Evidence Report/Technology Assessment
Number 110

End-of-Life Care and Outcomes

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. 290-02-0003

Prepared by:
Southern California Evidence-Based Practice Center
RAND Corporation, Santa Monica, CA

Principal Investigators
Karl Lorenz, MD
Joanne Lynn, MD

Director
Paul G. Shekelle, MD, PhD
Senior Statistician/Co-Director
Sally C. Morton, PhD
Project Manager/Policy Analyst
Margaret Maglione, MPP
Reviewers
Sydney Dy, PhD
Ronda Hughes, PhD, MHS, RN
Richard Mularski, MD
Lisa Shugarman, PhD
Virginia Sun, RN
Anne M. Wilkinson, PhD

Programmer/Analyst
Lara Hilton, BA
Database Manager
Shannon Rhodes, MFA
Research Assistant
Hsien Seow, BS
Staff Assistant
Cony Rolón, BA

AHRQ Publication No. 05-E004-2
December 2004

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Suggested Citation:
Lorenz K, Lynn J, Morton SC, Dy S, Mularski R, Shugarman L, Sun V, Wilkinson A, Maglione M, Shekelle PG. End-of-Life Care and Outcomes. Evidence Report/Technology Assessment No. 110. (Prepared by the Southern California Evidence-based Practice Center, under Contract No. 290-02-0003.) AHRQ Publication No. 05-E004-2. Rockville, MD: Agency for Healthcare Research and Quality. December 2004.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. This report was requested and funded by the National Institute of Nursing Research, National Institutes of Health (NIH). The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the healthcare system as a whole by providing important information to help improve health care quality.

We welcome comments on this evidence report. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to **epc@ahrq.gov.**

Carolyn M. Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.
Director, Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Patricia A. Grady, Ph.D., R.N., F.A.A.N.
Director
National Institute of Nursing Research, NIH

Kenneth S. Fink, M.D., M.G.A., M.P.H.
Director, EPC Program
Agency for Healthcare Research and Quality

Ronda G. Hughes, R.N., M.H.S., Ph.D.
EPC Program Task Order Officer
Agency for Healthcare Research and Quality

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Structured Abstract

Context: The "end-of-life" refers to a prolonged, difficult period for patients and caregivers. Nine-tenths of Medicare-insured elderly live with a serious, chronic condition before death. Due to our aging population, Americans will increasingly face such challenges.

Objectives: Focusing on the outcomes patient and family satisfaction; pain, dyspnea, depression and anxiety and behavioral problems in dementia; continuity; caregiving burden other than bereavement; and advance care planning, we conducted a systematic review to evaluate the following:

1. The scope of the end-of-life population.
2. Outcome variables that are valid indicators of the quality of the end-of-life experience for the dying person and surviving loved ones.
3. Patient, family, and healthcare system associated with better or worse outcomes at end-of-life.
4. Processes and interventions associated with improved or worsened outcomes.
5. Future research directions for improving end-of-life care.

Data Sources: MEDLINE®, Database of Reviews of Effects (DARE), the National Consensus Project for Quality Palliative Care, Toolkit of Instruments to Measure End-of-life Care (TIME), and citations recommended by an international expert panel.

Study Selection: We focused on studies in the Western literature related to adult patient or caregiver end-of-life outcomes published between 1990 and April 2004, excluding studies of chemotherapy, radiotherapy, and similar technical care.

Data Extraction: We identified a total of 24,423 citations from all sources; 5,216 went on to abstract review, of which 911 articles were considered for detailed review including 95 systematic reviews, 134 intervention, and 682 observational studies.

Data Synthesis: Evidence is strongest in cancer, reflecting the degree to which palliative care has been integrated into oncology practice. Studies demonstrate strong associations between satisfaction and communication, pain control, practical support, and enhanced caregiving. We identified high-quality measures of quality of life, satisfaction, quality of care, and symptoms. Strong evidence undergirds cancer pain and depression treatment, and small studies suggest that opioids benefit dyspnea. Caregiving studies demonstrated inconsistent effects and focused on dementia. Strong evidence supports interventions to improve continuity in cancer and congestive heart failure (CHF), although CHF studies lack generalizability and palliative outcomes. Inconsistent evidence supports advance care planning, although studies often measure utilization rather than patient and family-centered outcomes.

Conclusions: We identified a number of priorities including a need to (1) characterize the implications of alternative definitions of the "end-of-life"; (2) test measures in diverse settings and populations; (3) in studies of satisfaction, emphasize specific process, especially those less-studied (e.g., non-pain symptoms, spiritual support, and continuity); (4) address methodological

challenges in measurement; (5) conduct studies of the epidemiology and clinical significance of symptoms in non-cancer conditions; (6) conduct larger studies of interventions for dyspnea; (7) conduct studies of short- as well as long-term treatment of depression; (8) conduct studies of caregiving in populations other than cancer and dementia; (9) evaluate economic and social dimensions of caregiving; (10) in continuity research, emphasize common settings (e.g., ambulatory care) and studies of nursing home-hospital continuity and involving multiple providers; and (11) in studies of continuity in CHF, incorporate palliative domains and ensure that studies are generalizable to the sickest patients.

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Agency for Healthcare Research and Quality

Evidence Report/Technology Assessment

Number 110

End-of-Life Care and Outcomes

Summary

Authors: Lorenz K, Lynn J, Morton SC, Dy S, Mularski R, Shugarman L, Sun V, Wilkinson AM, Maglione M, Shekelle PG

Overview

To evaluate progress in the field of end-of-life care and clarify research priorities, the National Institute of Nursing Research (NINR), with the Agency for Healthcare Research and Quality (AHRQ), commissioned this evidence report as the basis for a State-of-the-Science Conference in December 2004. The need for such an assessment is clear. More than 75 percent of Americans now live past age 65, and 83 percent of Americans now die while covered by Medicare.[1] In 2000, the average life expectancy for Americans was 80 years for women and 74 years for men, compared to just 49 years in 1900.[2] By 2050, life expectancy for women and men will likely increase to 84 and 80, respectively.[3] A century ago, death came to most Americans suddenly. Today, many Americans live their last years with a chronic health condition, and about 40 million people, 15 percent of the adult U.S. population, are limited in activities from such a condition.[4, 5] Population aging patterns suggest that in the coming decades, larger numbers of Americans will be coping with serious impairments late in life. For the relatively healthy, a care system focused on curing acute intermittent illness is adequate. For persons living with advanced, chronic disease, neither prevention nor cure are ordinarily possible. Instead, patients and families struggling with serious illness have other concerns, including managing pain and other symptoms, coordinating care among multiple providers and settings, ensuring that treatments reflect preferences and balance benefits and harms as well as medical appropriateness, achieving empathic communication and care, fostering well-being (including spiritual concerns), maintaining function, and practically supporting family and caregivers through illness and bereavement.

Reporting the Evidence

This report addresses the following key questions:

1. **What outcome variables are valid indicators of the quality of the end-of-life experience for the dying person and for the surviving loved ones?**
   a. What individual outcome measures are most strongly associated with overall satisfaction with end-of-life care?
   b. What is the reliability and validity of specific instruments for measuring quality of life or quality of care at the end-of-life?
2. **What patient, family, and health care system factors are associated with better or worse outcomes at end of life?**
   a. What individual patient factors (e.g., age, gender, race/ethnicity, underlying illness, education, etc.) are associated with better or worse outcomes at end of life?
   b. What family factors (e.g., relationship to patient, race/ethnicity, etc.) are associated with better or worse outcomes at end of life, including both outcomes reported by the family and how the family affects outcomes experienced by the patient?
   c. What health care system factors (e.g., site of care, type of provider, support services, etc.) are associated with better or worse outcomes?

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3. **What processes and interventions are associated with improved or worsened outcomes?**
   a. What is the effectiveness of specific healthcare interventions for improving specific outcomes in patients at the end of life?
   b. Does effectiveness of specific interventions vary among different populations?
4. **What are future research directions for improving end-of-life care?**

Methodology

A multidisciplinary Technical Expert Panel (TEP) was formed to assist the Southern California Evidence-based Practice Center with its review and to guide the evidence report. The TEP included leading scientists and clinicians in nursing, gerontology, and palliative medicine, and others with a broad knowledge of relevant research and policy issues in both the United States and Europe. Research reviewers included an oncology nurse, an intensivist (a physician who specializes in the care of critically ill patients), a general internist, palliative care physicians, and gerontologists.

The sponsors decided to focus only on adults and identified as a priority the evaluation of interventions related to managing symptoms, enhancing communication, enhancing spirituality, withdrawing technology, facilitating family caregiving, and enhancing grief resolution. A decision was also made to focus on three clinical common, representative conditions. Thus, as an organizing principle, our analysis deliberately highlighted evidence that illuminated the end of life as lived with cancer, chronic heart failure, or dementia. Cancer patients experience a somewhat predictable decline and are often served by hospice in their final weeks. In contrast, patients with organ system failure (e.g., congestive heart failure [CHF], chronic obstructive pulmonary disease [COPD]) may experience stable but impaired function punctuated by unpredictable, severe illness and rather sudden death[6-8] and are rarely served by hospice. In further contrast, patients with dementia have prolonged declines and often reside in nursing homes.[9, 10]

TEP members were asked to prioritize potential topics for the report based on relative importance at the end of life, relationship to patient experience, feasibility, relevance to care and policy, the availability of recent reviews on the topic, ability of the topic to illuminate differences in the strength of research in important clinical areas of palliative care, and modifiability in clinical practice and policy.[11] With the TEP's assistance, we decided to focus on the following topics:

- Satisfaction with care.
- As patient-centered concerns, the symptoms of pain, dyspnea, depression, anxiety, and behavioral symptoms associated with dementia.
- As family and caregiver concerns, caregiver burden excluding bereavement.
- As health system concerns, continuity of care.
- As a concern that requires coordinated action among patients, caregivers, and the healthcare system, advance care planning (ACP).

Literature Search and Review

A comprehensive search of the medical literature was conducted to identify studies addressing the key questions. Staff reviewed relevant articles, compiled tables of study characteristics and results, appraised the methodological quality of the controlled trials, and summarized results.

Sources for our review included MEDLINE®, the Cochrane Database of Reviews of Abstracts of Effects (DARE), the National Consensus Project for Quality Palliative Care, and several recent systematic reviews from both Health Canada and National Institute for Clinical Excellence (NICE), United Kingdom. We also used the 2000 Toolkit of Instruments to Measure End of Life Care (TIME). Additional studies were identified primarily through searches by U.S. National Library of Medicine (NLM) staff, complemented by RAND library searches. The searches were limited to published articles in the English language, appearing in journals between the years 1990 through 2004, involving human subjects, and did not include individual case reports. NLM staff conducted the first search of PubMed® in April 2004.

At the title screening stage, citations that clearly met the following criteria were excluded: studies that enrolled only a pediatric population (age 18 years and under); those that were case studies with fewer than 30 cases; those that did not consider palliative care; those that enrolled a non-Western population or were published in a non-English journal; reviews that were not systematic; clinical trials of chemotherapy, radiotherapy, stent, laser, endoscopy, or surgery (unless effects of the interventions were considered beyond effects on the primary disease process); descriptions of ethical, legal, or regulatory issues; descriptions of research processes; editorials, histories, personal narratives, and other descriptive non-clinical articles; articles about professional education (unless clinical or patient outcomes described); articles about organ transplantation or donation; articles that presented data only from prior to the mid 1980s; and studies in which the outcomes were lab or radiological tests or other physiological indicators. Approved titles moved on to an abstract screening phase.

The Report

Studies that satisfied the inclusion criteria are summarized in the evidence tables. The evidence tables provide detailed information about the study design, patient characteristics, inclusion and exclusion criteria, interventions evaluated, and the outcomes. The study sample size offers a measure of the weight of the evidence. Within the report, summaries of systematic reviews and intervention studies appear in an abbreviated form in tables, using summary measures of the main outcomes. Narrative text summarizes the findings and provides qualitative analysis in response to the key questions for each topic area.

Peer Review

Nine peer reviewers and TEP members reviewed our report. We compiled the comments and made appropriate changes to the report.

Findings

Literature Review

Of the 21,745 titles identified through literature searches, 5,563 were considered to be of possible relevance and subject to abstract review. The literature search of the DARE abstracts identified 92 titles; 62 were considered potentially relevant to our topic areas and proceeded to abstract review. Another 71 were added to the library of abstracts from the NICE guidelines, the Health Canada reports, the Toolkit of Instruments to Measure End of Life Care, and the files of our content experts. After eliminating duplicates and considering only citations for which an abstract was available, a total of 5,165 abstracts were reviewed.

Responses to Questions

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

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

We identified 10 systematic reviews, 12 intervention studies, and 17 observational studies on the subject of end-of-life care and patient or caregiver satisfaction. The preponderance of the interventional and observational literature supports the effectiveness of palliative care for improving both patient and caregiver satisfaction. Subjective measures of the end-of-life care experience include both satisfaction and quality-of-care measures, and these tools overlap significantly. Satisfaction or quality-of-care instruments that assess focused aspects of end-of-life care have been most useful in demonstrating the effects of interventions. Nonspecific satisfaction instruments or studies that use measures not specifically adapted for or developed for palliative care settings have often demonstrated ceiling effects. Possibly for that reason, effects of interventions on satisfaction have been somewhat inconsistent.

Measures of satisfaction that are more specific and strongly related to explicit intervention aims or processes (e.g., communication, pain control, practical support and enhanced caregiving) have demonstrated greater sensitivity to change and support a process-outcome relationship among these variables. The relationship of other processes or attributes of care (e.g., treatment of symptoms other than pain, spiritual support, continuity and coordination of care) to satisfaction is less evident in the literature, although such relationships are supported qualitatively. The ability to demonstrate relationships between these aspects of care and satisfaction may be partially related to challenges in defining spiritual support as an intervention and measuring spiritual support and continuity of care.

With regard to measures, our review identified one high-quality, widely recognized resource (Toolkit of Instruments to Measure End of Life Care) available on the World Wide Web at www.chcr.brown.edu/pcoc/bibliographies.htm that systematically reviewed and compiled recommended instruments for end-of-life research up to the year 2000. We updated and superceded this review, identifying 48 new measures to supplement the 35 existing recommended measures within the Toolkit. Measure development is most advanced for cancer populations or mixed populations that consist largely of cancer patients. The largest number of measures evaluated quality of life, quality of care, and symptoms. The literature documents many measurement challenges including proxy respondents, timing of interviews, and cognitive thresholds.

Key Question 2a: What individual patient factors are associated with better or worse outcomes at the end of life?

Key Question 3a: What is the effectiveness of specific healthcare interventions for improving specific outcomes in patients at the end of life?

As our outcomes, we considered the specific symptoms of pain, dyspnea, depression and anxiety, and behavioral effects of dementia, as well as caregiver burden. We reviewed 27 systematic reviews or meta-analyses because they addressed selected symptoms of a palliative care population. Of those 27, 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 focused on patients with COPD, three focused on patients with dementia, and another six did not limit their reviews to only one disease

cohort. We also reviewed 18 intervention studies and 14 observational studies that fulfilled our criteria.

The evidence base supporting the effectiveness of interventions for cancer pain is quite strong, but additional descriptive information about the experience of pain at the end of life for conditions other than cancer is needed. Studies of opioid treatment to relieve cancer pain were among the strongest in terms of study design. Few complementary and alternative medicine (CAM) interventions had a beneficial impact on pain relief; acupuncture and massage produced short-term pain relief in cancer patients. Studies of non-pharmacologic interventions—both CAM and mainstream—are small and of varied quality. None of the review studies and only four of the intervention studies included non-cancer patients; none of these studies focused on a single disease.

Several small, promising studies support the beneficial effect of opioids on dyspnea; one meta-analysis and three intervention studies reported mostly beneficial results for cancer and COPD. Relatively few studies have described the experience of dyspnea, despite the fact that dyspnea is a characteristic symptom of several important end-of-life conditions (e.g., advanced cancer, COPD, CHF). The evidence from the reviews and individual intervention studies does not strongly support a role for oxygen therapy in the management of dyspnea in cancer patients. Exercise interventions may have a beneficial effect on those with severe COPD and CHF but have not been tested in cancer patients. In small, short-term studies, acupuncture, acupressure, and relaxation therapy showed some clinical benefit.

Effective interventions have targeted the pharmacologic treatment of depression in cancer, but relatively few studies have evaluated short-acting drugs (e.g., non-Selective Serotonin Reuptake Inhibitors [SSRIs]) or the treatment of depression in non-cancer conditions. We identified one extensive review of the intervention literature regarding depression treatment in cancer patients. Of the seven interventions considered by this review, five focused on cancer patients. The other review and two intervention studies focused on other disease cohorts (one study focused specifically on depression in CHF patients, the other on mixed disease). SSRI's have been shown to be effective in treating depression in palliative care populations. Behavioral and CAM interventions have demonstrated mixed results.

Given the potential survival time after a diagnosis of dementia, it is not clear what proportion of the populations in studies evaluating interventions for behavioral problems in dementia are clearly near the end of life. The literature addresses many symptoms including aggressive/disruptive behavior, agitation, wandering, and mood lability. These studies suggest that a variety of non-pharmacologic therapies may be effective. Pharmaceutical interventions were the subject of only a few studies we identified and produced mixed results. Because the literature on dementia is beset by many methodological limitations, it is difficult to make definitive statements about the best treatment for these patients.

With regard to burdens of caregiving other than bereavement, we identified eight systematic reviews and meta-analyses that were relevant to family or informal caregiving. Three dealt with outcomes of caregivers for patients with dementia or other chronic illness, while five dealt with cancer patients or other life-threatening illnesses. We identified 13 additional studies assessing interventions and caregiver burden and 18 observational studies. Of these, seven studies evaluated the effect of caregiving interventions on terminally ill patients, nine studies investigated the impact of two critical transitions faced by many caregivers (nursing home placement or the death of the care recipient, and only two studies examined the needs of terminally ill non-cancer patients and their caregivers.

In general, a variety of interventions were studied for a broad range of caregivers (e.g., spouses, adult children, others), primarily caregivers to dementia patients.[12, 13] Palliative care caregiver interventions were studied mostly in terminal cancer patient caregivers,[14-17] usually as a supplement to clinical palliative care services being provided to the terminally ill patient. Most studies, whether on dementia or end-of-life caregiver interventions, focused on caregiver burden (objective and subjective burden) as the main outcome measure, but outcomes also included psychological distress (stress, depression), anxiety, coping skills, life satisfaction, health related quality of life, satisfaction with services or care, morale, rate of patient home death, rates of patient institutionalization, and costs.

Two kinds of interventions were used to address caregiver burden: individual and group interventions. The interventions included education, counseling, support groups, home health, hospice, or palliative care services to caregivers, singly, or in some combination. For the most part, intervention studies have reported inconsistent results. Larger treatment effects have been found for individual interventions, although group interventions predominate in the literature. Multi-component interventions and some respite services have shown positive (though small) impacts on caregiver burden. The inconsistencies in the literature may be attributable to the differences in the caregiver outcome measurement, research design, and analytical methods used.

With regard to continuity of care, we identified 9 systematic reviews that potentially dealt with the subject of continuity. We identified an additional 20 intervention studies and 17 relevant observational studies that met our criteria. A preponderance of evidence from systematic reviews and interventions support the efficacy of interventions to improve continuity of palliative

cancer care. In addition, we found some lower quality evidence that palliative HIV care could improve continuity of care. Interventions embody a variety of successful approaches including aspects of management, informational, and interpersonal continuity as well as comprehensive integrated care such as palliative care services. We found evidence for the effectiveness of interventions targeting care at multiple levels—provider, patient, provider/patient interface, and multiple settings but particularly home and hospital. Our review is limited in that it identified no evidence related to improving continuity across multiple sites of care.

Although we identified many effective interventions for improving continuity in CHF care, few of these explicitly addressed or reported patient-centered palliative outcomes (e.g., improvement in dyspnea, greater advance care planning, caregiving impact). However, interventions that improved continuity (often measured as hospital re-admission) share features of successful interventions in general, including longer intervention periods, coordination among providers, and regular, structured home assessment. Many CHF interventions specifically excluded patients who were 'terminally ill,' limiting their generalizability. Most interventions have targeted re-admission to the hospital or other kinds of high cost care, but interventions are needed to understand how to improve continuity in other settings as well.

The usual practice of advance directives and advance care planning is supported by little reliable scientific evidence of efficacy in improving outcomes. Improved communication and planning has some tendency toward improved patient and family satisfaction, and certainly anecdotes and small series point to patient and family frustration and disappointment with seriously flawed communication. Nevertheless, high quality research designs have not often been applied to these questions and, when applied, have shown quite modest effects, even upon increasing the rate of making decisions in advance. Whether improved advance care planning actually improves the experience for patients and their families has only thin and equivocal evidence.

Recommendations and Future Research

Our literature review identified a very large and diverse body of literature reflecting the tremendous growth and importance of the field of end-of-life care over the last decade. This review of the scientific evidence underlying key parts of the field of end-of-life care illuminates strengths of the field as well as opportunities for research. We identified evidence supporting the association of satisfaction and quality of care with pain management, communication, practical support and enhanced caregiving. The literature review identified evidence to support the effectiveness of interventions to improve satisfaction; ameliorate cancer pain, relieve depression in cancer, non-pharmacologic interventions for behavioral problems in dementia, and foster continuity in cancer and CHF care. Evidence is strongest in cancer reflecting the degree to which palliative care has already been integrated into the research agenda and clinical practice of oncology.

We also identified several opportunities for future research to strengthen the evidence base for end-of-life care. Our recommendations are as follows:

1. Research would benefit from characterizing the implications of alternative conceptual and operational definitions of the "end of life," particularly for important conditions. Efforts to define populations with specific symptoms, informational and caregiver needs, and risks of discontinuity are needed.
2. Further measure development should emphasize testing the highest quality measures in important settings (e.g., hospital, nursing home, hospice, and ambulatory care). These measures need to be evaluated in diverse populations (e.g., racial/ethnic groups, non-cancer conditions).
3. Studies evaluating satisfaction should use specific measures that reflect processes of care, and studies should examine the relationship of satisfaction to less studied processes such as non-pain symptoms, spiritual support, and continuity.
4. Methodological challenges in measurement require focused research. Strengthened research infrastructure including collaborative networks should be considered.
5. Symptoms have been relatively well-characterized in cancer, but high-quality studies of the incidence and epidemiology of pain and other symptoms, the relationship among symptoms, and the clinical significance of symptoms are needed in non-cancer conditions.
6. Small, high-quality studies suggest the effectiveness of interventions to alleviate dyspnea. Larger studies of interventions to alleviate dyspnea in cancer and non-cancer conditions are needed.
7. Studies that evaluate short- as well as long-term treatment of depression in palliative care settings are needed.
8. Research supports the effectiveness of interventions for cancer and dementia caregiving. High-quality studies in other populations are needed. These studies need to pay special attention to methodologic issues such as careful, specific measurement of outcome variables.
9. The economic and social dimensions of caregiving need additional research.

10. Substantial evidence supports interventions to improve continuity between home and hospital. Continuity research needs to look at other settings in which most patients are cared for, e.g., ambulatory care. Additional study of nursing home-hospital continuity and studies that incorporate multiple settings and providers are needed.
11. Studies of continuity in CHF and other conditions should incorporate the palliative domains described above (e.g., physical and psychological symptoms, caregiver burden, advance care planning) and need to be more generalizable to the sickest patients. Such studies need to include patients with multiple comorbidities.
12. Rigorous research in advance care planning is needed to understand how to best achieve patient and family goals (as opposed to evaluating resource allocation), and such research needs to address fundamental processes of care planning.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the Southern California Evidence-based Practice Center, under Contract No. 290-02-0003. It is expected to be available in December 2004. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 110, *End-of-Life Care and Outcomes*. In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.

Suggested Citation

Lorenz K, Lynn J, Morton SC, Dy S, Mularski R, Shugarman L, Sun V, Wilkinson AM, Maglione M, Shekelle PG. End-of-Life Care and Outcomes. Summary, Evidence Report/Technology Assessment No. 110. (Prepared by the Southern California Evidence-based Practice Center, under Contract No. 290-02-0003.) AHRQ Publication No. 05-E004-1. Rockville, MD: Agency for Healthcare Research and Quality. December 2004.

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www.ahrq.gov
AHRQ Pub. No. 05-E004-1
December 2004

ISSN 1530-440X

Chapter 1. Introduction

Background and Context

Only a century ago, death was common at every age and dying usually quickly followed the onset of disease or injury. Now, public health measures and health care prevent or cure many previously fatal illnesses or injuries, allowing most Americans to live into old age. Medications and treatments now often allow prolonged survival with serious chronic conditions. More than 75% of Americans now live past age 65,[1] and 83% of Americans now die while covered by Medicare.[1] In 2000, the average life expectancy was 80 years for women and 74 years for men, compared to just 49 years in 1900.[2] By 2050, life expectancy for women and men will likely increase to 84 and 80, respectively.[3]

Rather than a brief, well-defined period, the "end of life" today refers to a prolonged, uncertain period of difficulty because many Americans today live their last years with a advanced, chronic illness. In fact, such conditions affect 15% of the adult U.S. population.[4, 5] Of these, one-twelfth have severe cognitive impairments,[6] almost one-third have difficulty walking,[7] and one-fifth have impaired vision.[8] With advancing age, the likelihood of disability increases dramatically.[9] After age 85, only one person in twenty reports being fully mobile.[10] Age and disability are strongly associated with further declines in functioning, recurrent hospitalization, institutionalization, and death, even after accounting for other risk factors.[11, 12]

An important group of chronic conditions consists of those that typically worsen and eventually cause death (e.g., cancer; chronic heart, lung, liver, or renal disease; dementia; and stroke). Nine-tenths of the elderly insured by Medicare live with one or more of these conditions in the year before death.[1] Most Americans will have a substantial period of serious illness before dying, with onset months or years before death. Already, half of Americans who live to be 85 years have major memory loss in their final years.[13] By 2030, persons over 80 years of age will increase from approximately 3% to over 5% of the population, numbering 19 million.[14] Trends in the rates of late-life disability are uncertain,[15] but the growing size of the aging population suggests that many Americans will face chronic illness and impairment when the baby boomers grow old.

Over the past several decades, analyses underscored the cost of caring for chronic illness during the last years of life. For example, more than one-third of lifetime expenditures are still ahead of a person who is alive at age 85, and more than half are still ahead of a person at age 65.[16] Reports have consistently and repeatedly demonstrated that the last year of life consumes about 30% of lifetime Medicare expenditures.[1, 17-19] The length of time a person lives is relatively unimportant in predicting total costs, and lifetime medical expenditures are similar for those who start retirement healthier and those who start more disabled, because even healthier persons eventually reach the disabled state at the end of life, and that period of time is very costly.[20]

Framework for the Systematic Review

For persons living with advanced, chronic disease, neither prevention nor cure is ordinarily possible. Rather than a simple, straightforward aim like survival, which makes sense as a priority for most of life, people who are living with advanced and eventually fatal illness have complicated priorities like living well as long as possible but not suffering unduly, and being

close to and cared for by family but also not being a weighty burden on them. In this phase of life, care must serve multiple and complex goals and is affected by patient, caregiver, and healthcare system factors. A comprehensive description of the experience of patients living with advanced illness and their caregivers requires consideration of a range of conceptually overlapping measures including satisfaction, quality of care, quality of dying, and quality of life.[21, 22]

Both expert opinion and research on the end-of-life experiences of patients, caregivers, and providers inform a description of the major domains for evaluating the end-of-life experience. These core considerations arise from the experience of both patients and caregivers and include[23-31]

- pain and other symptom prevention and treatment
- adequate support for families and caregivers including bereavement
- continuity of health care
- treatment consistent with patient and family preferences and medical knowledge
- effective, empathic communication about diagnoses, prognosis, and care plans
- well-being, including addressing existential and spiritual concerns
- function and self-determination
- length of survival.

For this report, we addressed several categories among these outcomes that are relevant to particular aspects of the patient's and family's experience, and healthcare system concerns. To examine the patient's experience, we focused upon symptoms, particularly pain, dyspnea, depression and anxiety, and behavioral issues in dementia. To examine the family's experience, we focused on caregiving (excluding bereavement). To examine on the healthcare system's performance, we focused on continuity of care. The joint endeavor of decision-making and providing care consistent with preferences focused on advance care planning.

Pain, Dyspnea, Depression and Anxiety, and Behavioral Symptoms in Dementia

When a person is living with advanced illness and coming to the end of life, effective prevention and relief of symptoms becomes a high priority. Symptoms are subjective indicators of distress and the primary reason patients seek care, and they remain important in and of themselves even when the underlying causes of illness are increasingly difficult to modify.

Effective pain management is a palliative focus for many conditions, and pain is among the most debilitating and feared symptoms that patients and families face. Studies demonstrate a pain prevalence of 70–100% among cancer patients,[32-34] and an Institute of Medicine conference recently named pain in advanced cancer as one of five high-leverage targets for national reform.[35] Undertreatment and inequitable access to pain treatment have been described among many cancer patients presenting with pain.[36, 37] Pain is also prevalent among patients with advanced health conditions other than cancer[38-40] underscoring the importance of evaluating the scientific evidence relevant to pain in both cancer and non-cancer conditions.

Dyspnea, or shortness of breath, is an especially troublesome symptom that is characteristic of conditions including advanced chronic obstructive lung disease (COPD) and congestive heart failure (CHF).[38, 40, 41] The Institute of Medicine also named improving palliative care for CHF and COPD as one of five national priority areas for quality improvement.[35] Understanding and treating dyspnea better would represent important progress in these priority conditions.[1] Dyspnea is also an important symptom in cancer—in primary malignancies (e.g., lung), metastatic disease (e.g., metastasis to the lung), and as a consequence of treatment or progressive disease (e.g., associated with anemia).

Depression has increasingly come to attention as a cause of suffering in advancing illness.[42] Similarly, the suffering that anxiety causes might well be mitigated with better care arrangements and medications.[43] These and other behavioral symptoms such as wandering are especially important as manifestations of dementia.[44] Such symptoms create difficulties for caregivers of demented patients, including nursing homes where Americans increasingly reside during their final years.[45] Certain approaches to these symptoms (e.g., restraints) can be particularly harmful, and disseminating effective alternatives could improve palliative care in nursing homes and other settings for these patients.

Caregiver Experience

Families and other informal caregivers are essential in meeting an individual's physical and psychosocial needs and in accomplishing treatment goals. Caregivers provide substantial amounts of assistance with daily living tasks, watching over symptoms and general health, monitoring and administering medications, and coordinating care among health and social service providers, as well as through emotional support. This is particularly true when patients live with prolonged illness such as dementia, which has a median life expectancy of 3.5 years according to a large, recent prospective cohort study.[46] Caregiver responsibilities do not end with admission to a nursing home because caregivers continue to provide significant personal support even in the nursing home.[47-49]

Families and other caregivers face emotional, physical, and economic consequences as a result and may lack reliable support for their responsibilities.[39, 50, 51] Emanuel surveyed nearly 1000 caregivers and found that 35% reported substantial care needs that consumed time, money, and affected employment and borrowing, and that financial and nonfinancial caregiving burdens were related to depression as well as thoughts about physician-assisted suicide and euthanasia.[52] Almost half of personal bankruptcy is associated with medical illness,[53] and adverse financial circumstances may affect family decision-making.[54] Caregiver stresses do not diminish even after institutional placement.[49]

Continuity of Care

Continuity is an important goal that is mostly the responsibility of healthcare providers to foster. When a patient has complex illness, care is often characterized by multiple providers and settings, and continuity is important and elusive. A recent review identified irreducible elements of continuity including a focus on the individual patient and a concern with care delivery over time.[55] Aspects of continuity include a patient's having an ongoing relationship with specific providers, standardizing approaches to care so that services are delivered in an integrated, consistent fashion, and ensuring that information about the disease process or the preferences and values of the individual follow the patient into every setting of care.[30, 55]

Evidence suggests that discontinuity is a significant but addressable problem at the end of life. Discontinuity has been demonstrated in communicating treatment preferences, and in events related to late transfers among settings of care.[56-58] Hospice might be effective in promoting continuity—family members of hospice patients are less likely to report that providers do not know enough about a family member's clinical situation to provide the best care.[59] Important aspects of care related to continuity include record keeping, various settings of care, and effective planning for the acute problems and symptoms patients face when they are near the end of life.

