the intervention group used less morphine than in the control (p=0.003) and had less opioid escalation (p<0.0005). The mean weekly pain intensity was significantly less after three weeks in the intervention group than in the control (p=0.005). The Jadad score for this study was 3.

Systems/Institutional Interventions: In a study published in 1998, Latimer and colleagues²²⁹ investigated the effectiveness and efficiency of a patient care traveling record in palliative care. The authors randomized 61 patients cared for by a palliative care service to receive or not receive the patient care traveling record, a record of the patient's care from all sources that the patient could take with him/her to all appointments with providers including names of providers, next of kin, prior hospitalizations, medications, advanced directives, etc. Of the original sample, only 21 remained at the end of the follow-up period. Patients who used the traveling record had a larger reduction in reported pain at follow-up as compared to the control group; however, the difference was marginally significant (p=0.05). The Jadad score for this study was 2.

Building on the literature from Higginson et al.^{74, 214} are two recently published studies examining the relationship between palliative care team interventions and patient outcomes. In the study by Jack et al. published in 2003,²²¹ the authors conducted a controlled clinical trial of hospital based palliative care teams with 100 cancer patients (50 in intervention, 50 in usual care control group) to improve pain and other symptoms. The intervention group had significantly better pain ratings than the control group at the second and third assessments (p=0.029 and p<0.001, respectively). The most recent study, published in 2004 by Rabow et al.,⁸⁶ reports on a randomized controlled trial to understand the influence of an outpatient palliative medicine consultation team on symptoms in 90 patients (50 intervention, 40 control) with chronic heart failure, COPD, or cancer. There were no significant differences in patients reporting any pain or in their average pain score based on the Brief Pain Inventory. The Jadad score for this study was 3.

Complementary and Alternative Medicine: Soden and colleagues²²⁴ conducted a randomized controlled trial of aromatherapy massage versus massage only or no treatment (control) with 42 cancer patients. There were no significant changes in pain assessments between baseline and follow-up for any group, nor were there significant between-group differences in pain assessment. The Jadad score for this study was 5.

Exercise: Simmons and colleagues²²⁷ reported on a study that explored the effects of an exercise and toileting program on pain among 51 incontinent nursing home residents in a randomized controlled trial. The intervention included toileting prompts every two hours, five days a week, between the hours of 8:00 AM and 4:30 PM by nursing staff. During this same time period, either before or after toileting, the staff would provide assistance for the resident to walk, wheel, or at least perform sit-to-stand movements. This intervention did not result in significant differences in pain reports between the intervention and control groups. The Jadad score for this study was 1.

Two studies examined the role of structured assessment in improving care processes for cancer patients through better information collection and patient-provider communication. Sarna²²³ examined the efficacy of a structured symptom assessment on symptom distress in a randomized controlled trial. The study included 48 subjects with advanced lung cancer. Patients were randomized to structured assessment or usual care and assessed several times over a six-month period. A total of 21 patients remained in the study at six months. Pain symptoms (frequency and severity) did not significantly differ between the intervention and control groups across time. The Jadad score for this study was 2.

In a study published in 2002, Detmar and colleagues²²² evaluated the efficacy of standardized health-related quality of life assessments in improving patient-provider communication and increasing provider awareness of patient needs. Patients undergoing palliative chemotherapy (n=214) were randomized to the intervention or to usual care. Intervention patients were assessed at three successive outpatient visits. The study reported no statistically significant differences on measures of pain at the final visit for intervention patients as compared to controls. The Jadad score for this study was 2.

Dyspnea

Systematic Reviews of Dyspnea

We identified five systematic reviews addressing the topic of dyspnea in the context of end-of-life care. One of the reviews focused specifically on dyspnea in cancer patients, one on patients with COPD, and three on mixed disease. The review described previously by Gysels and Higginson⁷² also included studies addressing dyspnea. In this review, the authors summarized six studies regarding dyspnea, including the systematic review by Pan et al.²¹⁶ Two additional studies were randomized controlled studies, two were qualitative, and one was observational. The sample sizes ranged from 34 to 207 patients and two of the studies focused specifically on dyspnea in a patient population with lung cancer. Interventions included a nurse (RN) clinical intervention, a nurse (NP) CAM intervention, home care with a focus on dyspnea treatment, palliative care services, and one with an unclear intervention. Four of the five interventions described in these research studies (excluding the systematic review) demonstrated beneficial results by reducing the symptoms of dyspnea and/or the anxiety associated with dyspnea.