Advance Care Planning

Advance care planning (ACP) depends upon forecasting the challenges that the patient and family will face due to illness, medical treatment, and other concerns. When an important decision can be anticipated, the decision-making process is usually envisioned as including a prediction of the situation, awareness of alternative care plans, elicitation of preferences, and a final melding of preferences and alternatives into a coherent plan. Closely related issues include the need to make advance care plans available when patients need them and across settings, implementing advance care plans, and understanding their overall effects.

The early emphasis of advance care planning was on legal initiatives, although the concept has been broadened to emphasize the need to plan ahead and shape the course of care.[60] The 1990 Patient Self-Determination Act (PSDA) required states to articulate their statutory provisions and healthcare providers to inform patients of their rights and record any advance directives (ADs). The legalistic origins of ADs emphasized protecting patients' rights by granting them enforceable authority to make their own decisions. A broader construction of ACP recognizes that concerned parties are allied to discern what course best serves the patient and to ensure specific steps to make that course more likely. In addition to ADs, this requires practical arrangements (e.g., having the right medications in place). A number of authors have suggested that ACP should be targeted based on age, medical conditions, the patient's health status, social circumstances, and beliefs.[60, 61]

Summary

Given these significant concerns, the present offers an opportune time to conduct a systematic review to inform the research agenda for palliative care. Research to target gaps in knowledge will facilitate the quality, effectiveness, and affordability of care as well as access to care for patients and caregivers living with advanced illness. Thus, in order to evaluate progress and to propose research priorities the National Institute for Nursing Research, with the Agency for Healthcare Research and Quality, commissioned this Evidence Report as the basis for a State of the Science Conference in December 2004.

Chapter 2. Methods

Task Order Questions

The National Institute on Nursing Research, National Institutes of Health, requested this systematic review in preparation for a State of the Science conference to be held in December 2004. The following key questions were originally posed in the Request for Task Order (RFTO):

1. **What outcome variables are valid indicators of the quality of the end-of-life experience for the dying person and for the surviving loved ones?**
    a. What individual outcome measures are most strongly associated with overall satisfaction with end-of-life care?
    b. What is the reliability and validity of specific instruments for measuring quality of life or quality of care at end of life?
2. **What patient, family, and healthcare system factors are associated with better or worse outcomes at end of life?**
    a. What individual patient factors (e.g., age, gender, race/ethnicity, underlying illness, education) are associated with better or worse outcomes at end of life?
    b. What family factors (e.g., relationship to patient, race/ethnicity) are associated with better or worse outcomes at end of life, including both outcomes reported by the family and how the family affects outcomes experienced by the patient?
    c. What healthcare system factors (e.g., site of care, type of provider, support services) are associated with better or worse outcomes?
3. **What processes and interventions are associated with improved or worsened outcomes?**
    a. What is the effectiveness of specific healthcare interventions for improving specific outcomes in patients at end of life?
    b. Does effectiveness of specific interventions vary among different populations?
4. **What are future research directions for improving end-of-life care?**

Overview

In order to proceed with the task order, we assembled a team of clinical and methodological experts and staff and worked closely with the directors and staff of the Southern California Evidence Based Practice Center. Dr. Karl Lorenz led the day-to-day work of the review and writing teams with the close assistance and regular involvement of Drs. Joanne Lynn, Paul Shekelle, and Sally Morton. Our team included eight literature reviewers (with Dr. Lorenz) whose interests span broad concerns in palliative care and represented nursing, medicine, and gerontology. Reviewers possessed diverse clinical experience and included an oncology nurse, one intensivist, and two general internist/palliative care physicians. Our gerontologist reviewers possess special expertise in nursing home and hospice issues. The overall team met weekly to review and refine the methodology of the task order. Meetings and teleconferences of the SCEPC staff with technical experts helped specify issues central to this report within the framework of the key questions provided by AHRQ and NINR. The SCEPC conducted a comprehensive search of the medical literature to identify studies addressing the key questions. Staff reviewed relevant articles, compiled tables of study characteristics and results, appraised the methodological quality of the controlled trials, and summarized results.

Technical Expert Panel—Scope and Approach to the Report

In consultation with our Agency for Healthcare Research and Quality (AHRQ) Task Order Officer and the NIH Conference Panel Chair, we created a Technical Expert Panel (TEP) to guide the evidence report. We invited a multidisciplinary group of leading scientists and clinicians with expertise in nursing, gerontology, and palliative medicine and a broad knowledge of research and policy issues in the field of palliative care in both the United States and Europe to participate. The list of potential technical experts and their curriculum vitae were submitted to the Task Order Officer for approval, and a list of members is included in Appendix F.

Project staff worked closely with AHRQ, the Chair of the State of the Science Conference, and the TEP to refine the research questions and focus on the relevant outcomes in the topic areas. Before the contract was awarded, the sponsors had decided not to focus upon children or drugs used in palliative care. In considering the scientific literature that our review might address, we found it necessary to further focus and narrow the research questions.

One consideration was to represent the field by focusing on important, representative clinical conditions. We wanted to address important settings of care and also to illuminate important aspects of the patient and caregiver experience. Cancer patients experience a somewhat predictable decline, and are often served by hospice in their final weeks.[1] In contrast, patients with organ system failure (e.g., CHF, COPD) may experience stable but impaired function punctuated by unpredictable, severe illness and rather sudden death[62-64]and are less often served by hospice. Patients with dementia have prolonged declines and often reside in nursing homes.[9, 65] As an organizing principle, our analysis deliberately highlighted evidence that illuminated the experience of living through the end of life with

- cancer
- chronic heart failure
- dementia.

A second consideration in approaching the topic is that the category “end of life” has been undergoing substantial changes in recent years, and the lack of a settled definition has greatly limited the coherence of the research literature.[21] Previous systematic reviews concerned with end-of-life care have focused on well-bounded disease states (e.g., cancer), clinical conditions, (e.g., pain), or specific treatments (e.g., palliative services).[66-69] In organizing a review around the “end of life” population, George observed variation among operational definitions used in research, including diagnosis; prognostic criteria including diagnosis; symptom expression; functional capacity; provider, patient, and family estimates of life expectancy; or particular healthcare settings (e.g., ICU).[21]

These varying operational approaches reflect a few clinically relevant distinctions. Some investigators may use “end of life” to mean the last few days or hours, roughly corresponding to what hospice nurses call “active dying.” Others mean a larger group of people who would be eligible for hospice with the six-month prognosis required for hospice admission or some other arbitrary prognostic interval. The broadest approach uses “end of life” to denote the part of life when a person is impaired with an eventually fatal condition, even if the prognosis is ambiguous. We did not distinguish among these approaches in our review and implicitly accepted the

broadest definition—of a period of time when a person and his or her family are living with the challenges of advanced illness.

The first of a series of calls was held April 28, 2004 with our Chair and the TEP, and we narrowed the scope in a fashion consistent with the sponsor's priorities not to include chemotherapy, radiotherapy, stents, surgery, and other similar medically invasive or technically complex procedures. The TEP and the project sponsor also added a preliminary question of the evidence underlying various potential definitions of the field. For that reason, in addition to the task order questions, we also examined a preliminary question (Appendix A) of prognostication within the end-of-life literature.

Furthermore, since the RFTO was organized around outcomes in the end-of-life literature, we discussed considerations related to specific outcomes with the TEP and conducted a modified Cambridge ballot (see Appendix G) to prioritize those outcomes for inquiry.[70] TEP members rated aspects of end-of-life care, on the basis of

- relative importance
- relationship to patient experience
- feasibility
- relevance to clinical care and healthcare policy
- the availability of recent reviews on the topic
- ability to illuminate differences in the strength of research
- modifiability in clinical practice and policy.

Each potential topic that included pain, affective symptoms, other symptoms, quality of life, spiritual or existential well-being, caregiver well-being and satisfaction, provider communication, advance care planning, continuity and coordination, utilization of services, and site of death was rated independently by each TEP member on each of the above attributes on a scale of 0–10. We totaled the score for each topic area and discussed the findings with TEP members, asking them to reflect on their rankings. The TEP and the sponsors agreed that the EPC search would not include grief and bereavement, spiritual issues, highly technical care (defined as surgery, stents, laser therapy, chemotherapy, and radiation therapy and similar technological innovations), or general issues of communication including giving bad news. Keeping in mind the sponsor's priorities of focusing on aspects of the patient and family experience, and healthcare system concerns, this process resulted in our final decision to focus on the following topic areas in addition to satisfaction with care (specified in Question 1a).

- The patient's experience, focused on Symptoms, particularly
  - Pain
  - Dyspnea (shortness of breath)
  - Depression or anxiety
  - Behavioral issues in dementia.
- The family's experience, focused on Caregiving (excluding bereavement).
- The healthcare system's performance, focused on Continuity.
- The joint endeavor of decision-making and providing care consistent with preferences, focused upon Advance Care Planning.

Table 1 illustrates the task order questions and how we organized the report to address the sponsor's priorities of the patient and family's experience, and the healthcare system's performance.

Table 1. Report Section by Key Question

Key Question	Section of Report
Preliminary	The scope of the population (Appendix A)
Q 1a	Chapter 3 A. Better and worse outcomes, especially patient and family satisfaction
Q 1b	Chapter 3 B. Measurement of outcome elements for the patient and family
Q 2 and 3	Chapter 3 C. The patient experience, especially symptoms Chapter 3 D. The family experience, especially caregiving Chapter 3 E. Health-care system performance, especially continuity of services Chapter 3 F. Decision-making, especially advance care planning
Q2 Q3	Chapter 3 G. Summary of patient, family, and health system factors associated with better or worse outcomes Chapter 3 H. Summary of the effectiveness of interventions
Q 4	Chapter 4. Future research directions for improving end-of-life care

The reader will note that this implements a general strategy of including a broad scope, but also providing focus on a specific important issue within each dimension of that scope. This strategy deliberately leaves some important issues incompletely addressed or not addressed at all. In addition to the exclusion of children and drugs mentioned earlier, this strategy means that this report does not address, except in passing, such issues as spirituality, bereavement, rehabilitation, withdrawal of life support, or any of an array of additional symptoms (fatigue, seizures, delirium, hallucinations, pressure ulcers, and so on). The report also does not focus on many important illnesses such as HIV/AIDS, multi-organ system failure, end-stage renal disease, chronic obstructive lung disease, frailty of old age, or neurological degenerative conditions other than dementia. Finally, articles on advanced illness but which did not include the search terms we used related to "end of life" in the title, abstract, or indexing terms were not are likely not to be included, except by nomination of one of the expert reviewers.

Analytic Framework

Donabedian's quality-of-care framework structures our examination of the associations among outcomes considered by the project. Donabedian described the relationship between outcomes, processes, and structure of care.[71] Quality of care, quality of dying, quality of life, and satisfaction are various distal outcomes that apply in varying degrees to both patients and caregivers.[21, 22] Other topics we chose to examine (e.g., pain and symptoms, advance care planning, caregiver burdens, and continuity/coordination) could be considered as both processes of care related to these more global outcomes or as outcome themselves. In addition, some of these concerns may be understood as processes that affect other considerations as outcomes (e.g., improved pain and symptom management could reduce caregiver anxiety or improved continuity could improve pain management).

Evidence Sources and Searches

Literature Searches

Sources for our review included Medline, the Database of Reviews of Effects (DARE), the National Consensus Project for Palliative Care, and several recent unpublished systematic reviews from National Institute for Clinical Excellence (NICE) and Health Canada. National Library of Medicine (NLM) staff performed most of the searches, complemented by RAND library searches. Members of the project team worked closely with the TEP and librarians at NLM to decide how to refine the search strategy. We limited the searches to published articles in the English language, appearing in journals between the years 1990 through 2004, involving human subjects, and excluding individual case reports. The first search of PubMed was conducted by NLM staff in April 2004. The main search strategy included an extensive list of terms intended to identify all research publications associated with

- palliative or end-of-life care
- both overall (e.g., quality of life, quality of care, quality of death, satisfaction) and specific outcomes (e.g., pain and other symptoms) of interest
- measures and measurement
- individual, family or caregiver, and health system factors
- the full scope of healthcare settings relevant to end-of-life care.

The initial search strategy can be found in Appendix B1.

RAND and NLM created supplemental search strategies (Appendix B2) one week after the initial searches to enrich the initial set of citations. One revised search included terms on psychological and physical symptoms (i.e., pain, depression, anxiety) and specific healthcare services (i.e., nursing homes, hospice, home care) related to end-of-life care. The other new search focused on our three exemplary clinical conditions: cancer, heart failure, and dementia. Given the large number of citations identified through Medline, additional searches of other electronic databases simply were not possible within the resources and time constraints of the project.

Database of Abstracts of Reviews of Effectiveness

DARE contains structured abstracts of high-quality systematic reviews published in the scientific literature. DARE also contains references to other reviews which may be useful for background information. The reviews are identified by searching through key medical journals, bibliographic databases, and less widely available "gray literature." DARE includes papers that review the effectiveness of healthcare interventions or organization. The quality of the database content relies upon ensuring that all reviewers work to specified guidelines, and that independent checks on the review process are carried out. DARE is produced by the Centre for Reviews and Dissemination (CRD) at the University of York, UK. Full information about the database is available on the DARE website at http://york.ac.uk/inst/crd/darehp.

As displayed in Appendix B3, we searched for systematic reviews on cancer, heart failure, dementia, palliative care, and the topics we focused on for this review. One of us (KL) searched DARE using relevant terms and conducted an implicit title review of the resulting citations.

National Consensus Project

In February 2004, the National Consensus Project (NCP) for quality palliative care published guidelines to improve the delivery of palliative care in the United States. NCP conducted a search of the end-of-life literature that, although not strictly systematic, was extensive and gathered the input of clinical, research, and policy leaders in palliative care selected through a national nomination process. Five palliative care organizations oversaw the National Consensus Project including the American Academy of Hospice and Palliative Medicine (www.aahpm.org), the Center to Advance Palliative Care (www.capc.org), the Hospice and Palliative Nurses Association: (www.hpna.org), the National Hospice and Palliative Care Organization (www.nhpco.org), and the Last Acts Partnership (www.lastactspartnership.org). We incorporated the entire reference list, eliminated duplicates, and screened studies that were not otherwise identified through our computerized searches.

Major Recent Systematic Reviews of Palliative Care

In addition to systematic review citations identified via DARE and Medline, the project identified several unpublished but important reviews (listed chronologically by recency) of the end-of-life literature relevant to our task order directives and topics. These were evaluated for quality, and those accepted as high-quality reviews (see below) were key sources for certain topics of the review.

2003 NICE Systematic Review of Supportive Care for Cancer. TEP member Prof. Irene Higginson provided a systematic review on Improving Supportive and Palliative Care for Adults with Cancer that was conducted for the National Institute for Clinical Excellence (NICE) in 2003.[72] This recently published review (available at http://www.nice.org.uk/page.aspx?o=110005) evaluated studies from Medline, EMBASE, CINAHL, Cochrane Registry of Controlled Clinical Trials (CENTRAL), Cochrane Database of Systematic Reviews, and an Effective Practice and Organization of Care (EPOC) specialist register published from 1966 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 and caregiver support. Of 5263 studies reviewed, 443 potentially eligible studies were accepted after abstract review.

2003 Health Canada Reports. Health Canada, Canada's federal department of health provided an unpublished review that evaluated studies from nine databases (Medline, EMBASE, CINAHL, AHMED, PsychInfo, Eric, HealthStar, Sociological Abstracts, and Cochrane and covered the period 1987–2003). This Health Canada project generated 32 recent reports on a wide variety of topics, our review by two project investigators identified 14 of these as relevant to our task order directive and principal topic areas. Titles of all 32 reports are listed in Appendix C.

2000 Toolkit of Measures for End of Life Care (TIME). TEP member Dr. Joan Teno published the Toolkit, which arose from a review of over 928 articles identified from 1967 through 2000 and which selected 293 measures as potentially relevant to end-of-life care research. The Toolkit review through 2000 recommended 35 unique measures based on the criteria that (1) measures should be patient-focused, family-centered, clinically meaningful, and manageable in their application; (2) measures should strive for reliability, validity, and responsiveness; (3) measures should be user-friendly and relevant to quality evaluation and improvement; (4) measures should incorporate both the patient and family perspectives; and (5) measures should examine both the process and the outcomes of care. The website, www.chcr.brown.edu/pcoc/bibliographies.htm, gives an extensive summary of the Toolkit. The Toolkit is a well-known and widely used resource within the palliative care community and served as a foundation for our review of measurement.

Gray Literature

We sought supplemental publications from experts on our team and others involved in the review process, including the occasional "gray literature." We did not make an exhaustive effort to solicit this information however because a recent and well-conducted systematic review that evaluated the efficacy of palliative care teams demonstrated that the gray literature did not affect the results.[73]

Title Screening, Abstract Review, and Selection of Individual Studies

Eight researcher reviewers, six with clinical backgrounds in palliative care and all with established research careers in the area, conducted the study selection process. We trained the group in the critical analysis of scientific literature. The principal investigators resolved any questions or needs for clarification that arose throughout the literature review. Reviewers screened all titles found through our NLM searches or the NCP database or that were submitted by content experts for pertinence to the key questions and therefore their relevance to this project. We established screening criteria to facilitate the identification of articles concerning patient, caregiver, or health system factors related to patient and family-centered outcomes. At the title screening stage, we marked for exclusion citations that were

- exclusively pediatric ($\leq$18 years of age)
- case studies with $\leq$ 30 cases
- not on palliative care content (e.g., not about people who are living with serious illness or not an appropriate outcome)

- exclusively non-Western (i.e., North America, Europe, Australia/New Zealand)—either the population or the journal of origin
- nonsystematic review articles
- clinical trials about chemotherapy, radiotherapy, stent, laser, endoscopy, surgery
- descriptive of ethics, legal, or regulatory issues (nonclinical discussions)
- descriptive of the process of research
- editorials, history, personal narrative or other descriptive, nonclinical articles
- about palliative care professional education (unless effects on clinical, patient outcome(s) are described)
- about organ transplantation and/or organ donation
- clearly discussing research data only from before 1990
- studies in which the outcome was a lab, radiological test, or physiologic indicator (articles about strictly medical/technical outcomes even in the appropriate population).

We only eliminated citations at the title screening stage that clearly met any of the above criteria; we generally retained ambiguous citations. Some of the exclusions warrant explanation. Of the above criteria, as noted, we took the broadest possible view of the "end of life" population. We did not accept articles from the non-Western literature or those that focused exclusively on non-Western populations because (a) health systems and cultural factors are known to vary profoundly, limiting their applicability, and (b) these studies have qualitatively made little to no contribution to major recent systematic reviews of palliative care.[72, 74] We did not include clearly nonsystematic reviews in the title stage because so many citations fell into this category and we searched secondary sources (e.g., DARE) to supplement systematic reviews of relevant topics in the most efficient fashion. We excluded articles arising from data before 1990 because George[21] found that articles published before 1990 constituted just 10% of her unlimited review and articles more than fifteen years old are harder to locate in a short time. We decided to limit on the basis of when the data were generated, rather than when the article was published, since articles can take varying times to be published. We eliminated small case reports because one of the principal investigators (KL) reviewed a random sample of 30 such citations and corresponding reports and determined that they would add little substantive information, even descriptively, to understanding the issues in this review.

Approved titles moved on to the abstract screening phase. We designed a one-page data collection instrument specifically for this project and pilot-tested it with all reviewers after training conducted by SCEPC staff. This abstract screener (see Appendix D1) contained questions about outcomes, population, age, location, design, research topics, and diseases studied. The abstract screener phase included the same exclusion criteria as the title review stage. We added additional exclusion criteria based on the outcomes within the scope of the review that were chosen in consultation with our TEP and Conference Chair. Therefore, we excluded abstracts that clearly dealt with topics other than

- “good death” or “quality of dying”
- patient or family satisfaction
- measures
- family or informal caregiver concerns (other than bereavement alone)
- advance care planning
- continuity and coordination
- ain
- dyspnea
- depression or anxiety
- behavioral issues in dementia.

We provided definitions of these topics that were consistent with the general approach and definitions articulated in the field (see Introduction). Articles that focused on background or prognosis were marked for separate examination, as described below. Project staff entered data from the forms into an electronic database and tracked all studies through the screening process. We ordered all articles that were accepted after abstract screening and sent them out for further review based on topic area.

Procedures to Reduce Bias, Enhance Consistency, and Check Accuracy

Because of the very large number of citations to be evaluated and the short time to completion, we determined that the EPC’s usual method of dual independent reviews of all titles was not feasible. Therefore, we used single review of titles and abstracts and employed the following techniques to improve the reliability and accuracy of our method.

- Reviewers were trained in principles of citation review and use of a “training set” for title review to encourage consistent application of the definitions and criteria of the project.
- One of the principal investigators (KL) served as the “gold standard reviewer.” Outlier sets were identified by a second abstraction of a random subset of titles within each reviewer’s citation set, and the proportion of retained titles was compared. Dr. Lorenz subjected high and low outlier title sets to a second review.
- Specific definitions were used for both exclusion criteria and categorization of abstracts as described above. These criteria were similar at the title and abstract review stages.
- Reviewers were instructed that in any situations where they were not certain of their categorization to request a “second review” of abstracts, both to facilitate reviewer learning and enhance concordance with the ‘gold standard’ reviewer.

- A second review of a random subset of abstracts from all reviewers was conducted.

Following title and abstract review, accepted articles were reviewed by topic teams. The teams of at least two reviewers reached consensus on inclusion of final article sets for each topic area as well as consensus on data abstraction from these articles. Because of the large number of articles and the short time for our review, in practice articles were not dual-abstracted even though team members worked together closely, but abstraction results and findings were reviewed by the principal investigators for accuracy.

Summarizing the Evidence (Key Questions 1–3)

Previous systematic reviews—Definitions

As described above, we had three sources of reviews: our DARE search, experts, and titles identified in broad library searches that abstract review identified as systematic reviews or meta-analyses, using the definitions above (nonsystematic reviews were excluded). Before we begin discussion of the screening and assessment of reviews, we note the definitions that we used:[75, 76]

- *Review:* A review article that summarizes a number of different studies and may draw conclusions about a particular intervention. The methods used to identify, select, and appraise the studies are not systematic or necessarily reproducible. The summary in a review is generally narrative.
- *Systematic review:* A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research and to collect and analyze data from the studies that are included in the review. Statistical methods are NOT used to analyze and summarize the results of the included studies.
- *Meta-analysis:* A systematic review that uses statistical methods to integrate the results of the individual studies. A meta-analysis contains at least one estimate formed by pooling results across individual studies, i.e., an overall odds ratio.

We applied these definitions in the following manner. If a publication addressed a number of studies, then it was a review. If it was a review, then we assessed if the methods (search methods, inclusion/exclusion criteria, quality assessment, etc.) were systematic. If it was a systematic review, then we assessed if it produced a pooled estimate, i.e., applied meta-analytic procedures. If a review was clearly not a systematic review or meta-analysis, then we simply called it a review.

Screening of Reviews

We assessed all resulting reviews using a Systematic Review Screener (Appendix D2). Mostly, we relied upon the abstract; but, if an abstract was not available, we obtained the original article for screening. We excluded all that were not true reviews (i.e., did not address more than one study); were not systematic reviews or meta-analyses; or were not appropriate to our topics (using the same exclusion criteria as on the general screener above). Generally, reviews were not appropriate if they did not address palliative care.

All systematic reviews and meta-analyses that passed screening were sent to the appropriate topic team. For example, if the review addressed symptoms and advanced care planning, it was sent to both the symptoms and advanced care planning teams. The topic teams read each review with particular attention to the team's specific topic. They recorded the publication date and the date that the search for literature ended. Using these dates as well as the topic the review addressed, they assessed how relevant the review was to their topic. All reviews that were considered "highly" or "possibly" relevant were then assessed for quality.

Implicit Quality Assessment of Systematic Reviews

Two reviewers (PS and SM) reviewed all highly or possibly relevant systematic reviews or meta-analyses for quality independently. They then discussed their findings and reached consensus on the quality determination. No situations arose in which consensus could not be reached.

The reviewers categorized each review as either good, fair or poor quality. Good and fair reviews were acceptable to be used by the topic teams as evidence. The quality assessment was implicit. In this assessment the reviewers considered several characteristics of the review, drawing upon guidelines for assessing the quality of systematic reviews and meta-analyses.[77, 78] Good systematic reviews and meta-analyses met almost all of the standards below, and fair systematic reviews or meta-analyses met the majority:

- The search should be comprehensive, systematic and reproducible. Publication bias should be minimized, its existence assessed, and its possible impact on the conclusions discussed.
- The inclusion/exclusion criteria for studies should be clear, reproducible, and defensible, and a flowchart of studies should be provided.
- The study quality assessment criteria and process should be described and evidence-based.
- Data abstraction should be done by two independent readers with a consensus process, or by one reader after a reliability test.
- Individual study characteristics should be presented and possible causes for study heterogeneity considered and investigated.
- If the review is a meta-analysis, the pooling methods should be described and appropriate.
- The results of the review should follow from the evidence presented. Potential biases in the review process and their possible impact on the conclusions should be evaluated and discussed.

All systematic reviews assessed as good or fair quality were summarized by the topic area teams with a narrative description including an in-text table.

Intervention and Observational Studies

Intervention studies included a variety of designs, and we included all types in our report, being sure to emphasize study design and quality in the narratives. We used the following definitions:

Randomized controlled trial (RCT): A trial in which the participants (or other units) are definitely assigned prospectively into either "control" or "study" groups using a process of random allocation (e.g., random number generation, coin flips). "Study" groups receive a specific procedure, maneuver, or intervention.

Controlled clinical trial (CCT); A trial in which participants (or other units) are either

a) definitely assigned prospectively to one (or more) "control" or "study" groups using a quasi-random allocation method (e.g., alternation, date of birth, patient identifier) OR
b) possibly assigned prospectively to one (or more) "control" or "study" groups using a process of random or quasi-random allocation.

Intervention trial with comparison group but not RCT/CCT: A trial in which the participants (or other units) receive one of two (or more) forms of health care; some or all participants are either:

a) not assigned to one of two (or more) forms of health care by the investigator, OR
b) are not assigned prospectively to one of two (or more) forms of health care (e.g., historical control).

Intervention study without comparison group. A trial in which all participants (or other units) receive the same form of health care (e.g., pre-post).

Observational studies. We also evaluated a variety of other observational designs employed in nonexperimental studies. These designs may be retrospective, cross-sectional, or prospective.

Assessment of Quality—Intervention and Observational Studies

To evaluate the quality of the individual intervention studies, we collected information on the study design, withdrawal/dropout rate, method of random assignment (and blinding), and method for concealment of allocation (the attempt to prevent selection bias by concealing the assignment sequence prior to allocation) consistent with requirements for ODS-OMAR-supported EPC evidence reports. The elements of design and execution (randomization, blinding, and withdrawals) have been aggregated into a summary score developed by Jadad. The Jadad score rates studies on a 0 to 5 scale, based on the answer to three questions:

1. Was the study randomized?

2. Was the study described as double-blind?

3. Was there a description of withdrawals and dropouts?

One point is awarded for each "yes" answer, and no points are given for a "no" answer. Additional points are awarded if the randomization method and method of blinding were described and were appropriate. A point is deducted if the method is described but is not

appropriate. Empirical evidence in other clinical settings has shown that studies scoring 2 or fewer points show larger apparent differences between treatment groups than do studies scoring 3 or more.[79, 80]

Observational studies were assessed using ODS-OMAR procedures. Because of the extremely large number of observational studies identified, we were forced to limit our review of observational studies by definitely accepting only those that met the following criteria consistent with the task order goals:

a) If the study dealt with the topic of race / ethnicity as a single description of a racial group OR in the results reports racial differences, THEN it was included. If it did not do that AND it did not meet other criteria (b or c), then it was rejected.

b) If the study dealt with a setting of care other than hospice or compared settings of care, then it was included. If it did not do that AND it did not meet other criteria (a or c) then it was rejected.

c) If the study deals with the topic of CHF or dementia it is included, OR if it dealt with a comparison of a non-cancer disease state with cancer, then it was included. If it did not do that AND it did not meet other criteria (a or b), then it was rejected.

We defined a *cohort* as "a group of people who share a common experience or condition." For example, a birth cohort shares the same year of birth; a cohort of smokers has smoking as the common experience.[81] We also distinguished prospective cohorts as those that were forward looking or longitudinal in design and in which the measurement of exposure preceded the measurement of the outcome. We included all prospective cohorts that met criteria a–c. Selected observational studies were included in the evidence tables at the implicit discretion of our expert reviewers if they addressed an important aspect of the topic even if they did not meet criteria a–c.

Qualitative research studies were included only in the discussion of satisfaction and its relationship to other outcomes (question 1a). These studies were reviewed by a single reviewer (KL) to examine common themes in the literature. Most qualitative studies involved focus groups or unstructured individual interviews.

Qualitative Data Analysis

We report the evidence in several forms. First, the evidence tables (in Appendix E—Interventions and Appendix L—Observational Studies) offer a detailed description of the studies that we identified, addressing each of the topic areas. At the end of the printed report, summary tables report on systematic reviews and intervention studies in an abbreviated form, using summary measures of the main outcomes. Narrative text summarizes the findings and provides qualitative analysis of the key questions as they relate to the topic area. The synergistic impact of multiple or sequential interventions is not considered with this methodology.

The evidence tables provide detailed information consistent with ODS-OMAR criteria about the study design, patient characteristics, inclusion and exclusion criteria, interventions evaluated, and the outcomes. The study sample size offers a measure of the weight of the evidence. (In general, larger studies provide a more precise estimate of the effect in question, although patient population governs more the applicability of any given study.) Again, we graded the quality of the studies according to the Jadad scale; this is also presented in the evidence tables. The

evidence tables are condensed into in-text summary tables to provide a concise overview of study results. Summarizing the data in such a way allows for ease of comparison among studies.

Review of Articles Relevant to the Scope of "End of Life"

Starting with the articles that the core literature review had identified as related to background and prognosis, and supplemented by articles pointed out by experts and other reviewers, three reviewers examined the titles and abstracts for this preliminary task of defining the scope of "end of life" care. They then categorized the articles into potentially useful categories and implicitly reviewed them for research quality. Then, the team categorized the articles and qualitatively described the implications for defining the "end of life" as a target for care. This work was essential to our overall effort but lies outside the scope of the RFTO and we have summarized it completely in Appendix A. Because this issue as a whole is also relevant to how we understood the literature, some of the insights from this preliminary task are discussed in Chapter 4.

Peer Review Process

We identified potential peer reviewers through project staff, the TEP and AHRQ. Based on these inquiries we contacted 12 individuals with wide expertise in the field and with deep knowledge of the literature, 9 of whom provided recommendations in addition to our TEP members. We selected reviewers because of their international stature, knowledge of both the North American and European literature, and research experience. The list of peer reviewers and their affiliations can be found in Appendix F.

A copy of the draft evidence report was mailed to each peer reviewer and TEP member. All reviewers were asked to respond with their comments. We compiled the peer reviewer comments and made appropriate changes to the draft report, based on these comments. The reviewer comments and the EPC's responses are provided in Appendix K.

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

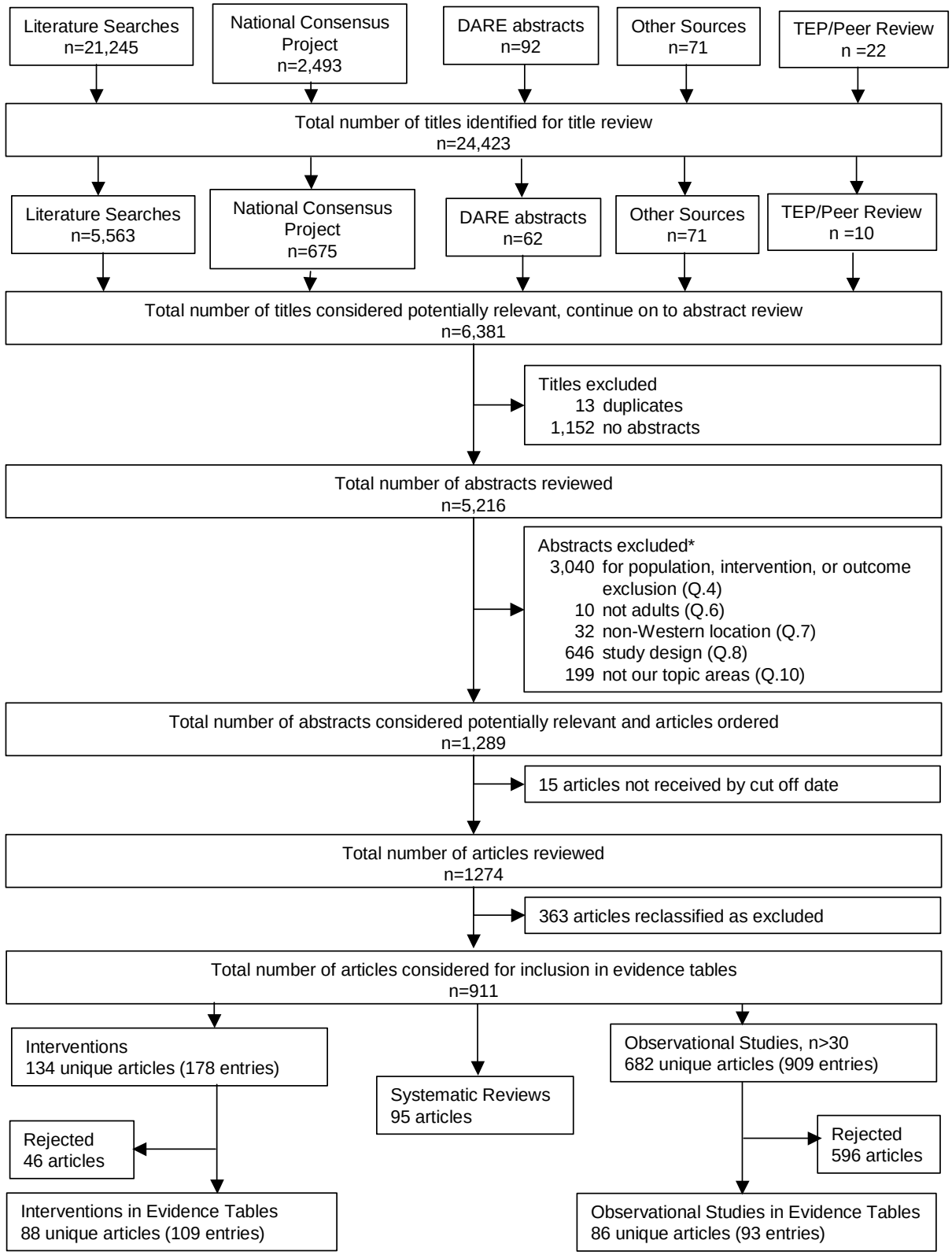
location. Six hundred forty-six studies were excluded due to study design: 239 were qualitative studies; 52 were nonsystematic reviews; 20 were other types of reviews; 138 were observational studies of less than 30 subjects; and 197 had unclear study designs. One hundred ninety-nine abstracts were excluded 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 satisfaction[74] 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 cancer[72] 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 an 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-tem 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 differences[96-98] 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 variable[98] 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 cancer[125] 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 Toolkit[30] 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 Karnofky 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 Toolkit[30] 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 scale[109] 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 Toolkit[30] 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 Toolkit[30] reviewed 41 measures and recommended five: Profile of Mood States, Memorial Symptom Assessment Scale, Center for Epidemiolgic 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 Toolkit[30] 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 Toolkit[30] 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 Toolkit[30] 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 Toolkit[30] 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 Toolkit[30] 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 Toolkit[30] 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. Hotgan 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 Toolkit[30] 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 al[216] 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 colleagues[225] 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 colleagues[226] 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 colleagues[229] 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 colleagues[224] 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 colleagues[227] 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. Sarna[223] 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 colleagues[222] 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 Higginson[72] 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 colleagues[213] 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 difference 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 colleagues[231] 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 colleagues[237] 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 controlled[230] 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 H_2O ($p<0.005$). 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 colleagues[232] 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 O_2 saturation or respiratory rate between the intervention and placebo groups. The Jadad score for this study was 0.

Abernathy and colleagues[235] 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=0.0.11) 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 colleagues[233] 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 reported. 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 colleagues[240] 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 Forbes[219] 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 colleagues[217] 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 trazadone 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.

D. 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 family experience, especially caregiving

Caregiver burden includes the full spectrum of potential concerns that families and other informal caregivers face in caring for someone with advanced illness. These concerns include but are not limited to mental and physical health, financial well-being including out-of-pocket costs and job loss, and interpersonal stresses. We did not generally assess bereavement, which we defined as after-death emotional concerns, but we otherwise considered the full impact of illness on caregiver well-being. If studies included bereavement as an outcome but also addressed other topics that were central to the review, they were included. However, studies on bereavement alone were excluded.

We evaluated six systematic reviews that potentially dealt with the subject of caregiver burden, addressed the project questions, and met implicit quality criteria. Three dealt with outcomes of caregivers for patients with dementia or other chronic illness; three others dealt with cancer patients or life-threatening illnesses. We went beyond the systematic reviews by including other interventions to reduce caregiver burdens at the end of life published after these systematic reviews or published at any time if not already addressed in a systematic review. In total, we reviewed an additional thirteen 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. Seventeen observational studies that met these criteria are discussed here.

The remainder of this section summarizes the systematic reviews, meta-analyses, intervention, and observational studies relevant to patient and caregiver burden. Summaries of the association of patient, family, and health system factors to caregiver burden and the effectiveness of interventions in improving caregiver burden are found at the conclusion of Chapter 3.

Table 5. Systematic Review—Caregivers

Systematic Review	Caregiver Outcomes	Date Search Concluded	Date Published
Acton & Kang [255]	Caregiver burden (dementia patients)	1999	2001
Acton & Winter [256]	Burden, stress, anxiety, coping, life satisfaction, morale, perceived physical health, and rate of institutionalization (dementia, advanced chronic illness patients)	2001	2002
Yin, Zhou, & Bashford[257]	Caregiver burden (dementia and frail patients)	2000	2002
Higginson, Finley, et al.[74]	Pain, other symptoms, quality of life, satisfaction, referral to other services, caregiver satisfaction, caregiver burden/morbidity, home death rates, health service use, costs (progressive, life- threatening illness patients)	1999	2002
Higginson & Gysels[72]	Caregiver burden, quality of life, satisfaction, anxiety, problem solving/coping skills, pain management, activity goals, knowledge, psychosocial status, stress management (cancer patients)	2001	2001
Wilson[258-260]	Patient and family satisfaction with care, well-being and quality of life, family needs, and EOL outcomes, including effects of case management on those outcomes	2003	Unpublished

Systematic Reviews and Caregiver Burden

We identified eight systematic reviews and meta-analyses that were relevant to family or informal caregiving and met implicit quality criteria (see Table 5). Three dealt with outcomes of caregivers for patients with dementia or other chronic illness; five others dealt with cancer patients or other life-threatening illnesses.

Acton & Kang (2001)[255] reviewed 46 studies (experimental, quasi-experimental, and one group pre-post designs) published between 1982 and 1999. Family caregivers of dementia patients were studied; no further details were given on the patients receiving the care. The caregivers were not caring for “terminally ill” patients or patients at the end of life. Twenty-four studies testing 27 interventions were included in the quantitative analysis (three studies tested two different interventions). Interventions included psycho-education (n=10), education (n=5), respite care (n=4), counseling (n=4), multi-component interventions (n=3), and support group (n=1). A total of 1,254 participants (range: 11 to 180, with a mean of 51 participants per study) were included in the meta-analysis (866 =T; 388=C). The outcome assessed was caregiver burden. The analysis reported that the interventions had no effect on caregiver burden, and in some cases the effect of the intervention was negative or the control group scores improved more than those of the treatment group. Only one multi-component intervention and one respite intervention significantly reduced caregiver burden. Pooled analyses of treatments that evaluated subjective and objective burden separately showed that interventions had no significant beneficial effect on either type of burden.

Acton and Winter,[256] in a review that partially overlapped the review conducted by Acton and Kang,[255] examined 73 published and unpublished research reports (1991 to 2001) and included controlled trials and pre-post designs. All types of caregivers of patients with dementia and other diseases were included. The studies appeared to span patients with all degrees of

severity; no “end of life” studies are specifically mentioned. Less than 50% of care receivers had dementia. A wide range of caregiver interventions designed to lessen the negative impact of caregiving or improve the positive aspects of caregiving for caregivers to patients with dementia or other diseases were included. Outcomes included burden, stress, anxiety, coping, life satisfaction, morale, perceived physical health, and rate of institutionalization. Studies were grouped by intervention type (education, support and education, counseling, respite, case management, and multi-component) and evaluated for strengths and weaknesses in design, sample, intervention, and outcomes. Overall, 32% of the study outcomes were changed in the desired direction after intervention.

Education interventions (23 studies, sample range: 2–95) focused on individualized, home-based programs delivered by nurses one-on-one over time periods ranging from one to eight months (resulting in higher intervention intensity than other education intervention strategies). About one-third of 90 outcome variables measured were reported to be statistically significant in the desired direction (depression, tension, anger, burden, negative affect). Knowledge, coping, and life satisfaction were significantly increased in three studies. Caregiver support and education intervention studies (14 studies, sample range: 26–53) were primarily delivered as individualized education to a caregiver. Only three studies were conducted in a group, community-based format and a fourth was a computerized intervention. Three of the 18 nursing outcomes were significantly changed in the desired direction (burden, stress, and decision confidence) and one study found stress and burden to be significantly increased. Counseling interventions, designed to help caregivers understand the behavioral symptoms exhibited by the demented care receiver and their own reactions to the behavioral symptoms, were tested in four studies (sample range: 5–39). One study reported significant changes in outcomes (increased knowledge and morale) after group counseling. Respite care, including eight studies evaluating day care and eight studies evaluating inpatient or in-home respite (sample range: 7–264) reported that the combination of use and duration varied considerably across studies, making it difficult to determine intervention effect. Intensity of interventions ranged from one to five days per week and duration ranged from one to four months. Case management (assessment, planning, coordination, collaboration, and monitoring by a professional case manager) was evaluated in six studies (sample range: 12–4,151). One study reported a significant reduction in stress**.** Twelve multi-component interventions (sample range: 5–86) were reviewed. Both positive and negative consequences of caregiving were measured as outcomes; most studies reported mixed results. Two studies found the rate of institutionalization significantly reduced. The results of the meta-analysis provide little support for the interventions studied.

Yin, Zhou, and Bashford (2002)[257] examined 26 studies that had comparison groups (single-group pre-post test designs were excluded), published between 1985 and 2000. All types of caregivers were included. The mean age of the caregivers was 60 years; 79% were women and 86% were White. An average of 80% of the caregivers lived in the same household as the care receivers. About half of the care receivers had dementia (the rest had other types of chronic illnesses). The care receiver’s mean age was 79 years old. There was no explicit identification of “terminally ill” patients or patients “at the end of life.”

The 26 studies included 18 addressing group caregiver interventions and 8 addressing individual caregiver interventions. The total sample size was 1,970 for the combined interventions and 472 for the individual interventions. Caregiver burden was the primary outcome in the group intervention studies (although only 10/18 used the same instrument—the

Zarit Burden Inventory). No details on the individual intervention outcomes were provided. Studies were evaluated on effect size, study design, type of intervention, duration and frequency of intervention, method of assignment, type of instrumentation, time of posttests, and study site, characteristics of the study samples, and characteristics of researchers.

The weighted mean effect size for all studies was .41 (95% CI, 0.32–0.51), indicating a moderate beneficial treatment effect of group interventions on caregiver burden. Subgroup analysis indicated the mean effect size was larger for individual intervention studies (0.48) than for group intervention studies (0.26). The mean effect size of the quasi-experimental studies (0.89) was more than three times that of the true-experimental studies (0.26) but generally consistent with other research.

Higginson, Finlay, Goodwin, Cook, Edwards, Hood, Douglas, and Normand[74] conducted an assessment of five systematic reviews (1977–1999, 43 studies) of palliative care team interventions on patients' pain, other symptoms, quality of life, satisfaction, referral to other services, and therapeutic interventions and on caregiver pre-post bereavement burden/morbidity and satisfaction with care. Disease severity, amount of family support, training and experience of team members in palliative care, whether the team had an occupational or physiotherapist, and team links to social services were not described in many of the caregiver-relevant studies and were thus excluded from the analysis. However, the general conclusions of each paper assessed were similar. Overall, the analysis indicated small beneficial effect of palliative care services on patient and caregiver outcomes, with the strongest support for home care services. Similar or improved outcomes were found for patient satisfaction, patient pain and symptom control, and family anxiety for hospice and palliative care services when compared to conventional care. There was a lack of good-quality evidence on which to base conclusions, and there was no evidence of an effect on other quality of life measures.

Gysels and Higginson[72] conducted a systematic review of the effectiveness of different interventions targeted at healthcare professionals, the structure of healthcare delivery, or the care delivered to improve supportive and palliative care to cancer patients. In this review, 22 interventions targeted at improving care for families and informal caregivers (including bereavement) were identified. Interventions included home nursing care (four studies), respite services (three studies), social networks and activity enhancements (two studies), problem solving and education (three studies), and groupwork (ten studies). Nine of the interventions were targeted to caregivers only. Limitations of the data included a lack of outcome evaluation designs, small sample sizes and a reliance on intervention descriptions and formative evaluations. Only two quasi-experimental evaluations were included. Interventions, patient and caregiver characteristics, and outcome measures were not well described in the review. The evidence in this analysis appears to contribute more to understanding the feasibility and acceptability of these interventions than to their effectiveness.

Caregivers reported high satisfaction with home care services and described them as useful. However, the high levels of psychological morbidity and unmet need reported in these samples of caregivers using home nursing care in both cancer and palliative care indicated that such generic supportive nursing care does not meet all caregiver needs. Caregivers using inpatient and home hospice care reported a greater reduction in anxiety and higher satisfaction compared to conventional care in one RCT. Another study of home hospice found caregiver quality of life remained stable over four weeks. An RCT of a hospital at home for terminally ill patients in the last two weeks of life reported no significant difference between the intervention and standard

care and low uptake of the intervention due to caregiver inability to cope. A formative qualitative evaluation of a community palliative care service (home care, day care, and respite as a single service) reported that caregivers valued the single point of contact, that it felt like a “home away from home,” and that it helped them overcome reluctance to access other services. A longitudinal RCT of home care nursing on caregiver psychosocial status of caregivers with and without physical problems of their own reported an improvement in psychosocial status for those caregivers with physical problems and at risk for psychological morbidity. A psycho-education program for cancer caregivers reported that perception of burden did not worsen even when caregiving tasks increased in intensity. Widely varying respite care services reported high satisfaction in caregivers.

Descriptive data were reported on respite care. One study, using a single group retrospective questionnaire (n=190), reported over 90% satisfaction among caregivers (though 33% felt the service had been offered too late). Social networks and “activation” programs for relatives of cancer patients aimed to promote increased social activity. One controlled trial was reviewed, with an age- and sex-matched comparison group (50 intervention and 45 comparison caregivers) and reported the intervention caregivers had significantly higher social activities during care receiver cancer treatments and significantly more involvement in personal activities preceding the death of the patient. One RCT of a one-to-one intervention designed to provide support, education, and build problem-solving and coping skills (n=38) reported the intervention effective only for a distressed sub-sample of cancer caregivers. This burdened sub-sample of caregivers was better at dealing with pressing problems following the intervention (n=11) compared to controls (n=18). Another one-to-one intervention on cancer pain education (n=50) reported significant improvements on knowledge/attitudes to pain, pain management, and caregiver burden. A multidisciplinary group support designed to alleviate caregiver stress from lack of knowledge is described, but no data are reported.

An RCT of group work interventions for patients and caregivers (n=25), designed to provide support and information to caregivers, reported that spouses who attended the intervention had significantly higher knowledge scores, achieved activity goals, coped better, and were more satisfied with care. However, psychosocial adjustment did not differ between the two groups. An observational study of group work on quality of life reported no differences in quality of life or coping strategies. A descriptive evaluation of a combined patients’ (n=73) and caregivers’ (n=54) group support for cancer care reported that the provision of information and education promoted understanding and facilitated coping, and the familiarity with the facts and feelings involved reinforced participants’ confidence. A retrospective single group evaluation of a monthly support group for cancer patients and families reported that 26% of the respondents felt more anxious/worried and 29% felt sadder. Another observational study of group support on quality of life in cancer patients and their family (n=12) compared to a control (n=12) and an ongoing support group (n=8) found no significant differences in quality of life or coping strategies.

The review supports the small body of evidence on the effectiveness of interventions for caregivers to cancer patients. Despite caregivers’ recognition of unmet need, they report some improved outcomes. However, one study indicated that these interventions could be detrimental to caregivers. Based on the analysis, the authors concluded that no single service model appears either acceptable or effective for the broad range of caregivers. Home care appears to produce high satisfaction. The authors concluded there is little evidence supporting the effectiveness of

respite services, support groups, and one-to-one individual interventions. Groupwork interventions reported the most effect but they had low uptake and are acceptable primarily to caregivers with specific profiles. The evidence suggests there is a high rate of unmet need in caregivers using palliative care services that highlights the limited scope of some of these interventions.

Wilson's systematic review (in press)[259] identified 11 studies and three systematic reviews of care/case management on end-of-life care. Of five research articles examining case management interventions on patient quality of life, two reported an increase in patient quality of life while three other studies reported no significant impact. However, the role of case management in the interventions varied significantly; in many cases, the case management function was not as care coordinator or problem solver. Three studies assessing the impact of case management on caregiver burden reported a beneficial impact on family caregivers. In general, case management was reported to be a means of reducing family caregiver burden, although only three studies were evaluated. In addition, the quality of the studies reviewed was poor, few RCTs were identified, and the exact interventions were inadequately described.

Additional Interventional Studies and Caregiver Burden

We identified 13 additional studies assessing interventions and caregiver burden.

One RCT[242] (n=203) reported no effect for nurse coordination for cancer patients in the community. Specifically, there were no significant differences in time between last follow-up and death, in symptom experience, or in use of pharmacologic treatments. A few significant differences arose in caregiver reports of type, severity, and effectiveness of treatment of patients' symptoms in last week of life. The groups did not differ on the hospital anxiety and depression scale, social support, and quality of life, ADL assistance needs, unmet needs, financial impact, use of social services, and satisfaction w/ care.

A multi-site RCT[147] compared enhanced home-based primary care (HBPC) in 16 VA hospitals compared to usual HBPC care. Enhanced care consisted of HBPC services plus systematic screening to identify high-risk patients, an emphasis on continuity of care, 24-hour telephone access, and the management of patients across organizational boundaries involving care management by HBPC physician serving as the primary care provider. Terminal patients in the intervention group significantly improved on eight health-related quality of life scales (emotional, social, bodily pain, mental health, vitality, general health), with the greatest improvement in emotional function. No difference was found in terminal patient satisfaction over the study period. Caregivers to terminal patients also reported significant health-related quality of life improvements ($p<.05$ overall) in all but two dimensions (vitality, general health), with greatest improvement in emotional function (13-point gain vs. usual care). Caregivers also reported significant gains in satisfaction with patient care ($p<.001$), except for one personal satisfaction item. An 8% reduction in hospitalizations and mean number of hospitalizations in enhanced HBPC program was reported in the first six months, but this was not sustained at 12 months. A 22% reduction in utilization was reported in those with the most disability. Patient and caregiver benefits were accompanied by a 6.8% increase in total costs of care at six months and 12.1% increase at 12 months. The Jadad score for this study was 3.

One RCT[261] evaluated an intervention designed to improve end-of-life decision-making and reduce the frequency of a mechanically supported, painful, and prolonged process of dying,

conducted in two phases. Phase I was a two-year prospective observational study with 4,301 patients, and phase II was a two-year RCT with 4,804 patients and their physicians (randomized by specialty group) to usual care or an intervention consisting of prognosis estimates to physicians, specially training nurses to improve communication and decision-making among seriously ill hospitalized patients, families, and healthcare teams. Phase I documented shortcomings in communication, frequency of aggressive treatment, and the characteristics of hospital death. Only 47% of physicians knew when their patients preferred to avoid cardiopulmonary resuscitation (CPR); 46% of DNR orders were written within two days of death; 38% of patients who died spent at least ten days in an intensive care unit (ICU); and, for 50% of conscious patients who died in the hospital, family members reported moderate to severe pain at least half the time. In the RCT, patients experienced no improvement in patient-physician communication (e.g., 37% of control and 40% of intervention patients discussed CPR preferences) or in five targeted outcomes, i.e., incidence of timing of written DNR orders (adjusted ratio, 1.02, 95% CI, 0.90 –1.15), physicians' knowledge of their patients' preferences not to be resuscitated (AR, 1.22; 95% CI, 0.99–1.49), number of days spent in an ICU, receiving mechanical ventilation, or comatose before death (AR, 0.97; 95% CI, 0.87–1.07), or level of reported pain (AR, 1.15; 95% CI, 1.00 to 1.33). The intervention also did not reduce use of hospital resources (AR, 1.05; 95% CI, 0.87–1.07). The Jadad score for this study was 3.

An evaluation of a hospital-at-home intervention[83] (n=198, 86% of 229 referred patients and 144 caregivers, 73% of 198 referred caregivers) on patient's quality of care, likelihood of remaining at home in their final two weeks of life, and general practitioner (GP) visits. The study reported no conclusive evidence that the hospital-at-home service for terminally ill patients increased the likelihood of remaining at home during the final two weeks of life. However, the service was associated with fewer GP out-of-hours visits. All respondent groups (GP, nurses, caregivers) rated the intervention favorably when compared to standard care but emphasized different aspects. Nurses rated services as better than standard care in terms of adequacy of night care and support for the caregiver; GPs positively rated the service in terms of the reduction of anxiety and depression in patients; and caregivers rated the service positively in terms of control of patient symptoms (pain and nausea). Overall, the authors concluded the service provided better quality of care. The Jadad score for this study was 3.

A cluster randomized trial of palliative care services for unspecified terminally ill patients and their caregivers[84] (discussed in satisfaction) measured the place of death and satisfaction with care. This same trial reported impacts of the palliative care intervention on caregiver quality of life[262] using a larger sample (517 caregivers) and reported similar results. Five of eight subscales of health-related quality of life scores declined between baseline and final follow-up (one to two months after patient's death). As expected, HRQOL returned to baseline by the end of the study. The intervention ameliorated declines in role limitation due to emotional problems and mental health, but scores for the other three subscales showed smaller and almost linear decline. There were extremely low response rates in both groups, which undermines the findings in this study. The Jadad score for this study was 3.

The Resources for Enhancing Alzheimer's Caregiver Health (REACH) project,[263-268] a six-year multi-site research program funded by the National Institute on Aging (NIA) and the National Institute of Nursing Research (NINR), focused on testing the most promising home and community-based interventions for maintaining and improving the health and quality of life of caregivers if dementia patients. Fifteen well-defined interventions (nine active and six control

group conditions) were implemented (Birmingham, Boston, Memphis, Miami, Palo Alto, and Philadelphia) and assessed common outcome measures. The interventions consisted of psychosocial and psycho-educational services, behavioral interventions, environmental modifications, and technology interventions. Three of the sites included a minimal support telephone contact control group and three sites included usual care control conditions. The study population (n=1,222) included African American, Cuban American, Mexican-American, and White American family caregivers of patients with Alzheimer's disease (AD) and related disorders (ADRD). A common set of measures was collected at all sites at baseline, 6 months, 12 months, and 18 months following random assignment to an intervention condition. Outcome measures included caregiver mental health or well-being and depression; social support; caregiver burden; religiosity; service utilization; caregiver and care recipient physical health and medication usage; and care recipient behavior and cognition.

The pooled effects of 15 site specific REACH interventions (nine active and six control group conditions) on caregiver burden and depressive symptoms following six months intervention and initial analysis of overall treatment effects by categories of caregiver race/ethnic identity, gender, educational level, and relationship to care recipient using an intent-to-treat model were reported.[263] Three sites (Birmingham, Boston, Philadelphia) tested a single active intervention (skills-training, telephone-linked computer [TLC], environmental skill building program [ESP]). Three sites implemented two active interventions: Memphis (behavior and enhanced care), Miami (family-based structural multi-system in home intervention [FSMII] and FSMII combined with computer telephone integration system (CTIS), and Palo Alto (coping with caregiving class and enhanced support group). Two sites used modified usual care control groups (Boston and Philadelphia) in which caregivers received information packets only. One site (Memphis) provided information and referral and three other sites (Birmingham, Miami, and Palo Alto) utilized a minimal support control (MSC; information and empathetic listening).

Using meta-analysis, the pooled treatment effect for burden was statistically significant (p=.022), although the difference was small. Overall, caregivers in the active interventions across the REACH sites showed lower values in burden associated with patient behavior problems than controls. No intervention showed a statistically significant effect for caregiver burden, although all scores did improve for active interventions. In contrast to burden, the pooled treatment effect for CES-D was not statistically significant (p=.095). Only one site (Miami) reported a significant reduction in depressive symptoms (p=.034) in the combined family therapy plus technology treatment condition compared to controls. The family-therapy intervention did not have a significant effect on depressive symptoms by itself. Overall, the REACH interventions produced only a modest treatment effect, but this is consistent with results of other recent meta-analyses. The magnitude of the effect sizes for the combined active REACH interventions on caregiver burden (0.15 standard deviation units) and Miami's FSMII +CTIS intervention on depressive symptoms (0.23 standard deviation units) fall within the range of effect sizes reported by others (Sorenson, et al., 2002).[269] The magnitude of change on burden for the REACH combined active intervention groups compared to control conditions was 10% (score range=0–96). This change is equivalent to the decrease or elimination of two very bothersome behaviors, such as repetitive vocalization or waking at night. The relatively small overall effects of REACH may be a result of the complex pattern of significant outcomes observed for various subgroups. Across sites, women and those with high school or less education who were in active interventions reported reduced burden compare to controls. In contrast, men and those with higher education levels did not show significant benefit from the interventions. Caregivers in active interventions who were

Hispanic, those who were non-spouses, and those who had less education reported lower six-month depression scores than controls. These findings suggest that the combined interventions had an effect for those caregivers in most need of support.

The Miami REACH project[264] investigated the efficacy of Structural Ecosystem Therapy (SET), based on the Brief Family Therapy intervention for treating behavior problems in dementia patients and SET+CTIS, a system designed to augment SET by facilitating linkages of the caregivers with their family and with supportive resources outside the home. The sample included 225 family caregivers (114 Cuban-American and 111 White American) of patients with Alzheimer's disease and related dementias (ADRD). Overall, there were significant differences by caregiver type, intervention, and ethnicity on depressive symptoms. Caregivers in the combined family therapy and technology intervention (SET+CTIS) experienced a significant reduction (five or more points for Cuban-American and White non-Hispanic daughters and Cuban-American husbands) in depressive symptoms at 6 months and at 18 months compared to all other intervention groups. Husband caregivers had lower CES-D scores than wife or daughter caregivers in all intervention groups, and Cuban-American caregivers (husbands and daughters) experienced the most benefit from the interventions, particularly the SET+CTIS.

The Memphis REACH[265] project compared two structured, parallel interventions, Behavior Care (BC) and Enhanced Care (EC) in a 24-month clinical trial. Behavior Care interventions focused only on improving the caregiver's management of the care recipient's behavioral problems using 25 pamphlets addressing particular behaviors. Enhanced Care interventions focused on these same behavior problems but also on improving the caregiver's own well-being in response to the behavior problems through 12 additional pamphlets geared to caregiver well-being. Both models were delivered by a master's prepared health educator in an office setting. One-hundred sixty seven caregiver-patient dyads were randomized into BC (n=85) and EC (n=82). At two months, 7 of the original 17 active caregiver-patient dyads remained for analysis. Difference in completers vs. noncompleters was based on length of caregiving (shorter length of caregiving more likely to complete). Of final caregiver-patient dyads (n=167), 66 were Black American, 99 were White-Caucasian, and 2 were other race. Caregivers were predominantly women and tended to be spouses or daughters. Results showed that caregivers receiving only BC had significantly worse outcomes for general well-being and a trend toward depression compared to caregivers receiving EC. There was an overall improvement in both groups for bother associated with care recipient behaviors. No racial/ethnic differences were reported.

The Birmingham REACH project[266] implemented a multi-component interventions intended to address the common needs of White and African-American family caregivers while remaining responsive to cultural issues. One hundred forty caregiver-patient dyads (White=70 and African American=70) were randomly assigned to either a skills training condition (ST) or a minimal support (MS) control condition. One hundred eighteen dyads completed the six-month assessment (White=70; African American=48). Significant differences between White and African American caregivers included: White caregivers more likely to be spouses and African American caregivers more likely to be non-spouses. White caregivers were significantly older and reported higher household occupational status than African American caregivers. African American care receivers had lower educational attainment and demonstrated greater cognitive impairment than White care receivers. Results demonstrated that both interventions were well received by caregivers. Caregivers in both groups and both races reported decreasing levels of problem behaviors and appraisals of behavioral bother, and increased satisfaction with leisure

activities over time. On one measure of appraisal of distress related to behavior problems, White caregivers showed more improvement in the minimal support control condition, and African American caregivers showed the greatest improvements in the skills training condition. No significant effects were found for race, treatment group, their interaction, or time for depression or anxiety. A significant treatment by race by relationship interaction was found with the largest decreases in the number of problem behaviors found for White spouse in the MS condition and for African American spouses in the ST condition.

The Philadelphia REACH[267] project examined the six-month effects of an Environmental Skill-Building program (ESB), as well as race, relationship, and gender on caregiver well-being and care recipient functioning. One hundred and ninety family caregivers of community-residing dementia patients completed the six-month follow-up. Caregivers were randomized to a usual care control group (UC) or intervention group (IG) that received five home contacts and one telephone contact by occupational therapists, who provided education, problem-solving training, and adaptive equipment. Baseline and six-month follow-up included self-report measures of caregiver objective and subjective burden, caregiver well-being, and care recipient problem behaviors and physical function. Compared with controls (n=101), intervention caregivers (n=89) reported less upset with memory-related behaviors, less need for assistance from others, and better affect. Intervention spouses reported less upset with disruptive behaviors; men reported spending less time in daily oversight; and women reported less need for help from others, better affect, and enhanced management ability, overall well-being, and mastery relative to controls. Statistically significant treatment differences were not found for hours helping with ADLs and IADLs, perceived change in somatic symptoms, White versus non-white caregivers, or care recipient outcomes.

The Boston REACH project[268] examined the 12-month effects of a computer-mediated automated interactive voice response (IVR) intervention designed to assist family caregivers managing persons with disruptive behaviors related to Alzheimer's disease (AD). One hundred caregivers were randomized into treatment (n=49) and control conditions (n=51). The intervention provided caregiver stress monitoring and counseling information, personal voice-mail linkage to AD experts, a voice-mail telephone support group, and a distraction call for care recipients. Measures of the caregiver's appraisal of the bothersome nature of caregiving, anxiety, depression, and mastery were repeated at baseline, 6, 12, and 18 months. Results showed a significant intervention effects for participants with lower mastery at baseline on all three outcomes: bother (p=04), anxiety (p=01), and depression (p=.007). Wives exhibited a significant intervention effect in the reduction of bothersome nature of caregiving (p=.02). Wives and those with low mastery and high anxiety benefited most from the automated telecare intervention.