In a separate review study, Salman and colleagues²¹³ searched three databases as well as the reference lists of selected studies and unpublished studies from meeting abstracts to identify RCTs that included interventions to relieve dyspnea through rehabilitation (either upper-extremity, lower-extremity, and/or respiratory muscle exercises) for patients with COPD. The study authors applied strict criteria for identifying studies with the intended population; however, it is not clear how much of the patient populations included were at the end of life. The authors

selected studies in which the clinical status of the patients was reported and in which patients had a diagnosis of COPD and had an forced expiratory volume (FEV1) < 70% of predicted value or an forced expiratory volume / forced vital capacity (FEV1/FVC) < 70% of predicted value. A total of 12 RCTs including in total 723 patients were identified that assessed dyspnea.

Intervention studies that included at least lower-extremity training (11 of 12 trials) reported significant improvements in dyspnea. Interventions lasting six months or longer had better outcomes for those with severe COPD while both short and long-term interventions improved dyspnea for patients with mild to moderate COPD. A meta-analysis of the selected studies yielded a beneficial overall effect (OR: 0.62, 95% CI: 0.26, 0.91). Among those with mild to moderate COPD, the total effect based on nine studies was not statistically significant (OR: 0.69, 95% CI: 0.24, 1.14). Among those with severe COPD, the total effect based on three studies was significant (OR: 0.42, 95% CI: 0.02, 0.84).

The study by Pan et al.²¹⁶ described previously also examined the literature on CAM in treating dyspnea. The interventions included in this review of the literature on dyspnea were acupuncture, acupressure, and behavioral/psychological therapies. A total of six intervention studies were identified; four of these studies explored dyspnea relief for patient populations with COPD and two addressed cancer-related dyspnea. We summarize the findings from this review below by type of intervention, and further details regarding these citations can be found in the systematic review by Pan et al.²¹⁶

Acupuncture: In a single-blind RCT, 24 COPD patients were randomized to receive 13 sessions of acupuncture over three weeks or sham acupuncture over the same time frame. At the end of the study, the intervention group had less subjective breathlessness and could walk further in a six minute walking test. In a prospective study of 20 patients with cancer-related dyspnea, 70% of patients reported symptomatic improvement lasting up to six hours after acupuncture treatment.

Acupressure: One study was identified that examined acupressure in a single-blind RCT (with crossover) as a treatment for dyspnea. In this study, 31 patients with COPD were randomized to a six-week course of self-administered acupressure alternating with six weeks of sham acupressure. Those in the intervention group experienced a significant reduction in dyspnea symptoms at the end of the study.

Behavioral and Psychological Therapies: Three studies were identified that addressed behavioral or psychological therapies with respect to dyspnea. In one RCT of 20 COPD patients, the authors randomized patients to an intervention of progressive muscle relaxation or usual care and advice to try to relax for 45 minutes a day. The study authors found that, in the intervention group, dyspnea symptoms improved with each session. However, there was no overall improvement over the course of the study. Another double-blind RCT of 65 patients with COPD reported less dyspnea when measured by the Fletcher scale for those who received nurse therapy (which consisted of reassurance without psychotherapeutic training) compared to those who received supportive therapy with psychoanalysis, analytic therapy, and a control group. There was however, no difference in the experience of dyspnea as measured by a visual analogue scale. A third RCT of 20 patients with small cell and non-small cell lung cancer incorporated a one-hour session with a nurse practitioner for three to six weeks in which the patient learned exercises, received counseling, relaxation techniques, and coping/adaptation strategies versus usual care to address dyspnea. After three months, the intervention group reported 35%

improvement in dyspnea, 53% improvement in distress, and 17% improvement in functional capacity.

The fourth review study, published by Jennings and colleagues,²¹⁵ considered the evidence regarding the use of opioids in the management of dyspnea. The authors searched eight electronic databases as well as hand searched reference lists of selected articles and textbooks on the subject. Only double-blind, randomized, placebo-controlled trials were included in this review. A total of 18 studies met the criteria for review. All studies had a crossover design. Nine of the studies examined the use of oral or parenteral opioids and nine examined the use of nebulized opioids. Meta-analysis of the studies (the subset of 13 with the necessary level of detail in the data) demonstrated an overall beneficial effect of opioids on the management of dyspnea (standardized mean difference (SMD): -0.31 ; 95% CI: $-0.50, -0.13$). Analyses were split by mode of opioid delivery (nebulized or non-nebulized) and the authors found a similar significant effect for the non-nebulized forms of opioid delivery (SMD: -0.40 ; 95% CI: $-0.63, -0.17$) but not for the nebulized forms (SMD: -0.11 ; 95% CI: $-0.32, 0.10$). An additional meta-analysis was conducted to explore the pooled effect of opioids on exercise tolerance, which failed to demonstrate a statistically significant beneficial effect (SMD: -0.20 ; 95% CI: $-0.42, 0.03$).

The most recently published review specifically addressing the research on the treatment of dyspnea was published by Booth and colleagues in 2004.²¹² The search strategy for this review included a search of three databases, the references of selected papers, and a hand search of key journals in the field. The authors identified 34 randomized controlled trials that examined the use of oxygen in the management of dyspnea for patients with COPD, advanced cancer, and heart failure. Studies were organized and evaluated both around the type of intervention (short- or long-term oxygen therapy) and by patient cohort (COPD at rest, COPD before, during, and after exercise, advanced cancer, and chronic heart failure). All studies, with one exception, included a crossover design. Short-term oxygen therapy for COPD patients at rest led to significant improvement in dyspnea in two out of five studies. Among the studies that included oxygen along with an exercise program, 18 out of 22 had a positive result; in most cases, the intervention led to a slower increase in dyspnea and/or increased endurance rather than simply reduced dyspnea on oxygen. Long-term oxygen therapy had little if any effect on COPD patients with dyspnea. Two of three studies focusing on the management of dyspnea in advanced cancer produced significant improvements in dyspnea with an oxygen intervention. Only one of three studies employing oxygen in the management of dyspnea for patients with chronic heart failure reported a positive finding.

Additional Interventional Studies of Dyspnea

An additional ten randomized controlled studies were identified that explored the role of different interventions on reducing dyspnea in palliative care populations.^{230, 231, 222, 232-236} These studies were all published between 1993 and 2003 and were not included in the systematic reviews described above either because they did not meet the disease cohort criteria or the intervention criteria. Eight of the intervention studies focused on cancer patients, one focused on patients with chronic heart failure, and one focused on patients with chronic obstructive pulmonary disease (COPD).

Three of the randomized controlled studies reported on interventions incorporating oxygen to relieve dyspnea in cancer patients.^{231, 236, 237} Booth and colleagues²³¹ administered oxygen or air

to 38 hospice patients with advanced cancer and dyspnea at rest in a single-blind randomized controlled trial with crossover (20 initially receive oxygen, 18 received air). Patients received either oxygen or air for 15 minutes and then were switched to receive the other. This treatment was repeated; however, the authors do not report the number of times the crossover took place. There was significant relief from dyspnea reported for all patients after receiving air ($p < 0.001$) or oxygen ($p < 0.001$) as compared to baseline. However, there was no significant difference in mean dyspnea scores between air and oxygen administration. Analyses of patients stratified by coexisting drug therapy indicate that those on morphine only, benzodiazepine only, or morphine and benzodiazepine had significantly reduced dyspnea with oxygen while those with neither drug therapy had non-significant differences in reported dyspnea with oxygen or air. The Jadad score for this study was 2.

In a double-blind randomized controlled trial with crossover, Bruera and colleagues²³⁷ assessed the effects of oxygen on the reported intensity of dyspnea in 14 patients with terminal cancer. Patients were randomized to receive oxygen or air for five minutes at which time patients were switched to the other. This process occurred twice each for oxygen and air. Reports for oxygen saturation, respiratory effort, respiratory rate, and the 100-point visual analogue scale (VAS) for dyspnea were all significantly better with oxygen than with air. The Jadad score for this study was 2.