Observational Studies and Caregiver Burden

A number of prospective cohort and observational studies examined the impacts of caregiving on family caregivers. Two of these were discussed previously (see Satisfaction).[27, 99] Seven studies evaluated the overall impacts of caregiving upon terminally ill patients. Covinsky, Goldman, Cook et al.,[270] in a prospective cohort study (n=2,129) of outcomes, preferences, and decision-making in seriously ill hospitalized patients found that one-third (34%) of patients required considerable caregiving assistance from a family member. In 20% of cases, a family member had to quit work or make another major life change to provide care for the patient. Even though almost all patients had health insurance, loss of most or all of the family savings was

reported by 31% of families, whereas 29% reported the loss of the major source of income. Patient factors independently associated with loss of the family's savings included poor functional status (OR 1.40; 95% CI 1.10–1.78), lower family income (OR 1.74; 95% CI 1.37–2.21 for those with annual incomes below $25,000 and young age (OR, 2.85; 95% CI 2.13– 3.82 for those younger than 45 years of age compared to those 65 or older). Families of younger, poorer, and more functionally dependent patients are the most likely to report loss of most or all of the family's savings to a serious or fatal illness.

Emanuel, Fairclough et al.[271] conducted a survey of 988 terminally patients and their caregivers in six randomly selected areas of the United States to determine how their needs for assistance were met and the frequency with which they received such assistance from family members and paid or volunteer caregivers. Of the 988 terminally ill patients, 59% were over the age of 65 years and 51.5% were women. The most frequent terminal illness was cancer (52%), followed by heart disease (18%), and chronic obstructive pulmonary disease (11%). Four percent of the sample were in an institution (nursing home, hospital, or residential hospice), the rest were living in the community. Seventy-two percent of caregivers were women and 96% of caregivers were family members. A need for assistance was reported by 87% of the patients, including help with transportation (reported by 62%), homemaking services (55%), nursing care (29%), and personal care (26%). Most patients relied completely on family members and friends for assistance. Only 15.5% of patients relied totally on paid assistance for more than half of the care they needed. Volunteers (unpaid helpers who were not family members) provided less than 3% of all care. In addition to medical care, dying patients often need many types of assistance. Family members, primarily women, provided the majority of assistance with non-medical care.

In a subsequent analysis of this data, Emanuel, Fairclough et al.[50] found that 35% of the sample had substantial care needs and that those with substantial care needs were more likely to report that they had a subjective sense of economic burden (44.9% vs. 35.3%; difference 9.6 percentage points [95% CI, 3.1–16.1]; p=0.005). In addition, 10% of these families household income was spent on health care (28% vs. 17%; difference, 11 percentage points [CI 4.8–17.1]; $p \leq 0.001$) and they or their families had to take out a loan or mortgage, spend their savings, or obtain an additional job (16.3% vs. 10.2%; difference, 6.1 percentage points [CI 1.4–10.6]; p=0.004). Patients with substantial care needs were more likely to consider euthanasia or physician-assisted suicide (p=0.001). Caregivers of these patients were more likely to have depressive symptoms (p=0.01) and to report that caring for the patients interfered with their lives (p=0.001). Caregivers of patients whose physicians listened to patients' and caregivers' needs had fewer burdens. This study demonstrated that substantial care needs are an important cause of the economic and other burdens imposed by terminal illness.

Brazil, Bedard, Willison, and Hode[272] examined the effects of palliative caregiving in the home for 151 family caregivers to terminally ill cancer patients. The majority of respondents were the female spouses (79%) of the patient. The numbers of caregivers providing assistance in specific functional activities were bathing (88%); mobility 81%); dressing and undressing (76%); toileting (67%); and assistance at night (64%). Forty-one percent of caregivers reported that they had been providing some form of care for over one year. Caregivers reported that physical demands in caregiving increased substantially during the last three months of the care recipient's life. As family caregivers provided more assistance in ADLs, they were at greater risk of reporting high caregiver burden.

Hodgson, Higginson, McDonnell and Butters[273] prospectively collected patient and family well-being data on all patients referred for care over a six-month period in six home care services in Ireland. Five hundred and eight patients died while in care; 75% of these patients died at home. At referral, 32% of families had severe or overwhelming anxiety. During the last week of care, anxiety remained severe for 26% of care givers. Patient and family well-being were inter-related and there were significant interactions between family anxiety and patient physical and psychological symptoms and communication. Family anxiety at referral strongly predicts family anxiety at last week of life. Excluding family anxiety at referral, other predictors for family anxiety were patient symptom control, sex of patient, diagnosis, and patient age. These data suggest that while severe anxiety is not inevitable for all family members caring for a terminally ill patient, patient characteristics play a role in predicting family anxiety. Family anxiety is associated with patient age, sex, diagnosis and physical symptoms.

Outcomes at Transitions (Placement or Death)

Eight studies reviewed investigated the impact of two critical transitions faced by many caregivers (nursing home placement or the death of the care recipient) on caregivers. Some of these studies overlap with the topic of bereavement, which we did not explicitly address. We include only those studies that were also relevant to understanding other caregiver burdens. One overall impact of these was highlighted previously (under Satisfaction).[114] Collins et al.[274] prospectively examined changes in depression among family caregivers to dementia patients at three “transition” periods: nursing home placement, bereavement, and continuing residential care over three time periods (pre-event, and two post-event points). A convenience sample of family caregivers (n=142) was included in the analysis focusing on depression (n=46 residential caregivers, 49 institutional caregivers, and 47 bereaved caregivers). The mean depression levels for the total sample declined slightly over the three measurement periods but did not reach statistical significance. Depression appeared to decline among male caregivers and for bereaved caregivers over time but this change was not statistically significant. A more complex relationship occurred between gender and transition groups. Female residential and female institutional caregivers had higher combined levels of depression over time than female bereaved caregivers. In contrast, male residential and institutional caregivers had lower depression than bereaved male caregivers. Finally, male institutional or residential caregivers had significantly lower depression than their female counterparts. Thus, gender has an influence on mental health outcomes for caregivers who continue to provide care as well as those experiencing bereavement.

Grant, Adler et al.[275] prospectively examined the extent to which the chronic stress of AD patient caregiving was alleviated by placement or death of the patient in 119 caregivers and 48 non-caregiving comparisons. Three assessments on caregiver mood, blood pressure, and symptoms were conducted at six-month intervals among caregivers who cared for the dementia patient at home for all three observations (n=38), who placed the patient at follow-up (n=28), whose spouse were placed and subsequently died (n=27), those whose spouses died at home (n=26), and 48 non-caregiving spouses. Caregivers who placed the care recipient in a nursing home or whose care recipient died showed significant improvement in depressive and physical symptoms at 6 and 12 months after the transition (placement or death) compared to caregivers who continued to provide care and the non-caregiving comparison group, both of whom had relatively stable depression scores over time. Caregivers who placed the patient at the later time reported fewer serious symptoms over time compared to no change in the other groups.

However, both placement and death of patient were associated with higher blood pressure during transitions, and this continued up to 12 months after the transition. These data suggest that both placement and death of the demented relative can have beneficial effects on the mood and serious symptoms of the caregiver but that this effect can take 12 months to become evident. The blood pressure data suggest that a lengthy period of physiological readjustment may be necessary after placement or death of the AD spouse.

Hays, Kasl, & Jacobs[276] prospectively examined depression, anxiety, and distress in 1,112 caregivers with seriously ill spouses who survived or died over a two-year period. For analysis, the sample was divided into five groups, depending on whether the subject's spouse had been hospitalized for a critical illness or elective surgery, whether the outcome of the illness was death, and when the death occurred. Depressive symptoms and feelings of helplessness/ hopelessness were higher in caregivers whose spouse was hospitalized for critical illness, regardless of the outcome. In addition, distress related to the incidence of bereavement was significantly higher than that of the control group and endured for at least six months after the spouse's death. Anxiety levels did not change in response to either transition (hospitalization and/or death). Depressive symptoms and general anxiety were higher among widows and wives at the time of hospitalization compared to males while gender differences disappeared at two and six months for all bereaved caregivers, regardless of gender. Middle-age subjects reported more hopelessness/helplessness at baseline and six months compared to elderly subjects.

Schulz, Mendelsohn, Haley et al.[277] prospectively examined the type and intensity of care provided by 217 family caregivers to persons with dementia during the year before the patient's death and assessed the caregiver' responses to the death. Overall, caregivers exhibited high levels of depressive symptoms while providing care to the relative with dementia (mean CES-D score: 15.8$\pm$ 11.7; median, 13). Forty-three percent of caregivers had scores above 15. At the death of the relative, depressive symptom scores spiked to 22. However, within three months of the death of the relative, caregivers had clinically significant declines in the level of depressive symptoms, declining to a level similar to pre-bereavement levels (mean, 16.2$\pm$12.3; median, 14). Within one year the levels of symptoms were substantially lower than at baseline (mean 11.5$\pm$9.4; median, 9) ($p=0.03$). Caregivers who cared for and then placed their relative in a nursing home had mean scores for depression of 17.1$\pm$11.9 (median, 15) before placement and mean depression scores of 18.1$\pm$13.0 (median, 15) after placement. One year after placement, depression scores remained high and were significantly higher among caregivers of patients who had been institutionalized than among those caregivers of patients who had died (mean, 16.2 vs. 11.5; median, 14 vs. 9; $p=0.02$). Use of antidepressant medication and anxiolytic drugs increased after the death of the relative (16.6% and 19.4% before the death, 21% and 18% after the death). While the death of a close relative is generally viewed as a powerful source of psychological stress, the caregivers in this study showed remarkable resilience in adapting to the death of their relatives.

Volicer, Hurley, and Blasi[278] conducted a survey of a nationwide sample of 156 family caregivers of demented individuals who had died during the preceding year. Twenty-two percent of patients died at home. The results indicated that end-of-life experiences of individuals with dementia differ according to setting of care. Patients cared for at home and receiving hospice care during the last 90 days had fewer symptoms vs. other groups and fewer signs of physical distress during the dying process. Hospice use did not affect caregiver burden but these patients stayed at home 23 days longer and were twice as likely to die at home than in an institution.

Caregivers of patients dying at home had increased time dependence burden but other burden scores were similar among all groups. Caregivers with patients dying both at home and in an institution were less satisfied with care than those cared for in only one setting. No effect on burden was found for use of formal or informal assistance. Psychiatric symptoms in the patient increased caregiver burden and were the most common cause of institutionalization. Receipt of psychiatric care was associated with longer stay at home. Presence of advance directive decreased hospital stays and increased the likelihood of dying in a nursing home. These results indicate that quality end-of-life dementia care can be provided at home by family, with hospice and psychiatric care.

Martikainen and Valdonen[279] prospectively examined the effects of the death of a spouse on caregiver mortality using census and death certificate data on all Finns who died between 1986 and 1991. Five thousand five hundred deaths of widowed individuals were examined to determine if income and education mitigated the negative effects of spousal death. The results indicated that both men and women experience excess mortality after the death of a spouse and that the relative excess mortality among the bereaved is broadly similar in all education and income subgroups analyzed. The absolute mortality difference between widowed and married persons, however, tends to be larger among less educated and, especially, low-income persons.

Markowitz, Gutterman, Sadik, and Papadopoulos[280] investigated the relationship of caregivers' health-related quality of life to the burden of caring for patients with Alzheimer disease and resource utilization in a sample of 2,477 dementia caregivers. Compared with a normative, age-adjusted sample, the dementia caregivers had lower mental and physical scores (for the latter, only those 54 years of age or older). Increased caregiver mental functioning was associated with caregiver support and perceived quality of patient care, fewer hours of caregiving, and fewer patient behavioral symptoms.

Caregiving for Non-Cancer, Non-Alzheimer's Disease

There has been little research done on palliative caregiving and non-cancer deaths, other than in patients and families with dementia. Two studies reviewed examined the needs of terminally ill non-cancer patients and their caregivers. McCarthy, Addington-Hall, and Ley[281] examined the needs, services, and outcomes of care for 600 non-cancer deaths (heart disease) from the Regional Study of Care of the Dying, a population-based investigation of dying people based on reports of their main informal caregivers after the death. Just under half (47%) of caregivers felt they had not been able to get all the information regarding the deceased's illness that they had wanted or when they had wanted it. Thirty-seven percent of caregivers said they had known the deceased was likely to die and 26% said they had "half-known," whereas 26% of deceased patients were reported to have known and 25% were reported to have "probably" known that they were likely to die. Of those deceased patients who were reported to have known or probably known they were likely to die, most were reported to have had to work this out for themselves: only 8% were said to have been told by a GP or hospital doctor. Moreover, only 44% of caregivers were told of the terminal prognosis. Half of the patients (54%) died in hospitals, 30% at home, and 4% in other places. Patients under age 75 were less likely to die in an institution and more likely to die at home than patients 75 or older. Women aged 75 or older more frequently died in residential or nursing homes than males. One-quarter of the deceased were reported to have expressed a wish to die sooner; more women than men were said to have expressed such a wish (30% vs. 17%, $p<0.01$). Moreover, decedents who were aged 75 or older were 2.6 times more likely to have expressed a wish to die sooner; those with four or more

symptoms perceived as “very distressing” were 2.3 times more likely; and those who had a poor quality of life wee 1.9 times more likely to expressed such a wish. These results indicate that healthcare providers rarely discussed prognosis with heart disease patients, even though the five-year survival rate of chronic heart disease is about 50%, comparable with many types of cancer. Better palliative care, with concern for symptom control and psychological care should be available to all dying patients. Open communication about death and dying is needed to allow for a patient-centered end of life.

Evangelista, Dracup, Doering et al.[282] surveyed 103 heart failure patient/caregiver dyads to investigate whether caregiver characteristics were related to the emotional well-being of heart failure patients. Overall, patients had significantly lower (poorer) emotional well-being scores than caregivers ($p<.001$). However, both gender and age influenced well-being. Female patients and caregivers had lower emotional well-being compared to males; however, the difference was only statistically significant for patients ($p=<.018$). Male and younger patients had higher (better) scores than female and older patients ($p<.05$). Patients’ age, gender, and caregivers’ emotional well-being accounted for 54% of the variance in patients’ emotional well-being. These findings suggest that caregiver emotional well-being is associated with the well-being of the heart failure patient. A focus on supporting caregivers and providing them with methods to support their loved ones would be beneficial to patients.

E. Key Question 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 healthcare system performance, especially continuity of services

Introduction

We used a multidisciplinary systematic review of the overall literature on continuity of care as a conceptual framework for our review.[283] Based on a systematic review of the literature through 2001 and feedback from an expert workshop, these investigators defined continuity as "the degree to which a series of discrete healthcare events is experienced as coherent and connected and consistent with the patient's medical needs and personal context." This review, and a second systematic review particularly interested in the concept of measurement,[283,30] identified several key elements of continuity across disciplines: informational, management, and relational. Although we make distinctions between these aspects of continuity in an effort to bring some clarity to the literature in our discussion, in practice, interventions and their measures overlap these boundaries to varying degrees.

We evaluated nine systematic reviews that potentially dealt with the subject of continuity. All nine addressed the project questions and met implicit quality criteria. We went beyond the systematic reviews by including other interventions to improve continuity at the end of life published after these systematic reviews or published at any time if not already addressed in a systematic review. In total, we reviewed an additional 20 intervention studies. Because reviews and interventions related to heart failure were distinctive, we discuss them after more general interventions targeting continuity.

The remainder of this section summarizes the systematic reviews, meta-analyses, intervention, and observational studies relevant to continuity of care. With regard to observational literature, we identified prospective, observational cohort studies addressing continuity and that also presented data separately by race, selected disease cohorts, or selected sites of care. Because there were so few studies that met the design criteria, we also identified several other of the largest studies that addressed important aspects of those questions. Nineteen observational studies met these criteria. All observational studies are discussed at the conclusion of this section. We first summarize information related to continuity in general, and then a series of reviews and studies of patients with congestive heart failure. Summaries of the association of patient, family, and health system factors to continuity and the effectiveness of interventions in improving continuity are found at the conclusion of Chapter 3.

Systematic Reviews

We found seven systematic reviews (Table 6). These systematic reviews are briefly summarized in Tables 6 and 7 and discussed in the text in more detail. Two of the reviews[72, 74] and a published paper (by the same authors) graded and summarized other systematic reviews.[284]

Table 6. Systematic Reviews for Continuity/Coordination

Study	Issues Addressed	Date Search Concluded	Date of Publication
Gysels, 2004[72]	Continuity/coordination Palliative care	March 2003	Unpublished
Smeenk, 1998 [285]	Home care programs for patients with cancer	1997	1998
Higginson, 2001[74]	Home death rate as outcome	1999	2001
Higginson, 2003[214]	Palliative care	2000	2003
Teno, 2004 [30]	Measurement of continuity	2000	2000 (web)
Wilson (Health Canada)[259, 286]	Continuity, case management	October 2003	Unpublished

Gysels et al.,[72] the review that explicitly addressed the issue of coordination, identified 11 relevant individual trials. Ten experimented with organizational changes in the usual available care. Many of these studies address palliative and home care interventions and are also addressed in systematic reviews on these topics. Not all studies in Gysels et al.[72] or Wilson (Health Canada)[259] were relevant to the end of life, so relevant interventions have been extracted and non-cancer or more recent interventions have been added.

With regard to improving continuity, we identified an extensive systematic review of the literature on improving supportive and palliative care for adults with cancer.[72] It found that specific interventions, such as structured symptom assessment, needs assessments, improved medical record documentation and sharing, coordination of services, information or education, support, and preparing patients for physician visits, may all improve utilization or various patient-centered outcomes or utilization. Multi-component interventions including these and other elements, such as home care, care protocols, nurse availability, team care, and involvement in discharge planning, often as a part of a palliative care intervention, have also shown some evidence of effectiveness. However, a meta-analysis found that benefits of palliative care interventions, although affecting several domains, appear to be relatively small. Multi-component interventions are often not targeted toward particular outcomes but attempt to address multiple domains, and are also often ill defined. Nevertheless, these studies provided some evidence for reduced hospitalizations from these interventions. The review recommended that further intervention research describe theoretical models, attempt to separate out effects of different components, and evaluate the processes of care in order to better understand how interventions affect outcomes.

Palliative care, home care, and hospice interventions include continuity as an integral component. These interventions vary greatly in the composition of the team and nature of the

intervention (e.g., consultation vs. direct care). Some of the systematic reviews assessed communication interventions, support of chemotherapy, and primary care. A meta-regression[74] reported that palliative care had small benefits in many areas but did not show benefits for home death. Results were consistent by the type of service. Less evidence is available for hospital at home.

Table 7. Summary of Results from Systematic Reviews Relevant to Continuity

Comparison	Results
Record continuity (patient-held records)	3 studies (including 2 RCTs) evaluated this type of intervention. 1 RCT was extremely small (only 21 patients completed). No clear benefits except for patient-reported use.[72]
Management continuity	
Use of protocols/pathways/guidelines	Only 2 studies (both observational and without control groups) evaluated those relevant to the terminally ill.[72]
Nurse coordinator/case manager	11 studies identified (although end-of-life relevance of many is unclear) (4 RCTs). Results of studies were conflicting, but studies were very heterogeneous.[259] Also see CHF section below for disease-specific reviews and interventions on this issue.
Relational continuity	All showed small benefits in a number of outcomes, but not home death.
Home palliative care	22 studies[72,74]
Hospital-based palliative care	9 studies[72,74]
Integrated inpatient hospice/home care and hospital advisory	6 studies[72,74]

A systematic review of case management at the end of life[259] used the Case Management Society of America's definition of case management, "a collaborative process which assesses, plans, implements, coordinates, monitors, and evaluates options and services to meet an individual's health needs through communication and available resources to promote quality, cost-effective outcomes." Eleven research articles were selected for review out of "over 200" identified, although it is unclear how they defined relevance. The applicability of this descriptive review to this report is unclear because studies of different quality were mixed together, many of the included studies do not seem relevant to the end of life (for example, patients with early Alzheimer's dementia or discharges from a general medical service), and few articles overlapped with our review. In the potential patient-related domains identified with the review, they found conflicting results for well-being and quality of life, patient satisfaction, hospital utilization, home death, and cost-effectiveness. Impact on family caregiver burden was promising but still had limited impact. In general, although they found anecdotal accounts of end-of-life case management, few research articles compared case management to other delivery models, and end-of-life populations or issues were often not included.

A systematic review using only the word "continuity" with end-of-life terms found 13 relevant research articles, 6 monographs, 14 non-research articles, and 2 primary websites.[286]

The review was very limited because of the single search term, and articles were almost all observational and quite heterogeneous.

Additional Interventional Studies and Continuity

Information/record continuity

The SUPPORT intervention[287, 288] and other studies that focused mainly on advance care planning are fully described in that section. Latimer et al.[229] randomized 61 patients to a patient care traveling record, and did report a marginally significant improvement in pain control (described in the Pain section above). An RCT giving patients audiotaped recordings of their multidisciplinary oncology consultations reported only higher "usefulness" of the clinic (described in detail under the Satisfaction section above).[90]

Management continuity

We identified two studies examining the effects of ethics consultations in the ICU.[91, 289] The second study was a multi-site trial based on the earlier study in a single institution. Although the interventions were not standardized across institutions, in general, ethics consultations involved coordinating care by interviewing "those involved in the patient's care who bore on the issues under consideration." Issues were framed in easily understood ethical terms with the involved parties; consultations and recommendations were documented in the medical record; and ethics consultants provided ongoing follow-up. These studies reported that, only in the subgroup of patients who did not survive to discharge from the hospital, patients receiving the intervention had fewer hospital and ICU days and days receiving ventilation than patients in the control group. Further details of these studies are described in the Satisfaction section.

Another study in the ICU reported that patients cared for by an attending physician who focused on continuity of care had lower lengths of stay than other patients in the ICU.[290] This single site quality improvement report involved two ICU clinical nurse specialists and an ICU physician who adhered to a structured communication with the family and the nurse specialists who also provided psychosocial support to families. The Jadad score for this study was 0.

A multi-site RCT of team-managed home-based primary care in the VA[147] focused on continuity and reported results separately for terminally ill patients. The study reported improvements in multiple domains and is described in detail in the Satisfaction section. Another RCT of nurse coordination in the community, described in the Satisfaction section, reported no effect in multiple domains.[242]

An RCT of hospital-at-home reported no difference in the location of death (58% controls, 67% intervention) in an intent-to-treat analysis.[291] Hospital at home provides practical home nursing support continuously for up to two weeks, typically at the very end of life. However, only 61% of patients offered admission to the home hospital actually enrolled; among those who used hospital at home, the frequency of home death was higher (78% vs. 58%). In addition, this RCT compared the service to standard care, which included a variety of hospice and cancer support services. The Jadad score for this trial was 2. An RCT of a hospital palliative care team, described in the Satisfaction section, did not report an effect on satisfaction.[85] A pre-post comparison of a Kaiser Permanente palliative care program, also described in the Satisfaction section, also reported significant improvements in satisfaction.[87]

DeCourtney et al.[292] developed a multidisciplinary quality improvement intervention to deliver end-of-life care services to remote Alaska Native communities, and in a pre-post evaluation of site of death records reported that home deaths had increased from 33% in 1997 to 77% in 2001. This approach (Helping Hands) relies on nurse case management in extremely remote villages and includes coordination with remote physicians, bush air support for nurse visits and medical supply provision, and remote communication using radio and phone. It mobilizes village youth to provide practical hands-on support to patients and families when medical professionals are not available.

Raftery et al.[146] performed a randomized controlled trial in the UK of the cost-effectiveness of a district coordinating service for terminally ill cancer patients. The nurse coordinators were based in the community; their role was to assess the need for different services, advise on how to obtain services or contact the agencies themselves when needed, and ensure that services were provided and of good quality. They acted as liaisons with other nurses but did not provide any clinical care themselves. Outcomes were all related to costs. The intervention did reduce health service costs, hospital days, and nurse home visits but did not affect indirect or direct costs borne by patients. The Jadad score for this study was 2.

Selwyn et al.[293] evaluated the impact of a multidisciplinary palliative care consultation service for patients with AIDS in an urban teaching hospital in an uncontrolled pre-post design. One of the components of this program includes coordinating care with primary HIV providers and community support and healthcare resources. They report follow-up data on 115 patients followed until death or problem resolution by an interdisciplinary team that worked across settings and attempted to integrate palliative care with usual AIDS care. Full problem resolution was 73% for care decision-making, 59% for conflict resolution, and 7%–67% for symptoms from the MSAS. 55% died while in care, 29% went to a nursing home with hospice, and 14% went to a nursing home for chronic care.

Stockelberg et al.[294] evaluated the impact of home nursing for 17 patients with hematological malignancies, and found that providing support and transfusions in the home avoided most ambulatory visits.

We identified two RCTs of continuity-related interventions for the frail elderly. Melin et al. conducted a study of elderly patients who had from 1-5 ADL impairments.[295] Intervention and control patients had a variety of diagnoses and a mean age of approximately 80. Intervention consisted of a team of physicians and nurses who made regular home visits for assessment and treatment as well as 24 hour phone support. Approximately 25% of the 249 patients (150–I, 99–C) died during the study. Relative to controls, the intervention group improved in IADL, social activities, and more were living at home at the conclusion of the study (79% vs. 63%). Hospital use was similar, but controls had more long-term care use and intervention patients used more home care days.

Mann et al. conducted[296] an RCT of 104 home-based frail elderly patients (52–I, 52–C) who were randomized to functional and home environmental assessment. These patients averaged 73 years of age and approximately 60% in both groups had been hospitalized in the previous six months. Intervention patients received assistive devices such as canes or walkers and environmental interventions such as ramps. Control participants declined on 7/9 functional measures during six months of follow-up compared to the intervention group. Pain scores were also lower at the conclusion of the trial in intervention group. There was no difference in total

costs—although intervention participants spent more on devices and modification, and control groups spent more on nursing homes and nurse visits.

Relational continuity

In a randomized, crossover trial, 214 patients receiving palliative chemotherapy completed a HRQOL questionnaire at three successive outpatient visits.[222] Physicians and patients were briefly educated about the intervention and were given a graphic summary of the questionnaire before each consultation. HRQOL-related issues were discussed more frequently in the intervention than in the control group, and physicians identified more patients with moderate-to-severe problems in feelings, social activities, and fatigue in the intervention than in the control group. Significantly more patients in the intervention group than in the control group received counseling from their physician on managing their health problems, the level of patient satisfaction with emotional support was higher, and significantly more patients showed improvement in mental health and role functioning. Seventy-nine percent of patients believed that the HRQOL summary increased their physician's awareness of their health problems. The Jadad score for this study was 3.

Specific populations

Heart failure

Many of the studies discussed in this area (in the context of systematic reviews or interventions) excluded 'terminally ill' patients and did not address other palliative domains. However, because these studies enrolled patients with advanced CHF who had high mortality and given the prognostic uncertainty in this condition, we determined them to be relevant for the purposes of the review. We identified five systematic reviews related to continuity and coordination in heart failure. One was a previous review that has now been updated[297] and one older review only included 7 articles;[298] these are not included here. These reviews all addressed the literature somewhat differently, with different definitions and inclusion criteria but some overlap; they are summarized briefly in the table below.

Table 8. Systematic Reviews Relevant to Continuity/Coordination in Heart Failure

Study	Issues Addressed	Date Search Concluded	Date of Publication
Phillips,2004[299]	Comprehensive discharge planning plus post-discharge support	2003	2004
McAlister, 2004 [300]	Multidisciplinary management programs (specialized multidisciplinary teams, enhancing patient self-care, and telephone contact)	2003	2004
Windham, 2003 [301]	Care management for older patients	2002	2003

In general, these reviews concentrated on utilization outcomes and mortality. McAlister et al.'s review of 29 RCTs[300] reported that trials that incorporated follow-up by a multidisciplinary team, enhancing patient self-care activities, or used telephone contact and advised patients to see their physician when needed all reduced heart failure hospitalizations. Reductions in mortality and all-cause hospitalizations were more variable. All interventions incorporated patient education.

Results for patient-centered outcomes were more equivocal. Windham et al.[302] and McAlister et al.[300] reported that approximately half of studies that examined HRQOL or functional status showed improvements. Phillips et al.[299] pooled QOL scores for 6 RCTs and reported a statistically significant difference: 26% improvement in the intervention groups compared to 14% in the control groups. Patient satisfaction was measured in only three of 32 studies evaluated in one review.[301] One review descriptively compared the characteristics of the 15 effective to the 17 ineffective case management interventions and concluded that education and close monitoring for CHF symptoms by nurses or care managers were important components. Eight of the 32 studies included a social worker as part of the intervention.[301]

Additional Interventional Studies and Continuity in CHF

We identified seven additional interventions related to continuity and coordination in CHF.[303-305,306-309,310]

Stewart et al. reported the outcome of a nurse case management intervention that included structured, intensive education, both patient and family activation, and coordination of care activities between both the primary physician and cardiologist.[303, 311] Twenty deaths (10%) occurred in six months of follow-up. Rates of unplanned readmission were lower in the intervention group 68 vs. 118, p=0.031), and costs were correspondingly lower. Quality of life improved among survivors in both groups. The investigators reported the effectiveness of the intervention on the most high risk patients and noted a mortality benefit as well in this subset analysis.[311] The Jadad score for this trial was 1.

Goldberg et al. randomized CHF patients to either a telephonic monitoring system linked to an electronic scale and trained CHF nurse case manager vs. usual care.[312] Patients with prognosis < 6 months were excluded as were those with advanced renal disease (dialysis or Cr. > 4.0) and other specific cardiac conditions although 13% (37/280) of enrolled patients died in six months of follow-up (lower in the intervention group 8% vs. 13%). There was no difference in re-hospitalization and quality of life improvements were similar in both groups. The Jadad score for this trial was 1.

Jaarsma et al. randomized 179 patients (84–I, 95–C) to a nursing education and one time telephone follow-up of CHF patients that was intended to increase self-care during the ten days after hospital discharge.[307] Exclusion included serious comorbidity. In nine months of follow-up, 38/179 (21%) patients died. Self-care behaviors attenuated strongly in control and intervention patients after discharge, although there was a small difference in persistence of self-care behaviors at nine months. This study failed to show a difference in utilization. The Jadad score for this trial was 1.

Philbin et al. conducted a hospital-level quality improvement cluster randomized trial.[313] Five intervention hospitals attempted to implement a critical pathway for CHF management. The intervention also included staff professional education. CHF survivors were followed for six

months post-hospitalization. All-cause mortality in these patients averaged about 20% among survivors at six months. This inpatient-only intervention noted no post-discharge benefits on mortality, utilization, or quality of life. The Jadad score for this trial was 1.

Goodyer et al.[314] performed an RCT of a three-month intensive medication counseling intervention in patients with chronic, stable heart failure. The study did not report mortality. The intervention significantly improved compliance and decreased edema and subjective breathlessness in the intervention group compared to the control group. The control group also had significant decreases in scores for energy and physical mobility that were not seen in the intervention group. The Jadad score for this trial was 1.

Heidenreich et al. reported an uncontrolled pre-post evaluation of an automated weight and vital signs monitoring device linked to physician and nurse manager alerts coupled with nurse education. Forty percent of these patients had moderate or greater reduction in left ventricular function. Survival was estimated as 82% at 12 months. Pre-post utilization and costs were lower in the intervention group, although quality of life was unchanged.

Gorski and Johnson reported a post-evaluation of a quality improvement intervention without a control group[306] that suggested benefits in self-care and utilization.

Observational Studies in Continuity

With regard to the association of ethnicity with continuity, although a prospective cohort study found that blacks received less intensive care in the hospital,[315] others have found that black nursing home residents tend to receive higher-intensity care and are more likely to die in the hospital.[316] Several studies provide potential explanations for these disparities. One study found that black residents tend to be concentrated in nursing homes with fewer available resources, which is associated with more hospitalizations.[317] Another study[318] examining non-English-speaking patients found that patients of different ethnicities had poorer understanding of their prognosis than English-speaking patients. Another[319] found that nurses spent less time at the bedsides of non-white dying patients.

In related literature about settings of care and continuity, we identified several studies that identified problems related to transitions in care in nursing homes.[316, 320, 321] Other observational literature (see Satisfaction and Advance Care Planning) highlighted the challenges of transitions and/or continuity involving other or multiple settings.[114] This literature also highlights the possible role of advance care planning (ACP) in reducing transfers.[316] One study highlighted an association between more intensive staffing and primary care in nursing homes and decreased risk for transfers.[322] Several studies suggest a higher preference for death at home than is typically observed.[323, 324]

With regard to disease, the observational literature underscores the risks of discontinuity in patients with CHF. One study highlighted the social factors, especially single marital status associated with a risk for re-admission.[325] Several other studies demonstrate that the risk of re-admission (up to 50%) is particularly associated with age and comorbidity, and in such unselected patients is even higher than in trials using more selected patients conducted in CHF.[325-327] We found no studies of other particular disease states or comparative studies of risk by disease.