In another more recent study by Bruera et al.,²³⁶ the authors explored the effectiveness of oxygen over air in decreasing dyspnea and fatigue and increasing distance walked during a six-minute walk test in a randomized, double-blind crossover trial. Of the 33 evaluable patients in this study, 31 had lung cancer and all had advanced cancer. Patients were randomized to receive oxygen or air during the first treatment and then switched to air or oxygen for the second treatment. In each treatment phase, the patients performed a six-minute walk test. Contrary to earlier findings by the same author, there were no significant differences between treatment groups in dyspnea, fatigue, or distance walked. The Jadad score for this study was 5.

One randomized controlled²³⁰ trial evaluated the effect of specific inspiratory muscle training (SIMT) on dyspnea in 20 patients with moderate heart failure. Ten patients received training in SIMT and the other ten received sham training. Both groups trained 30 minutes a day, six times a week over a three-month period. Inspiratory muscle strength measured by Pimax increased in the intervention group from 46.5 ± 4.7 to 63.6 ± 4.0 cm H₂O ($p < 0.005$). Endurance increased significantly in the intervention group ($p < 0.05$) but remained unchanged in the control group. Intervention group members were also able to walk further in a 12-minute walk test than control group members after completion of training ($p < 0.01$). Based on the dyspnea index (0–4 scale), intervention group members significantly improved ($p < 0.005$) while control group members remained unchanged. The Jadad score for this study was 2.

Three studies identified in our review examined the efficacy of morphine in relieving dyspnea.^{232, 234, 235} All three studies employed a randomized controlled trial design with crossover. Two of the studies employed patient samples with terminal cancer^{232, 234} and the third employed a sample with COPD.²³⁵ Mazzocato and colleagues²³² randomized nine patients with lung cancer to receive morphine subcutaneously or a placebo on day 1. The intervention crossed over to the control group on day 2. Morphine doses ranged from 5 mg to 11.25 mg q4h. Mean changes in dyspnea based on a 100-point VAS were -25 ± 10 mm and 0.6 ± 7.7 mm in the intervention and control groups, respectively ($p < 0.01$). Significant improvements were observed in the intervention group relative to the control based on the Borg scale as well ($p = 0.03$). There

were no significant changes in somnolence, pain, anxiety, respiratory effort, respiratory rate, and oxygen saturation. The Jadad score for this study was 2.

In the study by Bruera and colleagues,²³⁴ ten consecutive patients with terminal cancer were randomized to receive subcutaneous injections of morphine or placebo. Patients were crossed over on the subsequent day. Morphine provided substantial relief from dyspnea at 30-minute ($p<0.02$), 45-minute ($p<0.01$), and 60-minute ($p<0.01$) follow-up assessments. There were no significant differences in O₂ saturation or respiratory rate between the intervention and placebo groups. The Jadad score for this study was 0.

Abernathy and colleagues²³⁵ evaluated the efficacy of orally administered morphine in 48 patients with predominantly COPD and dyspnea. This study was the only one of the three that was explicitly described as a double-blind trial. Patients were randomized to receive 20mg of morphine sulphate with sustained release or placebo. After four days, patients were crossed over. Thirty-eight patients completed the trial. Based on a 100mm visual analog scale, patients receiving morphine had a mean improvement in dyspnea scores of 6.6 (sd=15) in the morning ($p=0.011$) and 9.5 (sd=19) in the evening ($p=0.006$). The Jadad score for this study was 5.

In the study by Detmar et al.²²² described above in the section on pain, the authors also evaluated the efficacy of standardized health-related quality of life assessments in improving patient-provider communication and increasing provider awareness of patient needs related to dyspnea. No statistically significant differences were found for measures of dyspnea at the final visit for intervention patients as compared to controls. The Jadad score for this study was 2.

The study by Rabow et al. investigated the influence that an outpatient palliative medicine consultation had on symptom relief.⁸⁶ In this study (described above in the section on pain), the authors reported a significant reduction in patient reports of the degree to which dyspnea interferes with daily activities ($p=0.01$) but no difference in the frequency that dyspnea limits activities ($p=0.07$). The Jadad score for this study was 3.

In another more recently published study, Jordhoy and colleagues²³³ examined how palliative care provided in cooperation between a hospital palliative medicine unit and community-based care improved on patient symptoms relative to usual care. Randomization in this study occurred at the community healthcare district. Cancer patients within these districts received the intervention or usual care ($n=235$ intervention; $n=199$ control) and followed for four months. No significant differences in patient ratings of dyspnea were found. The Jadad score for this study was 3.

Depression and Anxiety

Systematic Review of Depression and Anxiety

Our search identified two research evidence reports that covered the topics of depression and anxiety. We chose to address depression and anxiety together because many reports that address one also address the other, although that is not uniformly the case. One report addressed depression as part of a systematic review of the literature on the management of cancer symptoms.³⁴ This study was produced by the New England Medical Center Evidence-Based Practice Center and was described in detail earlier in the section on pain symptoms. The other report is an unpublished review of studies to improve supportive and palliative care for adults

with cancer.⁷² This report, produced by Gysels and Higginson, was also described in detail above in the section on pain symptoms.

The methods applied to develop the evidence report published by the New England Medical Center Evidence-Based Practice Center have been described previously. Only meta-analyses and randomized controlled trials in the topic of depression were included in this report. Eleven controlled studies were identified that explored the effects of medications on depressive symptoms. Nine were primarily treatment studies on depressive symptoms, and one was a study that explored both pain and depressive symptoms. One study was a depression prevention study. Four studies explored the efficacy of selective serotonin reuptake inhibitors (SSRIs) for depression in cancer patients. Other intervention medications included thioridazine, imipramine, methylprednisolone, mianserin, mazindol, alprazolam, trazadone, and amitriptyline. With the exception of two studies with mazindol and amitriptyline, all medications classified as antidepressants reported benefit for cancer patients. Three meta-analyses were identified that explored the efficacy of psychosocial interventions in treating depressive symptoms in cancer patients. Two of the meta-analyses focused on psychoeducational interventions for general cancer symptoms. One meta-analysis focused specifically on anxiety and depression. The interventions identified in this analysis included individual therapy, relaxation, group therapy, group therapy excluding psychoeducation, and group psychoeducation. A small to medium effect size was reported, but the low quality of the studies ultimately decreased the effect size.

The methods applied to develop the Gysels and Higginson review have been described previously. Twenty-four articles out of a total of 302 studies explored the topic of depression and anxiety. Six of the identified studies addressed depression alone or with other unrelated symptoms (i.e., pain, dyspnea), nine addressed anxiety alone or with other unrelated symptoms, and nine addressed both depression and anxiety. Of the 24 studies, 14 were randomized controlled trials, four were observational studies, one was qualitative, four were systematic reviews and one had an unclear design. Interventions in these studies included behavioral interventions (e.g., group/individual cognitive-behavioral therapy), systems/institutional interventions (e.g., hospital at home, hospice, palliative care teams), education, and complementary and alternative medicine (CAM). The behavioral interventions reported generally beneficial outcomes for anxiety and depression among cancer patients. Systems/institutional interventions produced mixed results; one study on comprehensive hospice care and one on palliative care teams did not report significant improvements in anxiety and/or depression. The other four studies with similar interventions reported beneficial results, however. An educational intervention to address cancer pain significantly reduced anxiety associated with pain. CAM interventions including homeopathy, relaxation, acupuncture, and massage demonstrated reductions in anxiety for cancer patients, but a nurse practitioner-run intervention of CAM did not yield improvements in depression among patients.

Additional Interventional Studies of Anxiety and Depression

Five studies were identified that included interventions to improve depression, and two were identified that addressed anxiety. Schofield et al.²³⁸ performed a pilot study using a randomized controlled trial design to investigate the use of the Snoezelen multisensory environment in a palliative day care setting for patients with anxiety. Twenty-six patients were recruited as subjects. The intervention consisted of access to the Snoezelen for one hour on two separate occasions. Control group subjects were given access to a quiet room. Assessments of anxiety were made immediately following access to these two environments. A brief semi-structured

interview was conducted with experimental group patients only at the completion of the trial session. A significant reduction in anxiety was seen with the experimental group, but the investigators reported no changes in quality of life. Semi-structured interviews revealed that experimental group patients experienced higher levels of relaxation. The Jadad score for this study was 3.

Soden et al.²²⁴ conducted a study to compare the effects of four-week courses of aromatherapy massage and massage alone on psychological symptoms (depression and anxiety) in patients with advanced cancer (this study was previously described above). There were no significant long-term benefits of aromatherapy massage in the improvement of anxiety. There were significant improvements in patients with depression and data suggested that aromatherapy massage may have a beneficial effect on sleep quality for advanced cancer patients.²²⁴ The Jadad score for this study was 5.