We identified several studies notable for particular mention related to the subject of continuity. Fisher et al.'s large national study of Medicare cohorts (described in the Satisfaction section above) descriptively highlighted the fact that ten or more physicians were involved in the care of 37% of chronically ill patients during the last six months of life.[115] A retrospective study of approximately 9000 decedents using administrative data demonstrated a strong association between higher physician primary care continuity measured using the Modified Continuity Index (MMCI) and lower emergency department use in the last six months of life as well as greater likelihood of home death.[328, 329]

F. 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 decision-making, especially advance care planning

Advanced directives (ADs) (including "living wills" and "instructional directives"), are formal, legally endorsed documents that state instructions for care (e.g., circumstances in which life-sustaining treatment is to be provided or forgone) or that name a proxy/surrogate decision-maker (e.g., "durable power of attorney" and "healthcare proxy") in the event of future decisional incapacity. The federal Patient Self-Determination Act (PSDA) (OBRA-1990) and legislation on practice in all 50 states provided legal enforcement for ADs that followed certain procedures. More recent efforts to elicit patient preferences have moved toward advanced care planning, which denotes a broader set of activities. Advance care planning requires a well-informed patient or surrogate to make decisions about future care so that treatments undertaken during a future period of decisional incapacity will still be in accord with the patient's preferences.

For this report, studies involving advance-care planning, advance directives, living wills, and "do not resuscitate" (DNR) orders were included if their targets were patients or families (rather than only reporting about clinicians). We evaluated four systematic reviews that potentially dealt with the subject of ACP. We went beyond the systematic reviews by including other interventions to improve ACP at the end of life published after these systematic reviews or published at any time if not already addressed in a systematic review. In total, we reviewed an additional 21 intervention studies. All observational studies that met our criteria are discussed at the conclusion of this section.

The remainder of this section summarizes the evidence from systematic reviews, intervention studies, and observational studies relevant to advance care planning, including ADs, living wills and DNR orders. Summaries of the association of patient, family, and health system factors with ACP and the effectiveness of interventions in improving ACP are found at the conclusion of Chapter 3.

Systematic Reviews

Four systematic reviews were identified that met implicit quality criteria (see Table 9), and reflected three separate reviews addressing the topic of advance care planning.

Table 9. Systematic Review for Advance Care Planning

Study	Aspect of Advance Care Planning	Date Search Concluded	Date of Publication
Baggs[330]	End-of-life care decision-making	2000	2002
Hanson et al.[331]	Interventions targeting patients, physicians or both, by their effect on increasing use of patient preferences and reducing use of life-sustaining treatments	1996	1997
Higginson et al.[332]	Communication, advance care planning, continuity	1999	2002
Walsh et al.[333]	Patient satisfaction, patient preferences	1997	1998

In the first of these, Baggs[330] systematically reviewed the literature for evidence on end-of-life care for older adults (over 44 years old) in ICUs and their families and caregivers, focusing in part on literature involving nursing. Ninety-one studies were evaluated, reviewing the literature on interventions, prospective cohort studies, and retrospective analyses. Baggs' review found that the characteristics of appropriate care for dying patients, particularly patients with DNR orders, are not clear. She also identified that advanced age, severity of condition, and DNR orders correlate with limited life-sustaining treatment. Two studies found that resource use decreased following placement of DNR orders. One study found that life-supporting interventions were withdrawn or withheld in 45 percent of ICU patients before their death. On the whole, age was not a factor in limiting care among patients once admitted to the ICU, but age has been a factor in limiting admission to the ICU for the elderly and some studies showed that the elderly appear to receive less aggressive care than do younger patients.

Furthermore, Baggs' review showed that end-of-life hospital care often involves inadequate communication and disagreement between patients and their families and physicians and nurses. Several studies, including the SUPPORT study, found that families and clinicians often have an incomplete understanding of patients' preferences. This inadequate communication can cause some elderly to receive technical interventions rather than their preferred comfort care prior to death. Since dying ICU patients are generally not capable of communicating their preferences, achieving accord on a plan of care is often challenging. Ongoing communication is important because many patients want relief of symptoms without prolonged dying, decision-making that requires both families and providers, and psychological support. Communication is important because, while some of those in ICUs experience a feeling of safety and security, many experience discomfort, cognitive impairment, and anxiety. In the SUPPORT project,[287] families reported that in the last three days of life, dying patients were most often in pain, experiencing dyspnea and fatigue. Baggs' review of clinical interventions also showed that hospital end-of-life care does not rely upon evidence-based guidelines.

The Hanson et al.[331] systematic review examined the literature between January 1990 and March 1996, on whether interventions aimed at physicians and/or patients affected AD completion and subsequent end-of-life care. Six of the eight randomized studies reviewed, each targeting only patients, increased the rates of AD completion or proxy choices when they

combined written materials on ADs with one or more discussions with physicians or a social worker about ADs. Five other studies, that targeted only physicians in single sites, used physician education in combination with reminders and feedback. This combined approach was successful in increasing AD completion and/or advance care planning discussions with patients. Three additional studies reviewed involved both physicians and patients. For example, SUPPORT showed that having an intervention to improve advance care planning did not alter the use of life-sustaining treatment or other outcomes.[287] From this review of a total of 14 studies, Hanson et al.[331] concluded that, for end-of-life populations, educational interventions for both patients and physicians combined with repeated treatment preference discussions between physicians and patients as well as accessible documentation of the patient's treatment preferences, could reduce the use of life-sustaining interventions at the end-of-life.

A systematic review of the literature and meta-analysis by Higginson et al.[332] focused on the impact of hospital-based palliative care teams on patient outcomes and on families. Some of the findings related to advance care planning, particularly reporting a modest effect on hospital length of stay, but the authors note that the study designs do not allow confidence in this assessment or generalization to other settings. The 13 studies incorporated in the Higginson review do not overlap with this report. This Higginson review also reported that hospital-based palliative care teams are somewhat beneficial in terms of reducing the length of hospital stay and having a small positive effect on addressing patient's symptoms.

In the other systematic review, Walsh et al.[333] examined the literature on conveying "bad news" concerning a life-threatening diagnosis or death, including publications between 1994 and August 1997. Ten RCTs examined how bad news is delivered and how the impact in doing so influences patients' knowledge of their diagnosis, psychological adjustment, and satisfaction. In eight RCTs, the impact of communication interventions on patient recall and information needs was inconclusive; half showing an increase in short-term knowledge and the others showing no effect. Of the eight RCTs examined for the effect of communication practices on psychological adjustment, seven reported no significant differences, but one RCT found lower adjustment levels and higher anxiety after receiving the "bad news" intervention. The authors noted that these findings were in contrast to an older meta-analysis of 45 studies that had found a positive effect. Patient satisfaction in six RCTs was also inconclusive; three showing an increase and the other three showing no difference.

Additional Intervention Studies of Advance Care Planning

We found an additional 21 intervention studies that were not discussed in the systematic reviews. A trial of ACP in nursing homes was discussed above in the Satisfaction section.[92] Studies varied in scope, methodology, duration, and outcome. These studies involved the following approaches to research involving advance care planning: 1) providing education about and the opportunity to complete an advance directive or participate in ACP discussions to patients; 2) having clinicians, patients, and families/surrogates discuss the patient's treatment preferences and prognosis for patients who are dying or are likely to die; 3) having clinicians receive consultations to assist their decision-making process with patients; and 4) determining if efforts to document ADs affect treatment. Of these 21 studies, six were RCTs. Two of the RCTs examined ACP discussions in hospitals, three in outpatient settings, and one in nursing homes; the other RCT assessed the impact of physician-initiated AD discussions in elderly outpatients who were not severely ill. Among these studies, the few reporting differences by race/ethnicity and gender are discussed below.

Within SUPPORT, Marbella et al.[288] examined the accord of patients and surrogates as to the patient's preferences, comparing the 386 paired patient and surrogate responses of the intervention group for whom trained nurses spent extra time with patients and families to explain and answer questions about prognoses and potential treatments with the 331 patient and surrogate pairs in the control group. No difference in concordance between patients and families followed the intervention. Among all patient-surrogate pairs, there was slightly less accord if the patient was older or the surrogate was not a close family member. Race and gender did not have a significant impact, though the trend was toward more accord in non-white patients and with female patients. The SUPPORT intervention study has a Jadad score of 3.

The Landry et al.[334] and Dexter et al.[335] RCTs focused on interventions aimed at increasing the number of adult and elderly patients with advance directives in outpatient settings. In the Landry et al. RCT,[334] 95 patients with no known life-threatening diagnoses were randomized to the intervention group from the 187 patients in an outpatient clinic. The intervention group participated in an educational seminar without their clinicians and received written materials on ADs, while the control group only received the written materials. AD completion was found to have increased in both groups, but the AD completion rates in the intervention group doubled. In the Dexter et al. RCT,[335] 1,009 patients age 75 and older, with no known life-threatening illness, were randomized to an instruction directive group, proxy directive group, instruction directive and proxy directive group or to the control group. Primary care physicians were given reminders on the computer-generated encounter form in the patient record to have advance directive discussions with the intervention group patients. Comparatively, there was a significant increase in AD discussions in the intervention groups, half of which resulted in the patient completing an AD. The Jadad score for both studies is 3.

In the Smucker et al.[336] RCT, 100 patients 65 years or older, in an outpatient clinic, were randomized to physician-initiated discussions on ADs or to discussions on health promotion and assessed on their subsequent emotional or attitudinal response. Patients in the intervention group did not experience adverse emotional or attitudinal effects, and those who had ACP discussions with their primary care clinicians were more satisfied, findings that were even more pronounced when patient's had higher educational levels and a long term relationship with their physician. This study has a Jadad score of 1.

In a pilot RCT, 61 ambulatory geriatric patients between the ages of 65 to 92 were randomized, either to the control group, which only received a healthcare proxy form, or to the intervention group, which received the form and participated in an ACP discussion with a skilled nurse. For the 31 intervention patients, discussions of ACP involved a program called "Respecting Choices," while 30 patients had no involvement in "Respecting Choices." Patients and their surrogates concurred as to the patient's preferences and more patients opted for less aggressive interventions in the intervention group. Interventions such as "Respecting Choices," where options are presented along with an actual living will form, have been tested in numerous studies, but generally only at one site of care.[337] This study has a Jadad score of 2.

We also identified an additional 15 non-randomized intervention studies aiming to improve ACP, six with a comparison group and nine without a comparison group. These studies fell into the following categories: five studies that used specially trained clinicians to discuss ACP, including the diagnosis and prognosis of severely ill ICU patients at high risk of dying with assessment of changes in utilization; three studies that used palliative care teams for ACP discussions for hospitalized patients; one study that used clinician education and

institutionalizing forms to assess patients who died; three studies that provided ACP discussions for patients receiving outpatient care; and three studies of end-of-life discussions in patients with advanced illness receiving non-hospice home care.

In one of the active communication studies in ICUs by Lilly et al.,[338] advance care planning discussions with dying patients did have some impact, unlike SUPPORT. As part of the intervention, indirect caregivers (e.g., social workers and care coordinators) and some nurses met with the patient following the intensive communication session with direct caregivers, but a standardized meeting template was used to convey information from the intensive communication meetings.[338] The improvements documented in the initial intervention were sustained over the ensuing four years. However, this study did not monitor whether the patients admitted to intensive care changed over time. In both of these studies, presenting information about clinical status and expected outcomes to patients having advance directives and their families was associated with increases in decisions to forgo some therapeutic interventions.[338]

Similar to the findings of the Schneiderman et al. RCT[91] described in the Baggs systematic review[330] (and also above in the Satisfaction section), two of the communication studies examined the impact of specially trained teams on changes in utilization prior to death. In the first of these two, clinicians of 31 of 99 ICU patients receiving mechanical ventilation discussed the patient's preferences and prognosis with a team of two ethical consultants before decision-making became problematic for the clinicians. These consultations resulted in an increase in decisions to forgo life-sustaining treatment and shorter lengths of stay in the ICU.[339] In the second study, Campbell and Guzman[340] enrolled MICU patients with global cerebral ischemia after cardiopulmonary resuscitation and multiple organ system failure with or without ADs. These patients and their surrogates were given the opportunity to discuss the patient's prognosis and treatment options with a palliative care team. As a result, patients opted for palliative care more often than for pursuing all possible therapeutic interventions.

The last of this group of ICU communication studies assessed the impact of a healthcare team that met daily to select how 83 ICU patients should be treated, whereupon the team would seek agreement from the family, particularly if it was recommended that treatment be withheld or withdrawn. While the investigators did find an increase the incidence of withholding or withdrawing treatments, the study did not report whether the withholding or withdrawal of treatment was in accord with the patient's AD or treatment preferences.[341]

Three studies assessed improving communication of patient's preferences in hospitals and assessing the impact on patient outcomes. Jack et al.[342] enrolled 50 cancer patients referred to the hospital palliative care team for symptom control, and compared findings to a control group of 50 patients. Subsequent analysis focused on the positive effect on the patients' understanding of their diagnosis and prognosis. Patients in both groups improved their understanding of their diagnosis and prognosis, but the intervention group had higher levels of understanding. The Butler et al.[343] study assessed the impact of institutionalizing a standardized DNR order form on the number of patients who died in the hospital with a DNR form. Compared to the period before the form was institutionalized (94 patients), there was an increase in the documentation of the 62 patients' treatment preferences and in patient involvement in treatment decisions while hospitalized. In the Monteleoni and Clark study,[344] the impact of a palliative care team communicating with attending physicians about the patient's treatment preferences was assessed. In assessing rates of feeding tube placement before the time when they initiated their

intervention, the study found no difference in placement of feeding tubes in patients having ADs, including ADs that documented refusal of artificial nutrition.

We found three studies that investigated the impact of ACP communication with patients with advanced illness receiving outpatient care. In a controlled interventional study, the effect of AD education on 50 COPD rehabilitation patients was compared to 43 patients not involved with the educational workshop. Following the AD education, the rate of intervention patients with a completed living will increased from 52% to 72% and the rate with completed durable powers of attorney increased from 34% to 86%, as well as an increase from 16% to 52% in patients discussing their life-support decisions with a physician.[345] Another of these studies involved using palliative care consultations for nephrologists caring for 19 patients with no comparison group. These consultations were intended to assist the nephrologists when they helped patients to select treatments, including symptom control and assistance with coping with their burden of illness. These consultations increased discussions of advanced care planning between the patient's nephrologists and surrogates, though the numbers of advance directives did not increase (also discussed above in the Satisfaction section).[88] Both of these studies found that less than half of the patients had ACP discussions prior to the intervention, and their physicians or surrogates did not understand the patients' preferences.

The third ACP communication intervention in outpatient settings involved 204 patients receiving clinical services from two hospitals. The health status and psychological well-being of all study patients were assessed. Of the 104 intervention patients offered an AD form, 67% completed the AD form. Furthermore, signing the AD form did not adversely affect the patients' overall health (both physical and psychological).[346]

From another vantage point, three studies without comparison groups reported facilitating ACP discussion with severely ill home care patients. An evaluation of the Comprehensive Home-based Options for Informed Consent about End-stage services (CHOICES) program, enabled by the comprehensive nature of managed care in Medicare + Choice, 208 enrolled patients with advanced chronic illness elicited treatment preferences (including modifying ADs for patients with ADs), arranged appropriate services, and eventually facilitated entry into hospice care. The focus of CHOICES was to understand a patient's multifaceted needs and to fashion treatment options to fit the preferences of the patients. During the study period, the length of time in hospice significantly increased among the 208 patients, more patients died at home, and enrolled patients spent less time in hospitals.[347] The second home care study investigated the effectiveness of discussions about end-of-life care in a patient's home. After such discussions, almost all the 84 adult patients with life-limiting illnesses were willing to have an advance directive and wanted end-of-life care at home.[348] Both studies facilitated increased utilization of hospice care and dying at home. The third home care study was a small investigation documenting the treatment preferences among 31 AIDS patients with no comparison group. The investigator, who assisted the patients with defining their AD, found that standardized AD forms did not fully capture the patient's treatment preferences.[349]

Prospective Cohort Observational Studies on Advance Care Planning

We found an additional 22 prospective cohort studies that were not discussed in the systematic reviews and that address aspects of advance care planning not covered by the aforementioned intervention studies. These employed various methodologies, including using different instruments and respondents. Eight of these were prospective cohort studies drawn from the SUPPORT intervention study. From these studies, three major themes emerge. First, the impact of efforts to increase AD communication, completion, and documentation was evaluated positively by participants, but has not been shown to be effective in altering treatment patterns. Second, patient preferences often change over time and as illness progresses. Third, communicating with families and involving them, as well as patients, in advance care planning is important when possible.

Two SUPPORT studies by Teno et al.[350, 351] found that, in most instances, ADs did not affect end-of-life decision-making,[350] especially when family members and physicians had a clear preference and the patient's vague advance directive generally disagreed.[351] In SUPPORT, the intervention did succeed in having more advance directives present in the medical record, but very few advance directives provided clear instruction that was applicable to the situation. Very few patients and physicians talked about preferences, even when patients actually prefer forgoing resuscitation.[352] However, communication and physician understanding of patient preferences improved when physicians have a longer relationship with the patient, have an accurate understanding of the patient's six-month survival, and discuss resuscitation preferences with the patient.[353]

Assuming that clinicians have the responsibility of initiating advance care planning discussions, efforts to help them increase AD communication, completion and documentation have been mixed. Assessment of the impact of the AD discussions among 686 patients initiated by primary care physicians resulted in patients being more satisfied with their physicians, and no significant differences were associated with race/ethnicity and gender.[354] One Curtis et al.[168] study of 31 AIDS patients also found that, when these conversations did take place, patients were more satisfied, but more so when clinicians knew their patients and their ADs. However, non-Hispanic Whites and those with higher incomes were more satisfied. Furthermore, a study of 642 hospitalized cancer patients found that generalists and oncologists discussed similar topics and demonstrated similar prescribed treatments, which were influenced by the perception of the patient's preferences and prognosis.[355]

Given the importance of patient-physician communication, barriers exist for physicians to initiate end-of-life care discussions. Another Curtis et al.[356] study of 57 AIDS patients found that patient-physician communication barriers often stemmed from the clinicians' lack of education about end-of-life care and lack of time for these discussions, as well as having the opinion that the need for end-of-life care discussions had not been evident. A study of 255 patients in a Swiss hospital found that, even among patients with DNR orders, physicians tended to make DNR decisions when they perceived patients as having a poor quality of life; a perception that is often lower than the patient's measured quality of life.[357]

As time passes, patient's preferences may change. In a study of 50 adults age 65 and older, selection of health impairment states worse than death were similar to the selection of specific life-sustaining treatment preferences; preferences that did change over time.[358] Some of these changes may be associated with specific health events, but the evidence is equivocal. In a study

of palliative chemotherapy treatment decisions in 203 cancer patients, changes in health related quality of life resulted in patients' opting to modify or discontinue treatment when there was evidence of tumor progression or treatment toxicity; not when the patient's health related quality of life deteriorated.[359] Another study of patient preferences for place of death among 98 cancer patients found that, when patients understood their disease and prognosis, almost two-thirds did not want to die in a hospital and their needs could be met at home.[323] Similarly, in a study of 80 cancer patients, patient preferences for information and involvement in decision-making often changed between consultations. Generally, female patients wanted more information than males, and patients with worsening conditions more often wanted physicians to make treatment decisions. Some differences in patient preferences for information were associated with which of the two study physicians was seen on a particular visit, so preferences might well relate to physician behavior during patient-physician communication.[360]

Over the course of illness, patients' preferences may also not reflect their actual prognosis or subsequent utilization. Findings from one of the SUPPORT studies found that patients with advanced colon and lung cancer estimated longer survival times than their actual prognoses, and this correlated with a greater likelihood of wanting life-extending interventions.[361] Another SUPPORT study found that decisions to withhold or withdraw life-sustaining treatments was not associated with the patient's race/ethnicity,[362] but those with advanced age and men were more likely to have dialysis withheld or withdrawn.[363] Another SUPPORT report found that a patient's prognosis and preferences appear to affect the timing of documenting DNR orders.[364] A related study, assessing hospital utilization among 241 patients with advanced illness, found that patients' prior preferences were not associated with actual hospital and life-sustaining treatment utilization.[365] Similar findings were observed in another study of 65 nursing home residents, where patients' prior treatment preferences were found not to reflect subsequent utilization, particularly when a patient's health deteriorated and family and physician chose to limit further interventions.[366]

The involvement of families in advance care planning and decision-making is also important, but not a standard of practice. In a study of families and friends of 600 heart disease decedents, almost half had limited information on the decedents' illness, yet half of the decedents were reported as having known their prognosis and likelihood of death—many of whom wanted to die soon because of uncontrolled symptoms.[281] In another study of 102 ICU patients in a Paris hospital, physicians did not communicate with half of the ICU patients' families when they were from another country, spoke a different language, were not the spouse of the patient, and did not have a healthcare background.[367] There may be communication barriers among clinicians, between clinicians and patients and their families, and between patients and families. In an assessment of end-of-life care communication and cancer patients in England, Ireland, and Italy, there were communication problems in 30% to 40% of instances between patients and their families, compared to communication problems in 10% to 20% of instances associated between clinicians and clinicians, or patients and their families. There were also more communication problems when patients died in inpatient hospice care, not when patients died at home.[104]

Additional Cross-Sectional and Retrospective Observational Studies and Advance Care Planning.

Beyond the findings of the intervention and prospective cohort studies, we reviewed an additional 74 cross-sectional observational studies and 57 retrospective studies. Among the cross-sectional studies, we found that 21 had study populations less than 100, 7 reported outcome differences by race/ethnicity, and 23 reported outcome differences by gender. Among the 57 retrospective studies, we found that 8 had study populations less than 100, 11 reported outcome differences by race/ethnicity, and 5 reported outcome differences by gender. The majority of these retrospective studies used large secondary datasets. Among the cross-sectional and retrospective studies, there were significant differences: in study subjects (e.g., health status, diagnosis, prognosis, and proximity to death), setting of care, survey design and data collection instruments, and study methodology, Educational studies have included providing written AD materials or an informational videotape, providing education on the importance of advance directives to patients and/or providers (e.g., using AD discussion guides and written information for consumers, identification of a central or uniform place for the advance directive, and educational seminars), or counseling activities (e.g., supplying written information on ADs and providing an opportunity to complete an AD or assisting patients with life-threatening diseases to make decisions about medical care). Hammes and Rooney[368] reported remarkable effects from a community-wide implementation of AD education, with 85% of all who died in La Crosse, WI, having a written AD at the time of death, virtually all of which were available and followed. Showing that at least one large healthcare delivery system can similarly increase the rate of advance care planning, the Veterans Health Care System designated advance care planning for six conditions as being a mandated goal for each of their geographically based networks. The VA system increased advance care planning for veterans with the designated serious illnesses by 15% system-wide in just three months.[369] Two recent reports from Oregon where a special form called the Physician Orders for Life-Sustaining Treatment (POLST) is in common use show that three-quarters of all out-of-hospital decedents[369] and of all nursing facilities[370] have the POLST completed and available.

G. Summary regarding outcome variations among populations (by patient, family, and health system characteristics)

We identified one systematic review that addressed the issue of outcome variations by race/ethnicity and by settings of care—the two issues that we chose to focus on due to time and resource limitations. Because this review did not map easily to the topics we chose, we discuss it here in introducing a summary of our own findings.

Table 10. Systematic Review of Outcome Variation

Study	Aspect of Variation	Date Search Concluded	Date of Publication
Wilson[371-374]	Cultural variation; variation by site of care (hospital, long-term care, and home care)	October 2003	Unpublished

Wilson et al. identified studies relevant to cultural variation in outcomes. The eleven studies were all observational in nature, and were relevant to advance directives, healthcare preferences, communication, and decision-making. These studies generally observed that religion and acculturation as well as ethnicity figured prominently in explaining cultural differences. African-American and Hispanic status was associated with preferences for life-sustaining treatment in several studies. Hispanic status was also associated with impaired communication secondary to language – not only about advance directives, but also pain. Several studies highlight cultural differences not only in preferences for treatment, but also in the process of decision-making with respect to disclosure and the family's role vis-à-vis the patient's autonomy with non-white patients more likely to prefer non-disclosure and group vs. individual decision-making.

The same review also highlighted studies related to home, nursing home, and hospital care. These reviews did not explicitly examine differences, but the individual reviews are useful by comparison. The study identified 11 studies relevant to hospital care at the end of life, 20 studies related to home death, and 22 articles related to long-term care death. With respect to hospitals, the review highlighted the fact that many patients experience a hospital death and that from the population perspective, bed supply is one of the more important determinants of site of death. Women and non-white patients were at higher risk of end-of-life hospitalization, according to several studies. Less than a third of hospitalized patients made advance care plans in several studies and high-intensity care was common, even among patients with dementia. This review highlighted the role of nursing education in palliative care—studies reported an association between education or experience in end-of-life care and management or attitudes. With respect to nursing home issues, the review highlighted descriptive studies of difficulties in pain management, personal care, communication, and caregiver support. Several studies reported an association between hospice use in the nursing home and family perceptions of better nursing home care compared to families whose loved ones did not receive hospice. With regard to home death, the review highlighted literature describing a discrepancy between preference for home death and its low rate of occurrence. Home support was associated with increased likelihood of death and care at home, although home death was also associated with emotional and practical stress on caregivers.

We identified a number of studies highlighting important healthcare system associations. Several of the highest-quality population-based observational studies that have compared the performance of systems of care have found relative deficiencies in symptom management, physician communication, emotional support, and being treated with respect in hospital and nursing home environments compared to hospice at the end of life. Observational studies of symptoms did not inform differences among settings, but did point out associations between treatment and symptoms of behavioral disturbance in dementia. Observational literature on continuity of care highlighted particular issues with continuity related to each setting of care—including hospital readmission, nursing home transfers, and multiple providers when patients are living with advanced illness.

We found little evidence to inform whether or not there are racial/ethnic differences in satisfaction, although we found evidence that racial/ethnic considerations could affect expectations regarding the quality of care, especially with regard to advance care planning and treatment preferences. A number of observational studies describe Hispanic, African-American, and other group preferences for indirect or non-disclosure, group rather than individual decision-making, and use of life-sustaining treatments. The highest-quality observational studies of pain and other symptoms also provided little information on racial/ethnic differences in pain, dyspnea, and depression and anxiety. Observational studies in caregiving and continuity similarly provided little information on racial/ethnic differences, although intervention studies of caregiving did more so (this is discussed in the summary of effectiveness of interventions). A few studies of advance care planning showed modest improvement in patient-surrogate accord with non-white race, and preferences for avoiding planning ahead for persons with poorer health or lower education. However, effect sizes were modest and studies were small and conducted in non-generalizable populations.

The observational literature was generally uninformative with regard to important differences by disease. To the extent that it does highlight differences, it is mostly a function of the fact that research on certain topics is commonly pursued in specific diseases. For example, the caregiving literature highlights problems with caregiving in dementia, although a few studies of advanced CHF also highlight the stress experienced by caregivers. For the most part, with regard to all topics, this shows our need to expand our understanding of how disease status might be associated with the kinds and chronology of needs that patients and families face.

H. Summary regarding the effectiveness of interventions

Satisfaction

Although the evidence is mixed, the preponderance of the interventional and observational literature supports the effectiveness of palliative care for improving both patient and caregiver satisfaction. Subjective measures of the end-of-life care experience include both satisfaction and quality-of-care measures, and these tools overlap significantly. Satisfaction or quality-of-care instruments that assess focused aspects of end-of-life care have been most useful in demonstrating the effects of interventions. Nonspecific satisfaction instruments or studies that use measures not specifically adapted for or developed for palliative care settings have often demonstrated ceiling effects on satisfaction. Possibly for that reason, intervention effects on satisfaction have been somewhat inconsistent.

Measures of satisfaction that are more specific and strongly related to explicit intervention aims or processes (e.g., communication, pain control, practical support, and enhanced caregiving) have demonstrated greater sensitivity to change and support a process-outcome relationship among these variables. The relationship of other processes or attributes of care (e.g., treatment of symptoms other than pain, spiritual support, continuity and coordination of care) to satisfaction is less evident in the literature although it is supported qualitatively. The ability to demonstrate relationships of these aspects of care to satisfaction may be partially related to challenges defining spiritual support as an intervention and measuring spiritual support and continuity of care.

Pain, Depression and Anxiety, and Behavioral Symptoms in Dementia

The evidence base supporting the effectiveness of interventions for cancer pain is quite strong, but better descriptive information is needed about the experience of pain at the end of life in conditions other than cancer. In cancer populations, experiments testing different opioids, different dosages of the same opioid, or different means of opioid delivery did not produce statistically significant results as highlighted in both reviews and intervention studies. These studies were among the strongest in terms of study design. Few CAM interventions had a positive impact on pain relief; acupuncture and massage produced short-term pain relief in cancer patients. Along with descriptive studies, studies of pain treatment in non-cancer conditions needs further study. None of the review studies and only four of the intervention studies included non-cancer patient samples in their studies; none of these studies were on a single disease. Studies of non-pharmacologic interventions are small and of varied quality.

Morphine and other opioids may have a beneficial impact on dyspnea; one meta-analysis and three small but promising intervention studies reported mostly positive results for cancer and COPD. No large studies have examined interventions to relieve dyspnea in cancer or non-cancer conditions, or attempted to describe the experience of dyspnea, despite the fact that dyspnea is a characteristic symptom of several important end-of-life conditions (e.g., advanced cancer, COPD, CHF). Dyspnea in advanced CHF appears to be the most understudied among these conditions. The evidence from the reviews and individual intervention studies presents relatively

negative results for the role oxygen therapy plays in the management of dyspnea in cancer patients. Exercise interventions may have a positive effect on those with severe COPD and heart failure but these have not been tested in cancer patients. In small, short-term studies, acupuncture, acupressure, and relaxation therapy showed some clinical benefits.

Effective interventions have targeted the pharmacologic treatment of depression in cancer, but relatively few studies have evaluated shorter-acting drugs, or the treatment of depression in non-cancer conditions. We reported on one extensive review of the intervention literature regarding depression in cancer patients. Of the seven interventions considered, five focused on the treatment of depression and/or anxiety in cancer patients as well. The other review and two intervention studies focused on other disease cohorts (one study focused specifically on depression in heart failure patients, the other on mixed disease). SSRIs have been shown to be very successful in treating depression in palliative care populations. Behavioral and CAM interventions have demonstrated mixed results.

The existing literature on dementia has focused primarily on Alzheimer's disease. Given the considerable amount of time one can live after a diagnosis of dementia, these studies are somewhat limited in the context of this review because it is not clear how many of them include a population clearly near the end of life. The literature addresses many symptoms for the dementia patient population: aggressive/disruptive behavior, agitation, wandering, and mood were the most common. These studies suggest that a variety of non-pharmacologic therapies may be effective for behavioral symptoms in dementia. Pharmaceutical interventions were the subject of only a few studies and with mixed results. There are many more methodological limitations in the literature on dementia making it difficult to make definitive statements about the best treatment for these patients.

Caregiving Burden

In general, a variety of interventions were studied for a broad range of caregivers (e.g., spouse, adult children, others), primarily caregivers to dementia patients[255-257] and to terminal cancer patient caregivers,[72, 74, 258, 259, 286] usually as a supplement to clinical palliative care services being provided to the terminally ill patient. Most studies, whether on dementia or end-of-life caregiver interventions, focused on caregiver burden (objective and subjective burden) as the main outcome measure, but outcomes also included psychological distress (stress, depression), anxiety, coping skills, life satisfaction, health related quality of life, satisfaction with services or care, morale, rate of home death, rates of institutionalization, and costs.

There were generally two kinds of interventions used to address caregiver burden: individual and group interventions. The interventions included education, counseling, support groups, home health, hospice, or palliative care services to caregivers singly, or in some combination. For the most part, intervention studies have reported inconsistent results. Larger treatment effects have been found for individual interventions,[257] yet group interventions predominate the literature (Knight, Lutzky, & Macofsky-Urban, 1993). In addition, only multi-component interventions and some respite services have shown positive (though small) impacts on caregiver burden. The inconsistencies in the literature may be attributable to the differences in the caregiver outcome measurement, research design, and analytical methods used.

The caregiving interventional literature provides some information about ethnic or racial differences in caregiving experience. Caregiver race was significantly associated with the effect size of some interventions. Several studies in our review demonstrated such differences with

regard to African-American and White caregivers. Race was significantly associated with caregiver intervention impact (p<.001), indicating that the treatment was more effective for non-white caregivers.[257] Hispanic men and Hispanic and White daughters experienced a higher impact from Birmingham REACH intervention than other groups.[264]

Overall, palliative care teams do appear to have a small but beneficial effect on patient outcomes. In contrast, small effects have been found related to caregiver outcomes. There is also no significant effect of palliative care teams on home death rates, no matter what the make-up of the team.[72, 74]

Continuity

The preponderance of systematic reviews and interventions supports the efficacy of interventions to improve continuity in the context of palliation of cancer. In addition, we found some lower-quality evidence that palliative HIV care could improve continuity. Interventions embody a variety of successful approaches including aspects of management, informational, and interpersonal continuity as well as comprehensive integrated care such as palliative care services. We found evidence for the effectiveness of interventions targeting care at multiple levels—provider, patient, provider/patient interface, and multiple settings but particularly home and hospital. Our review is limited in that it identified no evidence related to improving continuity across multiple sites of care.

Although we identified many effective interventions for improving continuity in CHF care, few of these explicitly addressed or reported patient-centered palliative outcomes (e.g., dyspnea, advance care planning, caregiving impact). However, successful interventions share features of successful interventions in general including longer intervention periods, coordination among providers, and regular, structured home assessment. Many CHF interventions specifically excluded patients who were 'terminally ill,' limiting their generalizability. We identified no palliative interventions targeting other conditions and continuity of care—other than in the context of unselected populations that were more commonly focused on cancer care. Most interventions have targeted re-admission to the hospital or other kinds of high-cost care, but interventions are needed to understand how to improve other aspects of continuity as well.

Advance Care Planning

The usual practice of advance directives and advance care planning is supported by little reliable scientific evidence of efficacy in improving outcomes. Improved communication and planning has some tendency toward improved patient and family satisfaction, and certainly anecdotes and small series point to patient and family frustration and disappointment with seriously flawed communication. Nevertheless, high-quality research designs have not often been applied to these questions and, when applied, have shown quite modest effects, even on increasing the rate of making decisions in advance. Whether improved advance care planning actually improves the experience for patients and their families has only thin and equivocal evidence.

However, studies provided several key insights involving advance care planning. First, advance care planning has to reflect changing preferences and circumstances; patients' preferences change over the course of their illness. Second, when clinicians and families understand and agree with patients' preferences and prognosis, patients are more likely to experience preferred outcomes. Third, physical and psychosocial support for patients and their

families is needed and can improve communication and decision-making among clinicians, patients, and families. Fourth, interventions limited to one type of strategy and one site of care, as well as those that have few study subjects, are not likely to change care patterns or have long term impact. For about half of the studies reviewed here, only one site of care was used and a small number of patients were enroll.

Chapter 4. Research Recommendations

Overview

Our literature review identified a very large and diverse body of literature reflecting the tremendous growth and importance of the field of end-of-life care over the last decade. This review of the scientific evidence underlying key parts of the field of end-of-life care illuminates strengths of the field as well as opportunities for research. We identified evidence supporting the association of satisfaction and quality of care with pain management, communication, practical support, and enhanced caregiving. The literature review identified evidence to support the effectiveness of interventions to improve satisfaction, ameliorate cancer pain, and relieve depression in cancer; non-pharmacologic interventions for behavioral problems in dementia; and interventions to foster continuity in cancer and CHF care. Evidence is strongest in cancer, reflecting progress in acknowleding the place of palliative care in the research agenda and clinical practice of oncology.

Limitations

Several issues related to the nature of the literature complicated this review.

- An important challenge at the present time is the lack of a settled definition of the "end of life." Although our review worked with the broadest definition, any choice would be unsatisfactory because the definitions in the literature are inconsistent and inexplicit. In addition, much of the literature on advanced stages of fatal illnesses is not indexed as "end of life," thus making it difficult to include in a broad review.
- We observed a lack of clarity concerning certain concepts and their measurement. One example was satisfaction, but the same issues affect other topics, a fact that hindered our ability to classify outcomes and their relevance to patients and families.
- Most of the literature in end-of-life care does not clearly describe and compare the characteristics and outcomes of groups of patients. Therefore, this review was not able to explore many of the distinctions among patient groups, such as those affected by cancer, CHF, or dementia.
- We found it necessary to focus on selected data sources and topics. We utilized various strategies to incorporate most of the articles that the field itself identifies as very relevant at this time, such as reviewing references of the National Consensus Project and systematic reviews. We were unable to include many symptoms, such as delirium or fatigue, that may be even more common that those we highlighted. Similarly, we did not review bereavement, spirituality, or other specific outcomes including functional status or length of survival. We also did not evaluate cost of care, although it has obvious distributive implications and is a significant societal concern as our population ages.
- These same considerations led to our exclusion of clinical trials of palliative chemotherapy, radiotherapy, stents, laser therapy, and other technically complex care. The omission of these topics, which can have major impact on palliation, suggests that there may be need for in-depth review of these areas to guide future palliative care practice. Costly and medically complex care such as implanted cardioverter defibrillators,

biventricular pacing, and ventricular assist devices also increasingly characterize care for advanced CHF, and understanding the risks and benefits of such procedures vis-à-vis palliation is extremely important, although also out of scope of our review.

- To understand associations, our review focused on the highest-quality evidence (e.g., randomized clinical trials, intervention studies, and prospective cohort observational studies) to examine whether certain patient (e.g., race/ethnicity, disease) or healthcare system (e.g., site of care) factors are associated with better or worse outcomes of palliative care. By not being able to review all observational studies, we may well have missed some important associations among patient, family, and healthcare system factors and outcomes. We also did not include nonsystematic efforts, such as clinical practice guidelines and consensus documents, and therefore have not included recommendations based on expert consensus.

Given these choices and parameters, we identified important research opportunities for the field. In this section, we focus first on the lack of a definition of the "end of life" population (Preliminary Question), then on gaps in evidence related to conceptualizing and measuring satisfaction and other outcomes relevant to patients and caregivers (Question 1). We offer conclusions related to understanding variations (Question 2) and the effectiveness of interventions (Question 3) to improve each of the specific outcomes we addressed in this report.

Definition of the "End-of-Life" Population Needed

The lack of consensus on the definition of "end of life" leaves what various researchers have called "the denominator problem." If one aims to reduce the rate of dyspnea, for example, one must have a stable, replicable, and meaningful definition of the population. In a previous review of this literature, George also observed the lack of a consistent conceptual and operational definition of end of life.[21] The undefined nature of the category is apparent in the widely varying populations in studies we identified. We examined substantial numbers of reports of prognostic modeling (see Appendix A) and found that this literature does not and probably cannot define a population that both includes most people suffering with fatal illnesses and includes them only for a short time (e.g., six months before death).

The correct definition of end of life may well depend upon what use is to be made of the definition. If the purpose involves public policy for a diverse array of patients with various serious illnesses and social situations and if the aim is to identify opportunities for tailoring services to match the needs of most of the group, the definition will need to encompass many very seriously ill people and will necessarily include some patients who live a long time. If the use involves securing care for the last hours of life, the definition will be much more narrow. Similarly, if the definition is meant to signal authorization for physician-assisted suicide, the tolerance for errors of over-inclusion will be small. For research purposes, a few clear definitions of the scope might well be enough to allow clear reporting of the denominator population for each study and to enable comparisons across time and setting.

We identified relatively few studies (especially studies in hospice or palliative care settings) that made clear distinctions or studied distinct categories of illness; even fewer studies set out to compare the end-of-life experience of various conditions. The patient and family experience of the end of life has been best described in cancer. Very few studies address even the most important end-of-life symptoms in non-cancer conditions, despite the fact that the few existing

studies suggest the importance of separately considering conditions, or perhaps major groupings of conditions. In the lives of many patients, of course, conditions occur together, and there is a separate need to understand how multiple comorbidities affect the end-of-life experience. Finally, attention to particular conditions would emphasize the extent to which the end of life is being affected by treatment innovation such as the proliferation of technologies in CHF treatment. For these reasons, we suggest:

- ***Consideration 1: Research is needed to characterize the implications of alternative conceptual and operational definitions of the "end of life," particularly for important conditions. Efforts are needed to define populations with specific unmet palliative care needs.***

Measures and Satisfaction with Care and the End-of-Life Experience

The field has made a promising beginning in developing sound tools for evaluating end-of-life care, but gaps in the availability of measures remain. While some instruments have been evaluated in cancer and mixed populations in which cancer predominates, few instruments have been tested in prevalent non-cancer conditions. Related methodological issues include assessing patients with cognitive impairment and better understanding the limitations of proxy response. Novel approaches to evaluating outcomes may be needed in certain populations, and the limits of observation and self-report need examination.[375] Indeed, a number of methodological challenges in end-of-life research need sustained attention. In addition to the problem of substitute respondents, the challenge of the variable timing of death and its effect upon measurement needs attention.

Whether measures respond to changes in care system performance has not generally been tested, and only a few of the most rigorously developed instruments have been tested or applied in different settings. The experience of health care differs among settings and, according to evidence we identified in reviewing satisfaction, by disease or by the nature of the caregiver's relationship with the patient. Thus, researchers need to develop specific tools depending on the research objectives, or at least to account for potential differences in their analyses when evaluating the effectiveness of palliative care interventions. High-quality studies generally have not yet addressed the experience of health care while dying from different cultural perspectives, but adapting existing instruments and evaluating differences will be important as our aging population becomes more diverse.

With regard to satisfaction, we noted that most studies do not offer any conceptualization of satisfaction, and there is much overlap among instruments that measure satisfaction and other aspects of end-of-life care. Indeed, satisfaction has some limitations as a measure of care performance. Most studies of satisfaction did not employ standardized instruments, or if they did, they are often instruments that were not specifically developed for end-of-life settings or that reflect the kinds of healthcare experiences that are specific to the end of life. Important differences in the experience of health care are suggested by disease trajectory and by caregiver perspective, and the importance of measuring specific attributes of medical care is suggested by the fact that studies that observe differences in satisfaction have often done so in the context of instruments that include detailed items rather than simple summary measures. Better understanding is needed of the relationship of satisfaction to treatment of symptoms other than

pain, spiritual support, continuity and coordination of care, in particular. For these reasons, we recommend:

- ***Consideration 2: Further measure development should emphasize testing the highest-quality measures in important settings (e.g., hospital, nursing home, hospice, and ambulatory care). These measures need to be evaluated in diverse populations (e.g., racial/ethnic groups, non-cancer conditions). Measures would benefit from being standardized for comparisons among studies.***
- ***Consideration 3: Studies evaluating satisfaction should use specific measures that reflect processes of care, and studies should examine the relationship of satisfaction to less-studied processes such as non-pain symptoms, spiritual support, and continuity.***
- ***Consideration 4: Methodological challenges in measurement require focused research. Strengthened research infrastructure including collaborative networks should be considered.***

Pain, Dyspnea, Depression and Anxiety, and Behavioral Symptoms in Dementia

The preponderance of the evidence we reviewed supports the effectiveness of pharmacologic and system interventions for cancer pain. Nevertheless, the stability of population rates of cancer pain presents a caution; having evidence from interventional research that showed effective relief of cancer pain in substantial populations would be most useful. More rigorous studies are needed to understand the use of non-pharmacologic therapies and how they should be combined or sequenced with pharmacologic therapies. Limited evidence is troubling in that it suggests that pain characterizes a variety of severe illnesses, but studies are needed to characterize both the basic epidemiology and the clinical interpretation of pain in non-cancer conditions.

With regard to dyspnea, some evidence supports the efficacy of a variety of pharmacologic and non-pharmacologic interventions to reduce dyspnea in cancer and non-cancer conditions. Studies of opiates have been promising, although these studies are small and heterogeneous. The basic epidemiology and clinical interpretation or meaning of dyspnea in cancer and non-cancer conditions need to be better described. As with other symptoms, research on implementation of known better practices remains a priority.

With regard to depression and anxiety, and behavioral symptoms in dementia, the preponderance of evidence supports the effectiveness of pharmacologic interventions for depression in cancer; however, few of these studies focused on patients with later-stage cancer or in palliative care clinical settings. A variety of studies support the efficacy of non-pharmacologic interventions. We also need to understand the sequencing and combining of pharmacological and non-pharmacological therapies. In addition, the research to date does not adequately characterize the merits of controlled environments, environmental stimulation, and medication in ameliorating behavioral symptoms. These observations give rise to the following recommendations:

- ***Consideration 5: Symptoms have been relatively well characterized in cancer, but high-quality studies of the incidence and epidemiology of pain and other symptoms, the relationship among symptoms, and the clinical significance of symptoms are needed in non-cancer conditions.***
- ***Consideration 6: Small, high-quality studies suggest the effectiveness of interventions to alleviate dyspnea. Larger studies of interventions to alleviate dyspnea in cancer and non-cancer conditions are needed.***
- ***Consideration 7: Studies that evaluate short-term as well as longer-term treatment of depression in palliative care settings are needed.***

Caregiving

With regard to caregiving, we noted a lack of intervention outcome evaluation designs and a reliance on intervention descriptions and formative evaluations in the literature. Caregiver outcome studies suffer from small sample sizes and the predominant use of convenience samples. Many studies were non-randomized and characterized by sampling homogeneity (e.g., little diversity in the characteristics of caregivers and care receivers). Interventions vary widely and caregivers were rarely screened prior to study entry for problems or need related to the specific intervention being tested or the measured outcomes. There is confusion in the field concerning the operationalization and measurement of major caregiver outcomes, diversity in length, duration, and intensity of specific interventions strategies. In addition, a better match between interventions and outcomes is needed. There was also little research to systematically evaluate variability in cultural expectations of care.

Methodological challenges in studying these interventions may mean that alternatives to randomized controlled trials should be welcomed as the best available data. Most caregiving literature has found that, while caregivers rate interventions favorably, objective and subjective indicators of overall burden show little change. It is critical to identify specific outcomes most likely to be changed by the intervention employed. Burden may be too global and multidimensional to be affected by interventions because it has both subjective and objective qualities and there is a lack of conceptual clarity about what actually differentiates the subjective from the objective.[376] Measures of objective burden often ask the respondent how they “feel” about a particular caregiving situation or the impact of caregiving. Many measures of burden may not sufficiently differentiate between objective tasks and feelings about the experience of caregiving.

Future research in family caregiving needs to increase sample sizes and homogeneity. Attention is also needed to determine whether standardized or individualized interventions produce the best outcomes in family caregivers. Theoretically, those interventions linked to caregiver needs should produce the best outcomes, but this idea must be tested and validated or refuted. Researchers must also evaluate the optimal length, duration, and intensity of specific intervention strategies. Researchers must select outcomes that are likely to be changed by the intervention being tested. Caregiver research must also account for financial and social effects of caregiving upon the caregiver and the family, and the societal vision of optimal family caregiving is itself worthy of research, especially regarding cultural expectations of care.

- ***Consideration 8: Limited research supports the effectiveness of interventions for cancer and dementia caregiving. High-quality studies in other populations are needed. These studies need to pay special attention to such methodologic issues as careful sample selection and measurement of specific outcome variables that reflect intervention aims.***
- ***Consideration 9: The economic and social dimensions of caregiving need additional research.***

Continuity of Services

The models of service delivery that yield optimal outcomes for patients and families are not yet clear. Research on integrated delivery models, such as PACE and hospice, have been descriptively useful, but well-controlled studies are rare. Research on primary care and simple continuity has not generally examined patients so sick as to be at the end of life. Our review provided limited evidence for the ability of interventions to improve what we have designated as management continuity at the end of life—partly, this may be related to the measures used, which are often focused on such indirect outcomes as site of death. We found more evidence for the ability to improve continuity of care related to communication.

Studies of continuity in CHF are very promising, and successful approaches to fostering continuity in CHF share some important features with multi-component palliative care interventions. Despite the strengths of this literature, limitations in the interventions, measures, and exclusionary criteria that characterize these studies restrict their usefulness in understanding how to achieve palliative goals for these patients. Studies that incorporate these considerations are needed to broaden our understanding of how to serve the sickest patients with CHF and similar conditions. Our recommendations include:

- ***Consideration 10: Substantial evidence supports interventions to improve continuity between home and hospital. Continuity research needs to look at other settings in which most patients are cared for—e.g., ambulatory care. Additional study of nursing home–hospital continuity and studies that incorporate multiple settings and providers are needed.***
- ***Consideration 11: Studies of continuity in CHF and other conditions should incorporate the palliative domains described above (e.g., physical and psychological symptoms, caregiver burden, advance care planning) and need to be more generalizable to the sickest patients. Such studies need to include patients with multiple comorbidities.***

Advance Care Planning

A fully informative research base would address the plausibility and outcomes of making advance care plans for future clinical scenarios for a diverse array of patients and would evaluate the optimal approach to implementing care system processes that yield better outcomes. The reported experience in La Crosse and the Veterans Health System suggests that it might be possible to document advance directives more commonly. However, advance care planning was associated with only minor changes in ICU time or costs and with no effect in the few RCTs that have addressed the issue. Most studies of the effectiveness of advance care planning are negative, studied small samples in one site, and are several years old.

The clinical situation often seems to call for anticipating what might otherwise be harmful complications, rather than to call for advance care planning as an expression of autonomy. But does considering future complications and the expected worsening of health benefit patients and families? Can it be done in a reasonable time, can decisions and plans be implemented over time and across settings? The generally lackluster performance of advance directives and advance care planning leads some to question whether alternative approaches to reducing the use of certain high-intensity treatments might be evaluated, at least in some circumstances. For example, rather than having every patient and family with early dementia document a decision about artificial feeding, it may be better to assume that patients with advanced dementia should not get a feeding tube unless the patient or family actively seek such treatment. Or it may be that improving advance care planning requires widespread community activation, as in the example of Oregon.

However, alternative approaches to advance care planning might have unanticipated effects. For example, will patients and families also be less informed about diagnosis and prognosis? Would certain approaches affect the ability of patients and families to engage in practical planning for family support and caregiving? The persistently limited success of advance care planning as shown in limited research also calls out for reevaluating more fundamental assumptions—such as that the future is largely shaped by decisions, that those decisions generally can be examined in terms of optimizing outcomes, that people have important and persistent preferences among the possible outcomes, and that they are willing to articulate decisions and abide by them.

- ***Consideration 12: Rigorous research in advance care planning is needed to understand how to best achieve patient and family goals (as opposed to evaluating resource allocation), and such research needs to address fundamental processes of care planning.***

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Appendix A. The Scope of the "End of Life"

People die in their own way, with highly individual courses near death and with no one's last chapter being quite the same as another person's. Yet, the courses do tend to be rather similar for people with similar medical conditions and co-morbidities, similar symptoms and disabilities, and ordinary living circumstances. At least as an initial organizing principle, looking to those patterns and highlighting a small number of very common patterns yields a productive anchor for designing care systems, organizing information, and catalyzing reforms.

A recent idea in end-of-life care is that of "trajectories" of the course while living with fatal illnesses. A trajectory is essentially the time course of care needs and patient experiences from the onset of serious illness to the end of life, and it might well be more useful in designing reliable and effective care arrangements than strategies that rely upon diagnoses, procedures, or settings of care. A limited recent literature builds the case for a relatively small set of trajectories that could warrant separate planning for care needs. Lunney et al[1] proposed one trajectory for a short course of rapidly progressive disability in the last two months of life (often seen with solid cancers), one for a longer course of slow decline with intermittent life-threatening exacerbations and usually a sudden death (often seen with chronic lung or heart failure), and one for a very long course of slow decline with self-care disability arising from dementia or frailty.

Teno et al[2] confirmed Lunney's claim that the time course of disability in the last year was quite different for persons living with cancer as compared to those with stroke, chronic obstructive lung disease, diabetes and heart failure. Teno found that cancer patients were much less disabled until their last few months, when disability accelerated substantially and rapidly became more severe than the relatively mild increases for other conditions. Covinsky et al[3] evaluated the time course of disability in the conditions of frailty and dementia, showing that they are characterized by serious disability with slow worsening, with dementia being more severely disabling than frailty but with similar trajectoryie of decline over time.

At what point in these courses would it be appropriate to label the person as having come to the "end of life"? As with many definitions, a consideration of how it will be used is important. The definition that targets support to the caregiver and advance care planning with the patient would usually include much more time than a definition that identifies imminent dying. Lack of consistent definitions hinders building a coherent body of work regarding end-of-life care. Teno and Coppola[4] and George[5] have pointed out the serious problems that affect research when the "denominator problem" has not been addressed or resolved. As George noted in her systematic review,[5] most studies simply do not articulate the population to which the results could be generalized. In reports that did articulate the population of focus, we found three basic concepts of the scope. Some use "end of life" to mean the patient's last few days or hours, when it is quite clear that the person will not live long, when family should gather and last words be said, and when there is little thought of adding new medical treatments that might still delay death. This corresponds roughly to what hospice nurses often call "active dying." Others use the term to mean people who would be eligible and appropriate for hospice, in that they have a prognosis of less than six months' survival and have decided that

treatment should be focused upon palliative efforts. A third approach uses the term to denote a broader category that includes the part of life when the person is seriously afflicted with an eventually fatal condition, even if the prognosis remains ambiguous and some people live in this way for many years. Initial conversations with the NINR and AHRQ project officers and the Technical Expert Panel (see chapter 2) made clear that our Evidence-Based Report was to use the third, broad, definition of the category; but we were directed also to summarize the evidence as to how well the available literature supported each possible definition of the category. To this end, the EPC marked each article that we found in the searches described in Chapter 2 as to whether that article spoke to the question of prognosis. We supplemented this list of articles with those contributed by experts on the staff, in the TEP, in systematic reviews, and in expert reviews. The results of this review of the evidence underlying the definition of the category itself are presented below.

Search Results

We identified 348 articles from our title search including 299 in the title or abstract review phase and 48 contributed by expert reviewers. Of these, 90 were not about prognosis, or not quantitative (e.g., a review or ethics reflection). Forty citations described the natural history of a cohort, including mortality and effects of treatments. We identified 66 of these titles as not about chronic illness. Fifty-two citations described worse or better prognosis with one or a few factors in strata or simple association and merely quantified an obvious relationship. Sixteen regarded prognosis for a year or more. Twenty-one concerned only prognostication for patients already enrolled in a hospice or palliative care program. We identified a total of 63 articles to inform the question of when 'end-of-life' begins.

Defining the "end of life" as "active dying"

In case reports written by hospice and palliative care providers, the phrase "active dying" commonly designates a period of time in which the patient is declining markedly, is having irregularities in vital functions like breathing and circulation, and is reliably expected to die without any recovery within a few hours or at most a few days. In the articles identified in our broad search, no article addresses how often the designation is in error (in that the patient actually has a substantial period of stability before dying), how reliably different nurses and others designate patients as "actively dying," how many patients have this discernible phase before dying, or what the rate of various characteristics turns out to be among those identified as "actively dying." Clearly, if some aspect of clinical care or research is to turn on this definition, some empirical description and regularizing of the definition is in order.

Defining the end of life by patient "readiness"

While enrollment in hospice in the U.S. requires that the physician certify that the patient has "six months or less" to live, hospice enrollment also requires that the patient sign a statement giving up efforts at "curative" medical treatment and providing consent to treatment in a hospice program. Perhaps, at least for typical hospice patients, the prognosis requirement is mostly permissive and actual enrollment depends on the patient,

family, and clinicians being convinced that the patient is best served by extensive supportive care, usually because the patient is so sick and disabled. Of course, this status is loosely tied to prognosis, but it also is tied to how the people involved perceive the patient, including age, social situation, religious outlook, depression, weariness with life, and other factors. Perhaps the very definition of the category of "end of life" might be allowed to depend on preferences and perspectives of patient and family, at least among patients who are sick enough to die. A patient who is fiercely trying to regain stability with heart failure and who won't talk of dying might place herself in the category of "usual patients," while a person with similar physical impairments who is weary of fighting for breath, tired of it all, and ready to die might thereby be in the category of "end of life" patients.

One article provides an important window upon the question of patient "readiness" by assessing the correlation of cancer patients' self-assessment of prognosis with their preferences for life-sustaining treatment. Weeks et al[6] reported that cancer patients who estimated that they had at least a 10% chance of dying within six months had markedly more likelihood of preferring to avoid resuscitation than did those who thought that they had a better chance to live longer. This finding persisted whether or not their perceptions were accurate, and whether or not their views were in accord with their physicians. This raises the interesting possibility that patient "readiness" turns on certain thresholds or experiences that are not tightly tied to specific prognoses.

Another report on patient readiness to address end of life issues supports this point. Pfeifer et al[7] showed that sicker patients with chronic obstructive lung disease (COPD) were no more or less interested in end-of-life discussions than were somewhat less severely ill patients. Since the typical course of COPD includes periods of nearly stable life, intermittent exacerbations, and rather sudden dying, more or less severe illness might well have little effect upon the patient's perception of urgency, especially if patients are waiting for a warning that time is short. Most COPD patients will never know that time is short until death is close at hand in an exacerbation that is not going well.

At least with the search strategy that we used, no articles addressed the performance characteristics of a categorization that would turn in part upon patient and family preference for priorities of treatment or goals of care.

Defining the "end of life' by severity of illness

One practical way to define a category of people who are coming to the "end of life" would be to articulate explicit thresholds of severity of commonly fatal illnesses and to include the part of life lived with illness that severe or worse. This would allow the criteria to be disconnected from their performance as prognostic elements and to use instead those markers of severity that are commonly available, or readily obtained, and that mark the onset of substantial disability or suffering. The indices of severity could be linked to specific illnesses, or to trajectories, with the latter having the potential advantage of accounting for multiple co-morbidities.

Discerning the category by severity underlies a question used to help clinicians find the patients who are at the end of life: "Is this patient sick enough that is would not be a surprise if he or she were to die within six months?" It might not matter much whether one uses the reference category of 3, 6, or 12 months, since the question mostly

encourages the clinician to recognize that the patient already has an illness that might well take his or her life. The question was first reported in a quality improvement endeavor at the Franciscan Health System in Tacoma, Washington[8] and has since become more widely used.[9] However, no research has evaluated its performance characteristics formally.

Defining the "end of life" by prognosis

Prognosticating the patient's course is one of the oldest and most controversial parts of medical arts. Hippocratic teaching admonished physicians both to "declare the past, diagnose the present, foretell the future" and to "give necessary orders…revealing nothing of the patient's future or present condition."[10] In modern times, commentators admonish physicians both to inform the patient accurately as to what he or she faces and to avoid taking away hope. In most of the discussion, little attention goes to discerning what it is that the physician could possibly say about prognosis.

Giving a prognosis as to how the future is likely to unfold requires seeing that certain things known now (a,b,c,…) allow us to predict the risk of dying at a time in the future. For example, an article or text might say that 90% of the people with inoperable non-small-cell lung cancer who take no chemotherapy or radiation will be dead within six months. The same idea could yield a continuous expression of the likelihood of being alive, or a contingent prediction that illustrates the effect of different treatments or events.

Some elements of these common strategies are important to highlight. First, all prognostications of mortality yield a likelihood of survival at a particular time or over time, not "how long does he have to live?" Second, no prediction of survival will capture all of the variation and be precise, both because the elements used in prediction are not all known or well-measured and because some of the elements that actually shape the future are actually unpredictable for individuals (though some of these might be predictable for large numbers of people). Third, all predictions of the future rely upon past experience, so, to the extent that important circumstances change over time, such as treatment possibilities or complicating co-morbidities, predicting the future becomes unreliable. Finally, all prognostications have certain performance characteristics that shape their usefulness: in particular, overall performance in explaining variance, calibration, discrimination, dispersion (especially into the extremes of likelihood), practicality (often especially regarding missing data), and applicability to a new population of interest.

By far the most common way that prognostication has been used to shape the field of "end of life care" has been the claim that the "end of life" is when prognosis is less than 6 months, and the patient is eligible for enrolling in a hospice program. It is intriguing, and perhaps illuminating, that the statute that set forth the 6-month prognosis limit as eligibility for hospice coverage in Medicare did not define that statistic further, and that it has not been defined formally in the twenty years since.[11] Not only does it fail to state any degree of confidence that one would need to have in stating the prognosis, but it even fails to state the threshold clearly. Should a prognosis of 6 months or less mean that the person has less than a 50-50 chance to be alive in 6 months, or does it mean that the person is virtually certain to be dead within 6 months – e.g., with a 90% or 99% probability?

The size of the population to be served is dramatically different with these different definitions. Only a very few people, who usually live for a very short time, can be known to have less than a 1% chance to live 6 months; but many people, for much longer times, can be known to have worse than a 50% chance to live 6 months.[12] In the Government Accounting Office investigations of hospice enrollment, the standard employed seemed to be something like "virtually certain to die," but the recent enthusiasm to use hospice more seems to employ something close to the "more likely than not" standard.[9]

The group of 63 articles that inform the use of prognostication in defining the end of life addressed four major topics. First are reports of multivariable models developed to predict survival over time or to a point in time. Second are reports of expert clinicians predicting survival. Third are tests of either of these approaches in specified patient populations. Fourth are reports that present largely theoretical models that aim to make sense of the contribution of competing causes of death when they are commonplace in a population. While we do not know of a scoring system for the quality of multivariable modeling to predict survival, an on-line text outlines the dimensions of quality[13] and one article catalogues the pervasiveness of shortcomings in prognostication articles concerning the end of life.[14]

Multivariable prognostic models

The first group of research articles raises the question of how well a multivariable model can predict the likelihood of surviving to a future point in time, usually six months. One of the most well-developed models for multiple diagnoses was reported by the SUPPORT project.[15] It allows one to draw a survival curve and to calculate a reasonable estimate of the variance in the estimate for each of nine diagnoses. The SUPPORT model showed that the five hospitals involved had the same adjusted mortality rates and the same associations of all predictive factors with mortality predictions. Furthermore, the SUPPORT intervention did not affect mortality. The SUPPORT models were well-calibrated, they discriminated well even at the ends of the prognostic spectrum, and they dealt with missing data in justifiable ways.

However, the SUPPORT models' performance with regard to finding a population that was likely to die within six months was disappointing. Most of the deaths that drive the equations in SUPPORT occur early after admission to the hospital. The estimates of error in populations with a "middling" prognosis at six months are substantial, often requiring a range of 30 percentage points to encompass 90% of likely estimates. Furthermore, the study population was biased in mostly unmeasured ways, a fact that would greatly complicate application in another population. For example, the SUPPORT patients had come to a teaching hospital and had survived 48 hours in order to be enrolled. The average age at death in SUPPORT was more than ten years younger than in the population as a whole. Roughly twice as many people sick enough to qualify for SUPPORT were not enrolled but were in the community served by one of the hospitals.[16] Either they did not come into the hospital or they died quickly after admission. The people who did not come into the study included many living in nursing homes or who were very old and presumably supported at home.