In a similar randomized study, Wilkinson et al.²³⁹ performed a study to assess the effects of massage and aromatherapy massage on cancer patients in a palliative care unit. A total of 103 patients were accrued. Subjects received either massage using an inert carrier oil (control) or a carrier oil plus Roman chamomile essential oil (intervention). Of the 103 subjects, 46 were randomized to the aromatherapy group and 57 to the control group. Unlike the Soden study, this study reported a statistically significant reduction in anxiety across all allocated groups. The aromatherapy group reported a significant decrease in psychological distress with improvement in QOL. The massage group reported improvements as well, but this was not statistically significant. The Jadad score for this study was 3.

In a third study employing CAM, Stephenson and colleagues²⁴⁰ tested the effects of foot reflexology on anxiety and pain in breast and lung cancer patients. In this study, 23 inpatients were allocated to the intervention or control in a quasi-experimental, pre/post crossover design. Anxiety, measured using a 100mm visual analog scale was significantly reduced in patients receiving reflexology relative to the control ($p < 0.0001$). The Jadad score for this study was 1.

Gottlieb et al.²⁴¹ explored the effect of an exercise program on patients with moderate to severe heart failure on performance and quality of life including depression. Thirty-three patients were randomized to usual care or an exercise program consisting of aerobic training three times a week for six months. Depressive symptoms, measured by the CES-D, did not differ significantly between the intervention and control groups. The Jadad score for this study was 2.

In a randomized controlled trial, Rabow et al.⁸⁶ explored the efficacy of an interdisciplinary palliative care team on psychological outcomes. This study was described above in the section on pain interventions. There were no significant changes in anxiety or depression levels in the intervention group. The Jadad score for this study was 3.

Addington-Hall et al.²⁴² conducted a randomized controlled trial to explore the efficacy of coordinating care for terminally ill cancer patients on the presence and severity of psychological morbidity. A total of 554 patients were accrued and randomized. Of this total, 318 were randomized to receive coordination care, and 236 were allocated to the control group. The intervention included access to a coordination care team (made up of community-based nurses) who assessed the need for services and offered advice on how to obtain these services. Overall, there were no significant differences between the presence and severity of psychological morbidity across both groups. The Jadad score for this study was 2.

Behavioral Issues in Dementia

Systematic Reviews of Behavioral Issues in Dementia

A total of three systematic reviews were identified that addressed behavioral symptoms in patients with Alzheimer's disease or some other form of dementia.²¹⁷⁻²¹⁹ We summarize the findings from these systematic reviews below. An additional four intervention studies were identified that were either published after the systematic reviews were completed or addressed the same symptoms in another way.

Three systematic reviews were identified that addressed the topic of dementia.²¹⁷⁻²¹⁹ All three reviews addressed dementia in the context of Alzheimer's disease. Two of the systematic reviews focused on interventions for behavioral symptoms in dementia.^{217, 218} One study by Forbes²¹⁹ described the use of different strategies to manage behavioral symptoms in Alzheimer's disease. The author searched published and unpublished literature specifically for interventions addressing the following symptoms/activities: aggressive/agitated/disruptive behaviors, social interaction, self-care ability, day/night disturbances, and wandering. Forty-five studies published between 1985 and 1997 were identified. Only one was rated methodologically sound, with the majority (38) being weak or poor. The interventions addressed in the studies to affect the symptoms/activities described included music therapy (most common intervention type), skills training, visual barriers, exercise, bright light therapy, pet therapy, sensory integration, reality orientation, presence, therapeutic touch, life review, and white-noise therapy.

The author reported that exercise in the form of a planned walking program, bright-light therapy, music therapy, written cues, and simulated presence therapy all produced improvements in behavior problems including agitation, aggression, and repetitive vocalizations. Therapeutic touch was the only intervention that did not report beneficial results on behavioral outcomes. Exercise was also successful in increasing communicative function in demented patients as were pet therapy, life-review therapy, and reality-orientation therapy. Music therapy and small-group activities reported non-significant trends toward improvements in communicative function. Music therapy and skills-training interventions were both successful in increasing self-care ability whereas a sensory-integration program did not have a significant effect on this outcome. Bright light therapy and music therapy were used in interventions to normalize sleep patterns and produced beneficial, clinically significant results, although it is unclear that those results were statistically significant. Visual barriers were somewhat effective in reducing episodes of wandering among patients with dementia, particularly Alzheimer's and Parkinson's disease patients.