Furthermore, the SUPPORT prognostic model requires a substantial array of laboratory tests and the patients were mostly getting hospital-level diagnosis and treatment, so the SUPPORT model will not function as well in a population that is not in the hospital. The SUPPORT model is a remarkably informative instrument, and it probably is useful in calibrating the effects of treatments or comparing the quality of life-sustaining care among hospitals or treatments, but it is not a well-calibrated way to sort patients by their prognoses at six months. Contrary to the common assumption that "terminally ill" people are evident, SUPPORT showed that, even very near to actual dying, prognoses stay quite uncertain for many patients. In SUPPORT, the median prognoses within the last week of life were often greater than 50% to survive six months, especially for chronic conditions with intermittent exacerbations like heart failure and chronic lung disease.[17, 18]

Other models for predicting prognosis have similar limitations in reliably splitting the population of very sick people into those who will live longer than six months (or another limit) and those who will die by then. Mitchell et al.[19] developed a model specifically for nursing home patients with dementia using high-quality methods and a large dataset. In testing for the adequacy of the model to predict 6 month survival, the performance characteristics were quite good (Area under the receiver-operating characteristic curve of 0.74 in the development set and 0.70 in the validation set). Nevertheless, that performance would leave many patients enrolled and surviving past six months and many others denied enrollment for what turns out to be their last few months.

In a model-building endeavor that paralleled the SUPPORT model approach, Teno et al[20] reported an initial estimate for frail hospitalized elders. The nomogram presented in this report illustrates the kind of useful translation of results that could anchor more widespread use of prognostic models. Nevertheless, the model has all the limitations of the SUPPORT model, and this one relied upon just 1266 cases and only 505 deaths in 4 sites.

Other papers have focused upon specific lab tests, special settings (e.g., Chow[21]), or especially dire clinical situations. A broad array of such papers might end up building a generalizable approach, but they also might build an incoherent patchwork. Certainly, at the present time, although the various models and approaches yield informative and clinically helpful insights for individuals and yield standards that can anchor research and quality improvement, the models have not been particularly useful in sorting people who should be considered to be "at the end of life" from those with serious diagnoses but longer expected survival.

Clinical Judgment

Rather than developing multivariable prognostic models, some reports tested the clinical judgment of physicians. In SUPPORT, the judgments of physicians were nearly as accurate as the multivariable model, on average, but physicians showed a strong tendency to use only a few points along the spectrum of possible prognoses (e.g., 10%, 25%, 50%, 75%, and 90%), thus reducing the calibration of their estimates and also their ability to separate patients of middling prognosis.

Christakis and colleagues have shown that physicians generally predict longer survivals than patients have, at least when prognosticating for patients being considered

for hospice.[22, 23] Addington-Hall et al[24] found that medical and nursing staff over-estimated survival substantially in 12% of cases and also under-estimated in 9%. SUPPORT found that physicians were accurate on average when the question was the likelihood of being alive in six months. The errors that physicians made in this task had a normal distribution, but fully 39% of the predictions were in error by more than 20% when compared with the SUPPORT multivariable model as the gold standard.[25] Mackillop and Quirt[26] assessed the discriminatory power of oncologists' estimates of survival at 3 months and at one year and found fair discrimination at 3 months (Area under the ROC =0.75) and very poor discimination at a year (A-ROC = 0.57). Higginson and Constantini[27]checked the accuracy of prognoses made by experienced palliative care teams concerning cancer patients referred to their care. They recommended that prognosis be presented as a range, since that doubled the rate of proving to be accurate, but they noted that prognosis "is still very often inaccurate, except very close to death." Indeed, the patient's actual survival time lay outside of the predicted range in 58% of cases.

Prognostication for heart failure seems to be especially difficult. In SUPPORT, the median prognosis for heart failure patients on the day that turned out to be the day before death was just about 50% to live for 6 months.[28] Poses et al[29] tested emergency room physicians providing care for heart failure patients with an acute exacerbation, evaluating the accuracy of their estimates for three months and for one year survival. Their discriminatory ability was modest, with areas under the receiver operating curve of 0.66 for 90 days survival and 0.63 for a year. Indeed, in that study, of 1173 patients with 1603 visits, only 15 patients were estimated to have less than a 10% chance to live 90 days, but one-third of these patients lived that long and 208 others died within 90 days.

Pirovano et al[30] formally combined key elements from physiology and demographics with the clinician's prediction of survival and the Karnofsky performance status measure, thereby forming the Palliative Prognostic Score. In cancer, that score does serve to define three groups with median survivals of 64, 32, and 11 days. The utility for sorting "end of life" from the rest of humanity is limited because the groups have substantial overlap, and the overall survival is short. The strong role of performance status in predicting survival time in cancer was underscored in Vigano et al's systematic review of prognostic factors in cancer[31] which showed that 13 of the 13 prognostic models reviewed had tested a performance status measure and found it to be significant in predicting survival among people with advanced cancer. Vigano identified a number of symptoms that also often appeared to be independent predictors in prior research, although this systematic review underscored the methodological limitations of the studies in existence in 1999.

In SUPPORT, the physicians' estimates were also entered into the multivariable prognostic model and the resulting model performed measurably better than either the physicians alone or the multivariable model alone.

Others have tested expert prognostications. Arkes et al[32] underscored the mismatch between patients, surrogates and physicians, showing that patients were remarkably over-optimistic and physicians generally over-pessimistic. Pearlman [33] presented one case with acute and chronic respiratory failure to 205 physicians and asked for an estimate of survival. The range was from one month to five years with a median of about six

months. Social and preference factors had a substantial bearing on the estimated survival.

Testing Prognostic Estimates

A few reports have tested a prognostic scoring system or model in a patient population, usually seeing the sensitivity and specificity of the test at 6 months. The SUPPORT article by Fox et al[34] showed the generally inadequate ability of the SUPPORT prognostic model to discern what patients with lung, heart, or liver failure were qualified for hospice. Testing a broad inclusion criterion, an intermediate one, and a narrow one, the sensitivity and specificity moves from 42% and 67% for the broad criteria to 1.4% and 99.5% for the narrow criteria. Obviously, the trade-off between sensitivity and specificity was extreme and the criteria did not provide a method by which to identify the potential hospice population without unacceptable error rates of inclusion or exclusion.

Most of the models built around a specific illness have used data from populations that have very few people who are quite elderly. SUPPORT, for example, has an average age at death that is more than a decade younger than the average age at death in the U.S. population. In general, then, the models do not take account of the contribution of advanced age or of multiple co-morbidities that are life-threatening. A series of reports has aimed to build a model for understanding the role of competing co-morbidities, especially in estimating the merits of treatments that affect the survival time from one illness.[35-38] When patients have multiple serious conditions, delaying death from one cause has the effect of making it more likely to come to the end of life with another. In populations like SUPPORT, few patients have more than one fatal illness. In older populations, frailty and lack of reserve capacity in various vital systems often creates a cascade of life-threatening complications. Indeed, Morrison and Siu[39] reported that pneumonia or hip fracture have only about 12% mortality within six months if the patients are cognitively intact, while those with serious dementia have more than 50% mortality. Multivariable models that take account of the interaction among causes of death in making prognostications are not in evidence, though a new specific statistical approach has been developed and applied to AIDS.

Many models do take into account a simple measure of co-morbidity such as the Charlson Co-Morbidity Index, the Adult Comorbidity Evaluation 27, the Index of Co-Existent Disease, and the Kaplan-Feinstein Comorbidity Index.. In all such reports, when adjusted for severity of the underlying illness, substantial additional co-morbidity increased the likelihood of dying. For example, in Piccirillo et al,[40] patients with severe co-morbidity had adjusted hazard ratio for death of 2.56 (95% CI, 2.35-2.81) and even mild co-morbidity carried an adjusted hazard ratio of 1.21 (95% CI, 1.13-1.30), in comparison with patients with no co-morbidity. These measures do add some explanatory power to predictive models, but Piccirillo's models have a C-statistic of 0.7-0.8. Co-morbidity and competing causes of death have multiple impacts upon the likely survival, from becoming primary causes of death or limiting the aggressiveness of treatment to altering the patient's and the family members' assessment of the desirability of undertaking troubling courses of treatment. Nevertheless, in general, the prognostic models that are available for predicting survival for individual patients either did not

include many patients old enough to raise these concerns or did not adjust for these factors.

Indeed, even how to weigh the role of treatment effects upon prognostication is not standardized. If prognosis could be much better with treatment, but the patient refuses or cannot get the treatment, then is the patient's prognosis simply that of the untreated patient? Does it matter if the patient who initially refuses could change his or her mind for a substantial period of time? These issues have not yet been part of the discussion over prognostication, perhaps because they are largely irrelevant in hospice enrollment when the patient's physicians must certify prognosis. In a gesture to limit the risk of choosing to accept an earlier death and thereby to qualify for hospice, enrollment now requires that the prognosis rely upon "the normal course of the individual's illness."[41]

One report did examine the association of age, aggressiveness of care, and survival, showing that older patients did get less aggressive care and did have shorter survival, but that these two findings were not themselves associated. At least in the SUPPORT database, survival was not affected by care patterns at each hospital or by the intervention, which aimed to increase communication and awareness of prognosis.[42] Volicer et al.[43] built a model for predicting survival of dementia patients after an episode of fever. The model's two strongest elements are treatment variables: the management strategy as to whether to pursue a palliative approach or a conventional approach, and the recency of having been admitted for long-term care. These had odds ratios of 4.25 for palliative care and 7.78 for having recently been admitted, while physiological severity and age had odds ratios only a little more than 1. It is not clear that prognostic models should simply incorporate treatment strategies. At least at the extreme, a treatment strategy can be self-enforcing with regard to survival: consider the effect of deciding to implement terminal sedation.

The status of the category "end of life"

This review of the literature shows that various concepts of the "end of life" are in actual use, and none of them have had substantial empirical validation of potential defining characteristics. Prognostication models and clinician estimates are useful for generally forecasting a patient's future; however, they are not sufficiently precise or generalizable for splitting those with short prognoses who are to be eligible for services tailored to the end of life from those with longer prognoses who are to continue to use the ordinary health care system. Furthermore, the definitional strategies other than prognostication have only clinical experience behind them, without any formal definitions or examination of their performance characteristics.

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Appendix B1. NLM Search Strategy

First Strategy for End of Life from NLM in PubMed – Trajectory Issues NOT included

April 8, 2004

1. palliative care[mh] OR attitude to death [mh] OR death [mh:noexp] OR terminal care[mh:noexp] OR hospice care[mh] OR hospices [mh] OR bereavement [mh] OR terminally ill[mh] OR "death and dying"[All Fields] OR "dying loved one"[All Fields] OR "dying patient"[All Fields] OR "dying patients"[All Fields] OR "dying people"[All Fields] OR "dying person"[All Fields] OR "end of life"[All Fields] OR "limited life expectancies"[All Fields] OR "limited life expectancy"[All Fields] OR "limited life span"[All Fields] OR "limited life spans"[All Fields] OR "limited lifespan"[All Fields] OR "limited lifetime"[All Fields] OR "imminent death"[All Fields] OR "imminent demise"[All Fields] Limits: All Adult: 19+ years, Publication Date from 1990 to 2004, English, Human **Total: 10,543**
2. health care quality, access, and evaluation[mh] OR "outcome and process assessment (health care)" [mh] OR consumer satisfaction[mh] OR personal satisfaction[mh] OR quality of life[mh] OR quality of health care[mh] OR value of life[mh] OR questionnaires [mh] OR interviews [mh] OR psychological tests [mh] OR clinical trial[pt] OR clinical trials[mh] OR psychotherapy[mh] OR reproducibility of results[mh] OR predictive value of tests[mh] OR psychiatric status rating scales [mh] OR (rating AND (scale OR scales)) **Total: 789,126**
3. #1 AND #2 **Total: 7,870**
4. sociology [mh] OR continental population groups[mh] OR socioeconomic factors [mh] OR education [mh:noexp] OR health education [mh] OR age factors [mh] OR sex factors [mh] OR sexuality[mh] OR life style[mh] OR interpersonal relations [mh] OR morale [mh] OR internal-external control [mh] OR social distance [mh] OR cooperative behavior [mh] OR attitude to health [mh] OR religion [mh] OR personality [mh] OR emotions[mh] OR mental competency[mh] OR family[mh] OR caregivers[mh] OR friends[mh] OR sexual partners [mh] OR social environment [mh] OR visitors to patients [mh] OR communication[mh] **Total: 261,455**
5. #1 AND #4 **Total: 5,258**
6. palliative care[mh] OR attitude to death [mh] OR death [mh:noexp] OR terminal care[mh:noexp] OR hospice care[mh] OR bereavement [mh] OR terminally ill[mh] OR "death and dying"[All Fields] OR "dying loved one"[All Fields] OR "dying patient"[All Fields] OR "dying patients"[All Fields] OR "dying people"[All Fields] OR "dying person"[All Fields] OR "end of life"[All Fields] OR "limited life expectancies"[All Fields] OR "limited life expectancy"[All Fields] OR "limited life span"[All Fields] OR "limited life spans"[All Fields] OR "limited lifespan"[All Fields] OR "limited lifetime"[All Fields] OR "imminent death"[All Fields] OR "imminent demise"[All Fields] Limits: All Adult: 19+ years, Publication Date from 1990 to 2004, English, Human **Total: 10,395**
7. health services needs and demand [mh] OR health facilities [mh:noexp] OR academic medical centers [mh] OR health facilities, proprietary [mh] OR health

facility environment [mh] OR health facility size [mh] OR hospital administration [mh] OR hospital units [mh:noexp] OR intensive care units [mh] OR hospitals [mh] OR residential facilities [mh] OR community health services [mh:noexp] OR community mental health services [mh] OR home care services [mh] OR home care agencies [mh] OR counseling [mh] OR suburban health services [mh] OR urban health services [mh] OR rural health services [mh] OR women's health services [mh:noexp] OR health services for the aged [mh] OR health services, indigenous [mh] OR health services [mh:noexp] OR community health nursing [mh] OR professional-patient relations [mh] OR public relations [mh] OR decision-making, organizational [mh] OR decision support systems, clinical [mh] OR institutional management teams [mh] OR patient care management [mh] OR role [mh] OR health personnel [mh] OR attitude of health personnel [mh] OR patient care [mh:noexp] OR critical care [mh] OR nursing care [mh] OR life support care [mh] OR health care economics and organizations [mh] OR resource allocation [mh] OR government [mh] OR government programs [mh]
Total: 158,202

8. #6 AND #7 **Total: 4,465**
9. #3 OR #5 OR #8 **Total: 8,944**
10. terminal care/economics OR terminal care/psychology OR terminal care/standards OR terminal care/trends OR terminal care/utilization OR terminal illness/psychology OR hospice care/economics OR hospice care/psychology OR hospice care/standards OR hospice care/trends OR hospice care/utilization
Total: 1,570
11. #9 OR #10 **Total: 9,154**
12. letter [pt] OR news [pt] OR editorial [pt] **Total: 83,393**
13. #11 NOT #12 **Total: 8,778**
14. #9 NOT #12 **Total: 8,585**
15. euthanasia [mh] OR suicide, assisted [mh] OR pregnancy [mh] OR pregnancy complications [mh] OR fetal death [mh] **Total: 60,908**
16. #13 NOT #15 **Total: 8,018**
17. #14 NOT #15 **Total: 7,912**
18. (palliative care OR bereavement OR grief OR terminal care OR hospice care OR terminally ill OR hospice OR hospices OR Kubler-Ross OR (attitude* AND death) OR "death and dying"[All Fields] OR "dying loved one"[All Fields] OR "dying patient"[All Fields] OR "dying patients"[All Fields] OR "dying people"[All Fields] OR "dying person"[All Fields] OR "end of life"[All Fields] OR "limited life expectancies"[All Fields] OR "limited life expectancy"[All Fields] OR "limited life span"[All Fields] OR "limited life spans"[All Fields] OR "limited lifespan"[All Fields] OR "limited lifetime"[All Fields] OR "imminent death"[All Fields] OR "imminent demise"[All Fields]) AND (in process [sb] OR publisher [sb]) AND 1990:2004 [pdat] **Total: 447**
19. #16 OR #18 **Total: 8,465**
20. #17 OR #18 **Total: 8,359**
21. #19 NOT case reports [pt] **Total: 7,047**
22. #20 NOT case reports [pt] **Total: 6,961**

Appendix B2. Q2-Trajectories Search Strategy

QUESTION #2:
DATABASE SEARCHED: PUBMED
TIME PERIOD COVERED: 1990-2004
OTHER LIMITERS: ENGLISH ONLY, HUMAN ONLY

SEARCH STRATEGY 1A:

heart failure, congestive OR dementia OR neoplasms

AND

terminally ill OR chronic disease OR critical illness OR metasta* OR advanced

AND

patients[majr] OR patient*[ti] OR family[majr] OR family[ti] OR families[ti]

AND

spirituality OR pain OR emotions OR dyspnea OR depression OR attitute to death OR population characteristics OR psychology[sh]

AND

quality of life OR quality of health care OR patient satisfaction OR patient advocacy OR decision making

NOT

gene OR genetic* OR chromosom* OR surgery[sh] OR radiotherapy OR drug therapy[sh] OR pathology OR epidemiology OR case report OR treatment outcome

SEARCH STRATEGY 1B:

heart failure, congestive OR dementia OR neoplasms

AND

terminally ill OR chronic disease OR critical illness OR metasta* OR advanced

AND

health care facilities, manpower and services OR quality of health care OR health services research OR health services OR insurance, health OR patient care management

AND

quality of life OR quality of health care OR patient satisfaction OR patient advocacy OR decision making

NOT

gene OR genetic* OR chromosom* OR surgery[sh] OR radiotherapy OR drug therapy[sh] OR pathology OR epidemiology OR case report OR treatment outcome

NUMBER OF ITEMS RETRIEVED FOR BOTH SEARCHES: 961

Appendix B2. Q2-Trajectories Search Strategy

Appendix B3. DARE Search Strategy

DARE -Database of Abstracts of Reviews of Effects

We searched DARE using the following individual terms:
Caregiver, coordination, continuity, advance care planning, advance care, DNR, resuscitation orders, communication, dyspnea.

We also searched for systematic reviews in the area of pain by combining 'pain' with the following disease-specific terms:
Cancer, neoplasms, COPD, CHF, chronic obstructive pulmonary disease, congestive heart failure, dementia, cirrhosis. The term 'pain' was combined with all other disease categories.

Category:	Number of Citations
caregiver(s)	31
advance care planning	0
resuscitation	21
DNR	1
dyspnea	12
continuity	20
coordination	20
communication	103
pain + disease-specific terms	92

One of us (KL) completed a title review on all citations identified, yielding a set of citations that was subjected to formal abstract review (using our systematic review screener).

Appendix B4. RAND Search Strategy

REVISED STRATEGY FOR END OF LIFE QUESTION 1, PUBMED
Roberta Shanman, 4/20/04

#1 Search death[ti] OR death[mh:noexp] OR "dying loved one" OR "dying patient" OR "dying patients" OR "dying people" OR "dying person" OR "last year of life" OR "end of life" OR "terminal illness" OR "terminal illnesses" OR terminal care OR "death and dying" OR "limited life expectancies" OR "limited life expectancy" OR "limited life span" OR "limited lifespan" OR "limited life spans" OR terminally ill OR critical illness OR frail elderly Field: All Fields, Limits: Publication Date from 1990 to 2004, English, Human 16:16:25 40006

#2 Search delivery of health care OR quality assurance, health care OR "outcome and process assessment (health care)" OR quality of life OR quality indicators OR quality of health care OR patient care management OR continuity of care OR outcome[ti] OR outcomes[ti] OR consumer satisfaction OR patient satisfaction OR personal satisfaction Limits: Publication Date from 1990 to 2004, English, Human 16:17:11 1418497

#3 Search pain/th OR pain/psychology OR "pain management" OR "pain assessment" OR "relieve suffering" OR "relieve symptoms" OR palliative care[mh] OR pain[ti] OR "pain relief" OR discomfort OR "physical comfort" OR "comfort care" OR "symptom distress" OR "symptom burden" OR "symptom control" OR "symptom intensity" OR "symptom management" OR "symptom relief" OR "pain distress" OR "pain easing" OR "pain free" Limits: Publication Date from 1990 to 2004, English, Human 16:18:17 72663

#4 Search "psychological distress" OR psychology[sh] OR wellbeing OR "well being" OR anxiety OR anxious OR anxiety disorders[mh] OR depression OR depressive disorder[mh] OR depressed OR "attitude to death" OR neoplasms/psychology OR "emotional health" OR spiritual OR emotions OR support[ti] OR supportive OR communication OR relationships OR religion OR religiosity OR "treatment decision" OR decisionmaking OR "decision making" Limits: Publication Date from 1990 to 2004, English, Human 16:19:56 445112

#5 Search home care services/standards OR home nursing/st OR hospice care/st OR "nursing assistance" OR nursing homes/st OR residential facilities/st OR intensive care units/st OR life support care/st OR "home care" OR hospice* OR "nursing homes"[tiab] OR "nursing home"[tiab] OR "intensive care"[tiab] OR icu[tiab] OR icus[tiab] OR "place of death" OR health care facilities, manpower and services OR caregiver* OR caregivers OR "care giving" OR family[mh] OR family[tiab] OR families[tiab] OR "social services" OR "social support" Limits: Publication Date from 1990 to 2004, English, Human 16:20:48 247909

#6 Search #1 AND #2 Limits: Publication Date from 1990 to 2004, English, Human 16:21:30 22453

#7 Search #3 OR #4 OR #5 Limits: Publication Date from 1990 to 2004, English, Human 16:21:51 669678

#8 Search #6 AND #7 Limits: Publication Date from 1990 to 2004, English, Human 16:22:07 14020

#9 Search #8 NOT (letter[pt] OR news[pt] OR editorial[pt] OR case reports[pt]) Limits: Publication Date from 1990 to 2004, English, Human 16:22:56 11505

#10 Search #9 NOT (ethics[mh] OR euthanasia[mh] OR suicide, assisted[mh] OR pregnancy[mh] OR pregnancy complications[mh] OR fetal death[mh]) Limits: Publication Date from 1990 to 2004, English, Human 16:24:59

TOTAL TITLES 8,284
When compared with NLM search, 3,748 new and unique titles identified by this search strategy.

Appendix C. Health Canada Reports

Table C1. Health Canada Reports- Relevant to Key Questions

Study	Report Title	Relevant to Key Questions
Wilson, D (in press) [1]	Outcomes and Evaluation of end of life care	Yes
Wilson, D (in press) [2]	The needs of dying persons	Yes
Wilson, D (in press) [3]	End of life case management	Yes
Wilson, D (in press) [4]	The needs of the families of dying persons	Yes
Wilson, D (in press) [5]	Continuity of end of life care	Yes
Wilson, D (in press) [6]	Managing End of life pain and other symptoms through non-pharmacological means	Yes
Wilson, D (in press) [7]	End of life spiritual and psychosocial issues	Yes
Wilson, D (in press) [8]	End of life care in acute care hospitals	Yes
Wilson, D (in press) [9]	End of life care in residential continuing-care facilities	Yes
Wilson, D (in press) [10]	Culture and end of life care	Yes
Wilson, D (in press) [11]	The home as a place of end of life care	Yes
Wilson, D (in press) [12]	Gender differences in the experience of the dying process	Yes
Wilson, D (in press) [13]	End of life care in intensive care units	Yes
Wilson, D (in press) [14]	End of life care in rural or remote areas	Yes

Appendix C. Health Canada Reports

Table C2. Health Canada Reports - Not Relevant to Key Questions

Author	Report Title	Relevant to Key Questions
Wilson, D (in press)	Australia site visit report	No
Wilson, D (in press)	Bereavement	No
Wilson, D (in press)	Canadian end of life care programs, models, and approaches	No
Wilson, D (in press)	End of life topics addressed in randomized controlled clinical trials research	No
Wilson, D (in press)	Palliative day care	No
Wilson, D (in press)	Integrated end of life care: a Health Canada synthesis research project	No
Wilson, D (in press)	New developments in end of life care	No
Wilson, D (in press)	Pediatric end of life care	No
Wilson, D (in press)	End of life prognostication	No
Wilson, D (in press)	Web-based questionnaire data analysis report	No
Wilson, D (in press)	End of life respite care	No
Wilson, D (in press)	Literature reviews that have focused on end of life care	No
Wilson, D (in press)	New Zealand site visit report	No
Wilson, D (in press)	International end of life care delivery models or approaches	No
Wilson, D (in press)	Provincial home care data analysis report	No
Wilson, D (in press)	Education in Canada for end of life care	No
Wilson, D (in press)	Canada site visit report	No
Wilson, D (in press)	Aboriginal end of life care	No

Appendix C. Health Canada Reports

Reference List

1. In: Wilson D. Outcomes and Evaluation of end of life care. Edmonton, Alberta Canada: University of Alberta. draft in press.

2. In: Wilson D. The needs of dying persons. Edmonton, Alberta Canada: University of Alberta. draft in press.

3. In: Wilson D. End of life case management. Edmonton, Alberta Canada: University of Alberta. draft in press.

4. In: Wilson D. The needs of the families of dying persons. Edmonton, Alberta Canada: University of Alberta. draft in press.

5. In: Wilson D. Continuity of end of life care. Edmonton, Alberta Canada: University of Alberta. draft in press.

6. In: Wilson D. Managing End of life pain and other symptoms through non-pharmacological means. Edmonton, Alberta Canada: University of Alberta. draft in press.

7. In: Wilson D. End of life spiritual and psychosocial issues. Edmonton, Alberta Canada: University of Alberta. draft in press.

8. In: Wilson D. End of life care in acute care hospitals. Edmonton, Alberta Canada: University of Alberta. draft in press.

9. In: Wilson D. End of life care in residential continuing-care facilities. Edmonton, Alberta Canada: University of Alberta. draft in press.

10. In: Wilson D. Culture and end of life care. Edmonton, Alberta Canada: University of Alberta. draft in press.

11. In: Wilson D. The home as a place of end of life care. Edmonton, Alberta Canada: University of Alberta. draft in press.

12. In: Wilson D. Gender differences in the experience of the dying process. Edmonton, Alberta Canada: University of Alberta. draft in press.

13. In: Wilson D. End of life care in intensive care units. Edmonton, Alberta Canada: University of Alberta. draft in press.

14. In: Wilson D. End of life care in rural or remote areas. Edmonton, Alberta Canada: University of Alberta. draft in press.

Appendix D1. Sample: Abstract Screening Form

End of Life Care and Outcomes

FINAL ABSTRACT SCREENER

1. Article ID: _____

2. First Author (last name): _____

3. Reviewer: **(CIRCLE ONE ONLY)**

Dy	1	Mularski	5
Hughes	2	Shugarman	6
Lorenz	3	Sun	7
Lynn	4	Wilkinson	8
Other	9	(specify_____)	

4. Population, intervention, outcome **exclusions**: **(CIRCLE ONE ONLY)**

Not about end of life care	1	**STOP**
Related only to sudden, violent, non-chronic deaths	2	**STOP**
Evaluating chemotherapy, surgery, stents, laser, or radiation interventions	3	**STOP**
No outcomes specified	4	**STOP**
Outcome unrelated to patients, family, non-professional caregivers	5	**STOP**
Primarily useful as a background paper	6	**STOP**
Primarily about prognosis or trajectories	7	**STOP**
Data is older than 1990	8	**STOP**
None of the above	9	

5. Study population: **(CIRCLE ONE ONLY)**

Human	1	
Non-human	2	**STOP**
Unclear	3	

6. Subjects: **(CIRCLE ONE ONLY)**

Adults (≥19 years) included	1	
Only children (≤18 years)	2	**STOP**
Mix or Unclear	3	

7. Study location: **(CIRCLE ONE ONLY)**

US, Canada, Europe, or Australia / NZ	1	
Non-Western	2	**STOP**
Mix or unclear	3	

8. Design: **(CIRCLE ONE ONLY)**

Qualitative research	1	
Systematic review or Meta-analysis	2	
Non-systematic review	3	**STOP**
Any observational study (< 30 cases)	4	**STOP**
Any non-intervention observational study (≥ 30 cases)	5	
Any intervention study (**Answer Q9**)	6	
Unclear	7	

9. Does the study report an intervention? **(CIRCLE ONE FOR EACH QUESTION)**

	Yes	No	Unclear
Does the investigator control assignment?	1	2	3
Is there a comparison / control group?	1	2	3
Is the intervention a non-chemotherapy drug?	1	2	3

10. Topic(s): **(CHECK ALL THAT APPLY)**

- A 'good death', 'quality of dying' ❑
- Patient/family satisfaction with terminal care ❑
- Methods paper (e.g. measure development) ❑
- Measures (outcomes or intervention related):
  - Family or informal caregiver concerns (*non-bereavement*) ❑
  - Family or informal caregiver concerns (*bereavement only*) ❑ **STOP**
  - Advance care planning ❑
  - Continuity and coordination ❑
  - Symptoms:
    - Pain ❑
    - Dyspnea ❑
    - Depression, delirium, anxiety, other affective/ behavioral symptoms ❑
    - Other symptoms (**STOP** if only one checked) ❑
  - Other (**STOP** if only one checked) ❑
- Unclear ❑

IF *OTHER SYMPTOM* OR *OTHER MEASURE* ONLY, THEN STOP

11. Type of disease(s): **(CHECK ALL THAT APPLY)**

- Lung cancer ❑
- Breast cancer ❑
- Colorectal cancer ❑
- Other or mixed cancer ❑
- Heart failure (CHF) ❑
- Other or mixed heart disease ❑
- Advanced chronic lung disease ❑ *(e.g. COPD or other)*
- End stage liver disease ❑
- End stage renal disease ❑
- Dementia ❑ *(e.g. Alzheimer's, multi-infarct, HIV, and other)*
- Stroke or other neurodegenerative disease ❑
- HIV / AIDS ❑
- Multiple chronic illnesses of aging – frailty ❑
- Other single cancer ❑
- Other mixed cancer ❑
- Unclear ❑

12. Secondary review required: **(CIRCLE ONE ONLY)**

Yes	1
No	2

Notes:

Last updated: 05/25/04

Appendix D2. Sample: Systematic Review Short Form

End of Life Care and Outcomes
SYSTEMATIC REVIEW FINAL SCREENER

1. Article ID: _____

2. First Author (last name): _____

3. Reviewer: **(CIRCLE ONE ONLY)**
   Maglione 1
   Other 2
   (specify_____)

4. Primarily useful as a background paper?
   Yes ..... ❑
   No ..... ❑

5. Topic: **(check ALL that apply)**
   A 'good death', 'quality of dying' ..... ❑
   Patient/family satisfaction with terminal care ..... ❑
   Methods paper (e.g. measure development) ..... ❑
   Measures (outcomes or intervention related):
   Family or informal caregiver concerns (*non-bereavement*) ..... ❑
   Family or informal caregiver concerns (*bereavement only*) ..... ❑ **(STOP)**
   Advance care planning ..... ❑
   Continuity and coordination ..... ❑
   Symptoms:
   Pain ..... ❑
   Dyspnea ..... ❑
   Affective/ behavioral symptoms ..... ❑
   Other end of life care ..... ❑ **(STOP)**
   Not end of life care ..... ❑ **(STOP)**

6. Type of disease(s): **(check ALL that apply)**
   Lung cancer ..... ❑
   Breast cancer ..... ❑
   Colorectal cancer ..... ❑
   Other or mixed cancer ..... ❑
   Heart failure (CHF) ..... ❑
   Other or mixed heart disease ..... ❑
   Advanced chronic lung disease ..... ❑
   (e.g. COPD or other)
   End stage liver disease ..... ❑
   End stage renal disease ..... ❑
   Dementia ..... ❑
   (e.g. Alzheimer's, multi-infarct, HIV, and other)
   Stroke or other neurodegenerative disease ..... ❑
   HIV / AIDS ..... ❑
   Multiple chronic illnesses of aging – frailty ..... ❑
   Other single cancer ..... ❑
   Other mixed cancer ..... ❑
   Unclear ..... ❑

7. Year literature search ended?
   (enter 9999 if not reported) ___ ___ ___ ___

8. Year of publication?
   (enter 9999 if not reported) ___ ___ ___ ___

9. Study Design: **(check ALL that apply)**
   Systematic Review ..... ❑
   Meta-analysis ..... ❑
   Review ..... ❑ **(STOP)**
   Other ..... ❑ **(STOP)**
   Unclear ..... ❑ **(STOP)**

10. Were the following study characteristics reported?
    (CIRCLE ONE ONLY)

	Yes	**No**	
Search strategy	1	2	**(If No then STOP)**
Inclusion Criteria	1	2	**(If No then STOP)**

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Appendix E4. IS - Satisfaction Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Bookbinder, 1996[1]	Design: Intervention, without comparison group Jadad: 0 Setting: Hospital (non-ICU) Funding: Not reported	Sample size: 698 patients, 1210 RN interviews, 335 focus groups with RN staff 2000 vital sign records Disease: Mixed disease: Not reported Severity: Unclear Race: Not reported Gender: Not reported	Comprehensive pain management care team, CQI type intervention.	Outcomes: Pain, Patient satisfaction, Medical provider satisfaction, Provider knowledge, Patient concerns, Patient preference of treatment. Results: Overall high rate of patient satisfaction (92%). Significant moderate correlations were found between overall dissatisfaction and longest time to wait for medication, extent of pain relief, and time to change medication.
Brumley, 2003[2]	Design: Intervention, comparison group Jadad: 0 Setting: Home health care Funding: Garfield Memorial Fund	Sample size: N=300 Disease: Mixed disease: Not reported Severity: Advanced Race: Not reported Gender: Not reported	Comprehensive palliative care team, Usual care.	Outcomes: Patient satisfaction, Utilization of health care services, Cost. Results: The labor of care giving emerged as the organizing core theme. The role of the caregiver in contributing to the quality of life of the patient was apparent in the initial phase of an illness as well as at the time of death.