Opie et al.²¹⁸ explored the use of psychosocial approaches to behavioral disorders in people with dementia. The authors conducted searches using four databases for materials published between 1989 and 1998. Forty-three papers were included in the review; one had a strong methodological rating, 15 were rated as moderate, and 27 as weak. The following interventions were identified for the review: changes to the physical environment; activity programs; exposure to music, voice, and language; behavior therapy; massage and aromatherapy; light therapy; multidisciplinary teams; and caregiver education.

Changes to the physical environment were made to reduce wandering in dementia patients. The results were mixed; studies that created grids on the floor to disrupt walking patterns were not effective, but covering the doorknobs with fabric or painting them the same color as the door

did reduce the number of exits among patients. Placing a mirror in front of the exit door also reduced the number of exits. Sensory stimulation through music, videos, conversation, and exercise was shown to reduce verbal outbursts and repeated requests for attention. Exercise was also successful in reducing wandering, aggressive incidents, and episodes of agitation. Music therapy was the topic of ten interventions in this review; all of these studies reported beneficial results with respect to distress and agitation in demented patients. Behavior therapy was not a common intervention identified in the literature; only two studies were cited and one was a case study. However, in both studies behavioral interventions were successful in training patients with dementia to change negative behaviors (verbal outbursts, entering other patients' rooms and taking personal items). Light therapy was reported as successful in three out of four interventions to reduce agitation and nocturnal disorientation. Massage and aromatherapy have been used with mixed results to reduce agitation among demented patients; two of three studies reported beneficial effects.

Finnema and colleagues²¹⁷ explored the efficacy of emotion-oriented approaches in the care for individuals suffering from dementia. The definition of emotion-oriented care provided by the authors focused on care aimed at improving emotional and social functioning. The authors searched six databases for studies published between 1990 and 1999 and focused on the following interventions: validation, sensory integration/stimulation, simulated presence therapy, and reminiscence. Six studies focusing on validation were identified; only one was a randomized controlled trial and the remaining five were observational studies of various designs. The RCT was not completed at the time the systematic review was published. The five observational studies reported improvements in behavior and mood using validation. However, the study designs had methodological limitations due to small sample sizes and lack of control groups. Six studies examined the role of sensory stimulation/integration on demented patients' behavior, mood and cognition. Most of these studies reported beneficial outcomes. However, again methodologic flaws in study designs limit our ability to draw conclusions regarding this intervention. Simulated presence therapy is a relatively new form of therapy to reduce aggressive behavior, agitation, wandering, and repetitive vocalizations in patients with dementia. Four studies were reviewed by the authors and reported some beneficial results. Five studies were identified that used reminiscence to reduce negative behavioral symptoms. The work in this area reported mostly beneficial results with regard to decreasing aggressive and attention-seeking behavior as well as disorientation and increasing social interaction.

Additional Interventional Studies of Behavioral Problems in Dementia

We identified four intervention studies published between 1996 and 2003 that addressed behavioral outcomes for dementia patients that were not otherwise summarized in the systematic reviews described above. Out of the five studies that explored dementia, two explored the efficacy of specific pharmacologic therapies on behavioral symptoms related to dementia. Manfredi et al.²⁴³ conducted an intervention study to determine the effect of opioids on agitation in demented nursing home residents who were unable to report pain. There was no comparison group for this study, and subjects were not randomized to intervention versus placebo. Subjects were administered placebo for four weeks, and the intervention consisted of a four-week regimen of long-acting opioids. Subjects and nursing home staff were blinded to the medication administered. Twenty-five subjects completed the regimen. Of the 25 evaluable subjects who were less than 85 years of age, no significant differences in agitation level was reported between the placebo and opioid phase. There was a decreased agitation level in 13 of the 25 patients who

were greater than 85 years of age at the end of the opioid phase. This decrease in agitation persisted after opioid dose adjustments for sedation. The Jadad score for this study was 0.

In a randomized, double-blind trial, Sultzer et al.²⁴⁴ explored the relationship between behavioral improvement in patients with dementia who were treated on either haloperidol or trazodone. Twenty-eight patients in a geropsychiatry unit with dementia and agitation or aggressive behaviors were recruited. The intervention consisted of either haloperidol 1 mg or trazodone 50 mg. Dose escalation of one capsule was initiated if agitated symptoms worsened. In the haloperidol treatment group, improvement in behavioral symptoms was not associated with baseline delusional scores or with change in delusional scores over the course of the treatment. In the trazodone group, behavior symptom improvement was associated with improving depressive symptoms and neurovegetative signs. The investigators concluded that the use of trazodone in demented patients with mild depressive symptoms was associated with greater behavioral improvement. The Jadad score for this study was 2.

Two of the five studies exploring dementia focused on improving dementia care in nursing homes. Rogers et al.²⁴⁵ examined the effectiveness of a behavioral rehabilitation intervention for improving morning care activities of daily living in nursing home residents with dementia. Eighty-five residents participated in the study. Interventions consisted of activities in two different conditions. Patients in the usual care (condition 1) group received assistance in care by nursing home staff who were consistently assigned to care for them. Patients in the condition 2 group received skill elicitation intervention by a research therapist designed to identify and elicit retained ADL skills. The condition 2 group also received habit training intervention to continue to reinforce and solidify retained skills. ADLs monitored included dressing, bathing, and grooming. The experimental group residents reported an increase in the proportion of time engaged in nonassisted and assisted dressing and increased overall participation of ADL. There was also a concurrent decrease in disruptive behavior for the residents who received the intervention. The Jadad score for this study was 0.

Rovner et al.²⁴⁶ explored the efficacy of a dementia care program to reduce behavior disorders in nursing home residents with dementia. A total of 89 patients were accrued and randomized, and 81 subjects completed the trial. The intervention included an activity program during the day, psychotropic drug management, and educational grand rounds for staff where discussions of individual cases were made. Control treatment included usual nursing home care. Forty-two patients were randomized to the experimental group, and 39 to the control group. After a six-month follow-up, 12 of the 42 intervention patients exhibited behavioral disorders compared with 20 of the 39 control subjects. Control group residents were twice as likely to receive antipsychotic medications and to be restrained. There was more voluntary participation from the intervention group residents. The Jadad score for this study was 3.

Observational Studies and Symptoms

We identified 14 prospective observational cohort studies that addressed one or more of the symptoms and the site of care/condition/race characteristics we considered. Of these 14, four addressed pain management, two addressed delirium in cancer patients, three addressed behavioral problems in dementia patients, and five considered depression in the context of cancer of CHF populations. We highlight the findings of some of these studies here. More detail about the selected studies can be found in the Observational Evidence Table.

None of the studies identified here or in the previously discussed literature reported results separately by race or ethnic groups. Much of the research addressing end-of-life care in different racial/ethnic groups has been done in cross-sectional observational studies and thus was not considered here. More research is clearly needed about how different interventions affect different race/ethnic groups.

In the study by Goodwin et al.,²⁴⁷ the authors compared patients receiving palliative day care to those receiving usual palliative care services (i.e., in the hospital or home). The palliative day care model did not produce better outcomes than usual care. The authors cite limitations of quality of life measures and their current inability to capture all the dimensions of quality of life important to an individual as part of the reason that no differences were observed.

Three studies were selected because they dealt with the treatment of symptoms in a dementia population and where the setting was the nursing home. Nursing home use is associated with an increased incidence of dementia.²⁴⁸ Two of the studies^{249, 250} examined the use of pharmaceutical interventions (e.g., risperidone for behavioral disturbance in dementia and antibiotics for pneumonia) in improving symptoms and quality of life for dementia patients residing in nursing homes. These studies demonstrate that such interventions can have an important impact on the care of demented residents and that nursing homes can be the site of active intervention and not just custodial care for such residents.

Four studies focused on heart failure and depression.²⁵¹⁻²⁵⁴ The exposure in each study was a diagnosis of depression; each demonstrated that depression was significantly associated with poor prognosis, worsening health status, poor functional status, and an increased utilization of health services. These studies indicate the importance of the diagnosis and treatment of depression in heart failure to improve a variety of clinical and quality of life outcomes.