ICU = Intensive Care Unit, RN = Registered Nurse, CQI = Continuous Quality Improvement, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, I = Intervention group, C = Control group, HRQoL = Health Related Quality of Life, outpt = Outpatient

Appendix E4. IS - Satisfaction Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Hanks, 2002[3]	Design: RCT/CCT Jadad: 2 Setting: Hospital (non-ICU) Funding: NHS (UK) National Cancer R&D Programme grant	Sample size: 261 Disease: Mixed disease: Not reported Severity: Advanced Race: Not reported Gender: Not reported	Comprehensive palliative care team.	Outcomes: Quality of life (patient), Patient satisfaction, Family/caregiver satisfaction, Medical provider satisfaction, Utilization of health care services, Re-admission to hospital. Results: Satisfaction with care in both groups was high and there was no significant difference between them.
Hughes, 2000[4]	Design: RCT/CCT Jadad: 3 Setting: Home health care Funding: VA HSR&D and Cooperative Studies Program	Sample size: 981 -I, 985- C - 289 of these were "terminally ill" Disease: Mixed disease: Not reported Severity: Advanced Race: Not reported Gender: Not reported	Discharge planning, 24 hour availability, Home-based primary care, Nursing palliative care, case managers.	Outcomes: Quality of life (patient), Cost, Patient satisfaction, Caregiver burden, Re-admission to hospital. Results: Team-managed home base primary care improved most HR-QoL measures among terminally ill patients and satisfaction among non-terminally ill patients. It improved caregiver HR-QoL, satisfaction with care and caregiver burden and reduced hospital readmission at 6 months.

ICU = Intensive Care Unit, RN = Registered Nurse, CQI = Continuous Quality Improvement, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, I = Intervention group, C = Control group, HRQoL = Health Related Quality of Life, outpt = Outpatient

Appendix E4. IS - Satisfaction Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Latimer, 1998[5]	Design: RCT/CCT Jadad: 2 Setting: Hospice Funding: Hamilton Civic Hospitals (Canada)	Sample size: 46 randomized/21 completed study Disease: Unclear Severity: Moderate Race: Not reported Gender: Not reported	Portable patient-controlled health record, Patient Care Traveling Record.	Outcomes: Pain, Patient satisfaction, Utilization of health care services, Mood, Uncertainty regarding present situation. Results: 21 patients completed the trial. With the exception of those aged 65+, patients using the Patient Care Traveling Record reported decreased levels of uncertainty on follow-up. There was no additional use of health care services, no differences in mood states, pain relief, or satisfaction with health care.
Rabow, 2004[6]	Design: RCT/CCT Jadad: 3 Setting: Ambulatory/outpt medical care Funding: Robert Wood Johnson Foundation	Sample size: 90 Disease: Mixed disease: Not reported Severity: Moderate Race: Not reported Gender: Not reported	Comprehensive palliative care team, Usual care, Outpatient Palliative Medicine Consultation.	Outcomes: Quality of life (patient), Physical symptoms (general), Utilization of health care services, Affective/behavioral symptoms, Degree dyspnea interferes, Frequency dyspnea limits activities, Sleep, Spirituality, Cost, Pain, Anxiety, Depression, Patient satisfaction. Results: The intervention group patients had less dyspnea and anxiety, and improved sleep quality and spiritual well being, but no change in pain, depression, quality of life or satisfaction with care.

ICU = Intensive Care Unit, RN = Registered Nurse, CQI = Continuous Quality Improvement, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, I = Intervention group, C = Control group, HRQoL = Health Related Quality of Life, outpt = Outpatient

Appendix E4. IS - Satisfaction Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Ringdal, 2002[7]	Design: RCT/CCT Jadad: 2 Setting: Hospice Funding: Norwegian Cancer Society, Swedish Cancer Society, Norwegian Medical Association Fund for Quality Improvement	Sample size: 180 Disease: Mixed disease: Not reported Severity: Advanced Race: Not reported Gender: Not reported	Comprehensive palliative care team, Usual care.	Outcomes: Family/caregiver satisfaction. Results: The majority of respondents reported high satisfaction with care. The respondents related to the patients in the intervention group reported significantly higher satisfaction with care than the respondents related to patients in the control group.
Grande, 2000[8]	Design: RCT/CCT Jadad: 3 Setting: Hospice Funding: Elizabeth Clark Charitable Trust, NHS (UK)	Sample size: 229 Disease: Mixed disease: Not reported Severity: Advanced Race: Not reported Gender: Not reported	Intensive home-based palliative care, Usual care.	Outcomes: Physical symptoms (general), Medical provider satisfaction, Place of death or care at end of life, Provider workload. Results: While the Cambridge hospital at home service was not found to increase the likelihood of remaining at home during the final two weeks of life, it appeared to be associated with better quality home care.
Scneiderman, 2003[9]	Design: RCT/CCT Jadad: 3 Setting: Hospital (ICU) Funding: AHRQ RO1 HS10251	Sample size: 278 - I, 273 - C Disease: Mixed disease: Not reported Severity: Advanced Race: Not reported Gender: Not reported	Ethics team consultation.	Outcomes: Patient satisfaction, Family/caregiver satisfaction, Hospital length of stay, ICU length of stay, TISS reduction (hospital resource use measure), Death. Results: Ethics consultations were useful in resolving conflicts that may have inappropriately prolonged non-beneficial or unwanted treatments in the intensive care unit.

ICU = Intensive Care Unit, RN = Registered Nurse, CQI = Continuous Quality Improvement, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, I = Intervention group, C = Control group, HRQoL = Health Related Quality of Life, outpt = Outpatient

Appendix E4. IS - Satisfaction Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Molloy, 2000[10]	Design: Intervention, without comparison group Jadad: 1 Setting: Nursing home Funding: AHRQ Grant (RO1 HS07878-02S1)	Sample size: 527-I, 656-C Disease: Mixed disease: Not reported Severity: Advanced Race: Not reported Gender: Not reported	Let-Me-Decide advance directive forms, Skilled nurse advance directive facilitator - patient / proxy meetings.	Outcomes: Patient satisfaction, Family/caregiver satisfaction, Completion of Let Me Decide advance directive, Utilization of health care services. Results: Systematic implementation of a program to increase use of advance directives reduced health care utilization without affecting satisfaction or mortality.
Weisbord, 2003[11]	Design: Intervention, without comparison group Jadad: 1 Setting: Ambulatory/outpt medical care Funding: Project Death in America Faculty Scholars Program, Greenwall Foundation, Ladies Hospital Aid, International Union Against Cancer, LAS Trust Foundation, American Society of Nephrology, NIH T32HL07820-05	Sample size: 19 Disease: Single disease: End stage renal disease Severity: Advanced Race: Not reported Gender: Not reported	Palliative care team consultation.	Outcomes: patient report of DPAHC, patient report of advance directives discussion with MD, quality of life, symptom burden. Results: No differences were observed in symptoms, HRQoL or number of patients establishing advance directives as a result of the intervention.

ICU = Intensive Care Unit, RN = Registered Nurse, CQI = Continuous Quality Improvement, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, I = Intervention group, C = Control group, HRQoL = Health Related Quality of Life, outpt = Outpatient

Appendix E4. IS - Satisfaction Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Reigel, 2002[12]	Design: RCT/CCT Jadad: 3 Setting: Ambulatory/outpt medical care Funding: Pfizer, Inc	Sample size: 281 MD's randomized, unit of analysis is patient (358 / 573 eligibles participate in analysis) Disease: Single disease: Heart failure Severity: Moderate Race: Not reported Gender: Not reported	Dextromethorphan (DM).	Outcomes: Pain rating scale using VAS, Pain intensity, Edmonton staging system for cancer pain, Medication effectiveness, Patient satisfaction. Results: Heart failure hospitalization rate, hospital days, multiple readmissions, and costs were all significantly lower in the intervention group. The intervention group had higher patient satisfaction.
Bruera, 1994[13]	Design: RCT/CCT Jadad: 5 Setting: Ambulatory/outpt medical care Funding: Not reported	Sample size: 60 Disease: Single disease: Mixed cancer Severity: Advanced Race: Not reported Gender: Not reported	Tape recording of consultation with MD.	Outcomes: Satisfaction with care (general), Pt-family communication about illness, Understanding of treatment plan and illness. Results: Addition of an audiocassette to written communications significantly increased patient satisfaction and improved recall of the information given during the consultation.

ICU = Intensive Care Unit, RN = Registered Nurse, CQI = Continuous Quality Improvement, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, I = Intervention group, C = Control group, HRQoL = Health Related Quality of Life, outpt = Outpatient

Appendix E4. IS - Satisfaction Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Pietersma, 2003[14]	Design: Intervention, without comparison group Jadad: 1 Setting: Hospital (non ICU) Funding: Alberta Palliative Care Research Initiative	Sample size: 27 Disease: Mixed disease: Not reported Severity: Advanced Race: Not reported Gender: Not reported	Electric food cart, Usual care.	Outcomes: Satisfaction with food provided. Results: The patients on oncology/palliative unit significantly preferred their meals to be delivered via a food cart rather than thermal trays, with respect to the timing and appeal of the meal, appropriateness of food types and food portions and the variety of the food choices.

ICU = Intensive Care Unit, RN = Registered Nurse, CQI = Continuous Quality Improvement, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, I = Intervention group, C = Control group, HRQoL = Health Related Quality of Life, outpt = Outpatient

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ICU = Intensive Care Unit, RN = Registered Nurse, CQI = Continuous Quality Improvement, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, I = Intervention group, C = Control group, HRQoL = Health Related Quality of Life, outpt = Outpatient

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ICU = Intensive Care Unit, RN = Registered Nurse, CQI = Continuous Quality Improvement, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, I = Intervention group, C = Control group, HRQoL = Health Related Quality of Life, outpt = Outpatient

Appendix E1. IS - Advance Care Planning Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Anderson, 1994[1]	Design: Intervention, comparison group Jadad: 2 Setting: Clinical services in 2 large hospitals Funding: Not reported	Sample size: 104-I, 100-C Disease: Other Severity: Advanced Race: Not reported Gender: Not reported	Let Me Decide advance directive forms.	Outcomes: Level of quality of well being. Results: No differences between health status and psych well being between intervention and control groups.
Campbell, 2003[2]	Design: Intervention, comparison group Jadad: 0 Setting: Hospital (ICU) Funding: Not reported	Sample size: 40-retrospective analysis vs. 41-proactive cohort Disease: Single disease: Stroke or other neurode Severity: Advanced Race: Not reported Gender: Not reported	Meet with family daily to discuss patient's prognosis & treatment goals, Implementing DNR orders and Comfort measures.	Outcomes: Hospital - length of stay, Death/Mortality. Results: Proactive case finding approach decreased hospital length of stay, decreased time between identification of poor prognosis and establishment of comfort care goals, and decreased use of non-beneficial resources.
Heffner, 1997[3]	Design: Intervention, without comparison group Jadad: 1 Setting: Ambulatory/outpt medical care Funding: Greenwall Foundation	Sample size: 50-I vs. 43-C Disease: Single disease: Advanced chronic lung disease Severity: Unclear Race: Not reported Gender: Males and females	Educational workshop on AD and other end-of-life issues, Patients given pamphlets on AD, printed living will, durable powers of attorney for health care.	Outcomes: Physician-patient agreement/understanding on goals of care, including DNR, Patient report of living will &/or is in chart, Patient report of DPAHC &/or is in chart, Patient report of life support discussion with MD, Patient report of advance directives discussion with MD. Results: The educational group had an increase in all five study outcomes, while control group had an increase in three of the outcomes.

I = Intervention group, C = Control group, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive, MD = Physician, ACP = Advance Care Planning, AD/DPA = Advance Directive/Durable Power of Attorney, HRQoL = Health Related Quality of Life, T = Treatment group, DPA = Durable Power of Attorney

Appendix E1. IS - Advance Care Planning Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Holzpfel, 2002[4]	Design: Intervention, without comparison group Jadad: 1 Setting: Hospital (ICU) Funding: Not reported	Sample size: 475-I Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Males	4-step protocol for decision making in end-of-life care, Changes in treatment pattern required agreement.	Outcomes: Simplified acute physiologic score (SAPS), Use of mechanical vent, Use of mechanical vent > 48 hours, ICU - length of stay, Death/Mortality, Death after withholding, withdrawing life support (vent or other). Results: Withdrawal of life support was performed in 17% of ICU patients. Mean ICU stay was 10 days.
Jack, 2004[5]	Design: Intervention, comparison group Jadad: 1 Setting: Hospital (non-ICU) Funding: Not reported	Sample size: 50-I vs. 50-C Disease: Single disease: Advanced cancer Severity: Advanced Race: Not reported Gender: Males and females	Palliative care team consultation.	Outcomes: Palliative Care Assessment Tool. Results: Patients in the intervention group had significantly greater improvement in their insight scores.

I = Intervention group, C = Control group, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive, MD = Physician, ACP = Advance Care Planning, AD/DPA = Advance Directive/Durable Power of Attorney, HRQoL = Health Related Quality of Life, T = Treatment group, DPA = Durable Power of Attorney

Appendix E1. IS - Advance Care Planning Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Lilly, 2000[6]	Design: Intervention, without comparison group Jadad: 0 Setting: Hospital (ICU) Funding: Brigham and Women's Hospital, Boston, MA	Sample size: 134-pre-I vs. 396-I Disease: Mixed disease Severity: Advanced Race: African-American, Hispanic and other Gender: Males	Attending physician-led meetings with patients and their families.	Outcomes: Mortality rate, Consensus among providers. Results: Intensive communication significantly reduced the median length of stay.
Lilly, 2003[7]	Design: Intervention, comparison group Jadad: 0 Setting: Hospital–ICU Funding: Brigham and Women's Hospital, Boston, MA	Sample size: 134-pre-I vs. 396-I vs. 2361-4-year follow-up Disease: Mixed disease Severity: Advanced Race: African-American, Hispanic and other Gender: Males and females	Intensive communication sessions among providers, patients and families.	Outcomes: ICU - length of stay. Results: Intensive communication produced significant and durable reductions in both length of stay and ICU mortality.
Ratner, 2001[8]	Design: Intervention, without comparison group Jadad: 0 Setting: Home health care Funding: Allina Foundation	Sample size: 83 Disease: Unclear Severity: Unclear Race: Not reported Gender: Not reported	Discussion of ACP process with patients and their families during home visits, Documentation of health care directives using an ACP tool.	Outcomes: Chart based completion of advance directive, Time between ACP and death, Location of death, Use of hospice and palliative care. Results: Of patients expressing a clear preference for location of end-of-life care, 82% wanted this care to be at home.

I = Intervention group, C = Control group, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive, MD = Physician, ACP = Advance Care Planning, AD/DPA = Advance Directive/Durable Power of Attorney, HRQoL = Health Related Quality of Life, T = Treatment group, DPA = Durable Power of Attorney

Appendix E1. IS - Advance Care Planning Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Schwartz, 2002[9]	Design: Intervention, comparison group Jadad: 3 Setting: Ambulatory/outpt medical care Funding: Fairlawn Foundation, the Umass Memorial Foundation, and the Stoddard Charitable Trust in Worcester, MA	Sample size: 31-I vs. 30-C Disease: Unclear Severity: Unclear Race: Other Gender: Males and females	Facilitated "Respecting Choices" interview with informational pamphlet vs. nondirective interview.	Outcomes: Attitudes towards end of life decision-making (questionnaire), Patient-surrogate concurrence in end-of-life care, Change in treatment preferences. Results: Intervention achieved higher congruence between agents and patients in their understanding of patients' end of life care preferences. Intervention patients became less willing to undergo life-sustaining treatments for a new serious medical problem and less willing to tolerate poor health states.
Stuart, 2003[10]	Design: Intervention, without comparison group Jadad: 1 Setting: Home health care Funding: RWJ Foundation	Sample size: 208 Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Males and females	Implementing the "CHOICES" home care management program.	Outcomes: Location of death, Use of hospice and palliative care. Results: Preliminary evidence supports the program's feasibility and acceptability to patients, families, physicians, and agency partners.

I = Intervention group, C = Control group, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive, MD = Physician, ACP = Advance Care Planning, AD/DPA = Advance Directive/Durable Power of Attorney, HRQoL = Health Related Quality of Life, T = Treatment group, DPA = Durable Power of Attorney

Appendix E1. IS - Advance Care Planning Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Weisbord, 2003[11]	Design: Intervention, without comparison group Jadad: 1 Setting: Ambulatory/outpt medical care Funding: The Project on Death in America Faculty Scholars Program, the Greenwall Foundation, Ladies Hospital Aid Society of Western Pennsylvania, the International Union Against Cancer, Yamagiwa-Yoshida Memorial International Cancer Study Grant Fellowship, and the LAS Trust Foundation.	Sample size: 19 Disease: Single disease: Kidney disease/Renal failure Severity: Unclear Race: Not reported Gender: Not reported	Palliative care physicians performed an initial evaluation (using a standard intake form and doing a comprehensive history and physical exam) during dialysis visit, Written recommendations developed at weekly team meeting given to patient and their nephrologists.	Outcomes: Patient report of advance directives discussion with MD, Completion of AD/DPA and treatment preferences, Satisfaction with palliative care. Results: No differences were observed in symptoms, HRQoL or number of patients establishing advance directives as a result of the intervention.

I = Intervention group, C = Control group, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive, MD = Physician, ACP = Advance Care Planning, AD/DPA = Advance Directive/Durable Power of Attorney, HRQoL = Health Related Quality of Life, T = Treatment group, DPA = Durable Power of Attorney

Appendix E1. IS - Advance Care Planning Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Teno, 1997[12]	Design: RCT/CCT Jadad: 3 Setting: Hospital (ICU and non-ICU) Funding: RWJ Foundation	Sample size: 9,105 patients (4,301 in Phase I 4,804 in Phase II), patients & physicians randomized into T (n=2,652) or C (n= 2,152). Disease: Mixed disease Severity: Advanced Race: African-American and other Gender: Males and females	Physicians in the intervention group received computer- based estimates of the likelihood of 6 month survival for every day up to 6 months, outcomes of CPR, and functional disability at 2 months, A trained RN communicated w/ patients & families regarding treatment preferences, communicated these preferences to care team to improve understanding and patient-physician communication.	Outcomes: Time to comfort care goals/time when written/DNR, Physician-patient agreement/understanding on goals of care, including DNR, Frequency, severity of pain, Cost of care / resource intensity. Results: No evidence that the intervention enhanced the effect of advance directives on 3 measures of resuscitation decision-making.
Dowdy, 1998[13]	Design: Intervention, comparison group Jadad: 1 Setting: Hospital (ICU) Funding: Bon Secours-St. Mary's Health Care Foundation and the Trigon Blue Cross and Blue Shield of Virginia	Sample size: 37-C1, 31-C2 vs. 31-I Disease: Unclear Severity: Unclear Race: Not reported Gender: Females	Ethics service intervention after patient received >96 hours of continuous mechanical ventilation.	Outcomes: Frequency and documentation of treatment discussions with patient, Completion of AD/DPA and treatment preferences, ICU - length of stay, Cost of care / resource intensity, Death/Mortality. Results: More frequent and documented communications, more frequent decisions to forgo life-sustaining treatment, and reduced length of stay in the ICU for the proactive consultation group.

I = Intervention group, C = Control group, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive, MD = Physician, ACP = Advance Care Planning, AD/DPA = Advance Directive/Durable Power of Attorney, HRQoL = Health Related Quality of Life, T = Treatment group, DPA = Durable Power of Attorney

Appendix E1. IS - Advance Care Planning Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Schneiderman, 2003[14]	Design: RCT/CCT Jadad: 3 Setting: Hospital (ICU) Funding: AHRQ Grant	Sample size: 278-I vs. 273-C Disease: Mixed disease Severity: Advanced Race: African-American, Hispanic, Asian and other Gender: Females	Ethics consultation (not the standard of care at the time).	Outcomes: ICU - length of stay, Hospital - length of stay, Life-sustaining treatments in patients not surviving to discharge. Results: The intervention and usual care groups showed no difference in mortality. The intervention was associated with reductions in hospital and ICU days and life-sustaining treatments with ventilation in those patients who ultimately did not survive to discharge.
Molloy, 2000[15]	Design: RCT/CCT Jadad: 3 Setting: Nursing home Funding: AHRQ Grant (RO1 HS07878-02S1)	Sample size: 636-I vs. 656-C Disease: Unclear Severity: Unclear Race: Other Gender: Females	Let Me Decide AD program involving education of staff, residents, and families about Ads and forms to complete.	Outcomes: Patient satisfaction, Cost of care / resource intensity, Completion of AD/DPA and treatment preferences, Death after withholding, withdrawing life support (vent or other), Death/Mortality. Results: Satisfaction was not significantly different between interventional and control nursing homes. Intervention nursing homes reported fewer hospitalizations per resident and less resource use.

I = Intervention group, C = Control group, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive, MD = Physician, ACP = Advance Care Planning, AD/DPA = Advance Directive/Durable Power of Attorney, HRQoL = Health Related Quality of Life, T = Treatment group, DPA = Durable Power of Attorney

Appendix E1. IS - Advance Care Planning Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Dexter, 1998[16]	Design: RCT/CCT Jadad: 3 Setting: Ambulatory/outpt medical care Funding: AHRQ Grant	Sample size: 1009 (253-Control group, 219-Instruction directive group, 260-proxy directive group, 277-instruction directive and proxy directive group Disease: Mixed disease Severity: Advanced Race: Asian Gender: Females	Computer-generated reminders to discuss ADs, Computer-generated reminders for proxy directives, Computer-generated reminders to both instruction and proxy directives.	Outcomes: Completion of AD/DPA and treatment preferences. Results: MDs who received reminders discussed advance directives with 24% of patients, compared to only 4% of patients with control group MDs.
Rubin, 1994[17]	Design: RCT/CCT Jadad: 0 Setting: Ambulatory/outpt medical care Funding: Kaiser Foundation Research Institute, Institute of Mental Health grant, and RWJ Foundation	Sample size: 1001 (552-I, 549-C) Disease: Mixed disease Severity: Unclear Race: African-American, Hispanic, Asian and other Gender: Males	Patients mailed durable power of attorney (DPA) informational brochure and DPA form.	Outcomes: Frequency and documentation of treatment discussions with patient. Results: 18.5% of the intervention group completed a durable power of attorney compared to 0.4% of the control group.
[18]	Design: RCT/CCT Jadad: 1 Setting: Ambulatory/outpt medical care	Sample size: 95-I vs. 92-C Disease: Unclear Severity: Unclear Race: Other	Educational workshop on AD and other end-of-life issues, Patients given pamphlets on AD, printed living will, durable powers of attorney for health care.	Outcomes: Completion of AD/DPA and treatment preferences. Results: At one-month follow-up, the AD intervention group revealed a 38% completion versus control group's 24% completion of advance directive. Further,

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Appendix E1. IS - Advance Care Planning Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
	Funding: Department of Clinical Investigations, Walter Reed Army Medical Center	Gender: Not reported		73% of the AD group discussed advance planning as compared to 57% of control group.
19	Design: RCT/CCT Jadad: 2 Setting: Hospital (ICU and non-ICU) Funding: RWJ Foundation	Sample size: 386-I vs. 331-C Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	A trained RN communicated w/ patients & families/surrogates regarding treatment preferences to promote patient-surrogate agreement.	Outcomes: Patient-surrogate concurrence in end-of-life care. Results: The SUPPORT intervention was not successful in increasing agreement between patients and surrogates. Other findings suggest that improvements in communication are particularly needed when patients are older and when the surrogate is not a patient's immediate relative.
20	Design: RCT/CCT Jadad: 1 Setting: Ambulatory/outpt medical care Funding: Summa Health System Foundation, Family Practice Clinical Research Center, Kent State University Applied Psychology Center and the Department of Family Medicine at the Northeastern Ohio Universities College of Medicine grant D15 PE55048-01 from the Depart	Sample size: 85-I vs. 15-C Disease: Unclear Severity: Unclear Race: Not reported Gender: Not reported	Physician-initiated discussion of AD.	Outcomes: Attitudes towards end of life decision-making (questionnaire), Patient perception of MD - pt agreement / understanding of preferences, Patient mood or affective state. Results: Neither group had adverse emotional or attitudinal responses. The AD group showed positive affective and attitudinal responses to the discussion, including an increase in positive affect, an increased sense of physician-patient understanding, and increased thought and discussion about life-support issues in the week following the AD.

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CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive,
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Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Ahrens, 2003[1]	Design: Intervention, comparison group Jadad: 0 Setting: Hospital (ICU) Funding: Local grant (Barnes-Jewish Foundation)	Sample size: 151 (43 - I, 108 - C) Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	Communication - MD / nurse specialist communication team.	Outcomes: ICU length of stay, Charges/costs, ICU mortality, Hospital LOS. Results: Compared with the control group, patients in the intervention group had significantly shorter stays in both the intensive care unit and the hospital and had lower fixed and variable costs.
SUPPORT, 1995[2]	Design: RCT/CCT Jadad: 2 Setting: Hospital (non-ICU) Funding: RWJ	Sample size: 4804 (2652 - I, 2152 - C) Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	Communication - MD / nurse specialist communication team, Feedback/benchmarking, Pain assessment, Eliciting patient preferences.	Outcomes: Pain, ICU mortality, DNR orders, Physician awareness of pts HRQOL (physician agreement with patient report). Results: Compared to control patients, intervention patients experienced no difference in patient-physician communication, or in the 5 targeted outcomes. The intervention also did not reduce use of hospital resources.

ICU = Intensive Care Unit, I = Intervention group, C = Control group, MD = Physician, LOS = Length of Stay, RCT/CCT = Randomized Controlled Trial / Clinical Controlled Trial, DNR = Do Not Resuscitate, HRQoL = Health Related Quality of Life, ICU = Intensive Care Unit, outpt = Outpatient, QI = Quality Improvement, CHF = Chronic Heart Failure, Pt(s) = Patient(s)

Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Detmar, 2003[3]	Design: RCT/CCT Jadad: 3 Setting: Ambulatory/outpt medical care Funding: Dutch Cancer Society	Sample size: 214 patients, 10 physicians (pairs) Disease: Predominately one disease: Breast cancer Severity: Advanced Race: Not reported Gender: Not reported	Pre-visit HRQOL questionnaire with standardized reporting to the physician.	Outcomes: Communication summary score - audiotape derived, Physician awareness of pts HRQOL (physician agreement with patient report), HRQOL-related patient management, Patient satisfaction, and Physician satisfaction. Results: Health-related quality of life issues were discussed significantly more in the intervention than in the control group. MDs in the intervention group identified a higher percentage of patients with moderate-to-severe health problems. All MDs and 87% of patients believed that the intervention facilitated communication and expressed interest in its continued use.
Hughes, 2000[4]	Design: RCT/CCT Jadad: 3 Setting: Home health care Funding: VA HSR&D and Cooperative Studies Program	Sample size: 981 -I, 985- C - 289 of these were "terminally ill" Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	Nursing palliative care / case managers, 24- hour availability, Discharge planning, Home-based primary care.	Outcomes: Quality of life, Charges/costs, Patient satisfaction, Caregiver burden. Results: Team-managed home base primary care improved most HR-QoL measures among terminally ill patients and satisfaction among non-terminally ill patients. It improved caregiver HR-QoL, satisfaction with care, and caregiver burden and also reduced hospital readmission.

ICU = Intensive Care Unit, I = Intervention group, C = Control group, MD = Physician, LOS = Length of Stay, RCT/CCT = Randomized Controlled Trial / Clinical Controlled Trial, DNR = Do Not Resuscitate, HRQoL = Health Related Quality of Life, ICU = Intensive Care Unit, outpt = Outpatient, QI = Quality Improvement, CHF = Chronic Heart Failure, Pt(s) = Patient(s)

Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Latimer, 1998[5]	Design: RCT/CCT Jadad: 2 Setting: Ambulatory/outpt medical care Funding: Local grant (Hamilton, Ontario civic hospitals)	Sample size: 21 (12 - I, 9 - C) out of 46 randomized Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	Patient-carried medical record (Patient Care Traveling Record).	Outcomes: Pain, Mood, Patient satisfaction, Utilization, Patient uncertainty. Results: 21 patients completed the trial. With the exception of those aged 65+, patients using the Patient Care Traveling Record reported decreased levels of uncertainty on follow-up. There was no additional use of health care services, no differences in mood states, pain relief, or satisfaction with health care.
Marbella, 1998[6]	Design: RCT/CCT Jadad: 2 Setting: Hospital (non-ICU) Funding: RWJ	Sample size: 386 - I, 331 - C Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	Communication - MD / nurse specialist communication team, Feedback/benchmarking, Pain assessment, Eliciting patient preferences.	Outcomes: Patient - surrogate agreement on preferences for care. Results: Intervention did not have an effect on surrogates' agreement with patients' resuscitation wishes.

ICU = Intensive Care Unit, I = Intervention group, C = Control group, MD = Physician, LOS = Length of Stay, RCT/CCT = Randomized Controlled Trial / Clinical Controlled Trial, DNR = Do Not Resuscitate, HRQoL = Health Related Quality of Life, ICU = Intensive Care Unit, outpt = Outpatient, QI = Quality Improvement, CHF = Chronic Heart Failure, Pt(s) = Patient(s)

Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Smeenk, 1998[7]	Design: Intervention, comparison group Jadad: 1 Setting: Home health care Funding: National Committee of Chronic Diseases in the Netherlands Scientific Fund of the Catharina Hospital, Eindhoven	Sample size: 79-I, 37-C Disease: Single disease: Mixed cancer Severity: Advanced Race: Not reported Gender: Not reported	Discharge planning, 24- hour availability, Patient-carried medical record (Patient Care Traveling Record), Eare protocols.	Outcomes: Quality of life, Re-hospitalization. Results: Patients in the intervention group underwent significantly less re-hospitalization during the terminal phase of their illness. The intervention contributed significantly to the patients' physical quality of life. A higher, but not significant (p=.06) percentage of patients in the intervention group died at home.
Grande, 1999[8]	Design: RCT/CCT Jadad: 2 Setting: Home health care Funding: Elizabeth Clark Charitable Trust and NHS R&D program	Sample size: 186 - I, 43 - C Disease: Predominately one disease: Mixed cancer Severity: Advanced Race: Not reported Gender: Not reported	24 / 7 in home nursing care.	Outcomes: Home death / site of death. Results: Results were inconclusive; study attained less statistical power than initially planned.

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Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Goldberg, 2003[9]	Design: RCT/CCT Jadad: 1 Setting: Ambulatory/outpt medical care Funding: Alere Medical, Inc.	Sample size: 280 (138 - I, 142 - C) Disease: Single disease: Heart failure Severity: Moderate Race: Not reported Gender: Not reported	AlereNet (electronic monitoring system for weights and symptoms).	Outcomes: Quality of life, Patient satisfaction, Mortality, Emergency department use. Results: No differences in hospitalization rates were observed, but there was a significant reduction in mortality for the intervention group.
Gorski, 2003[10]	Design: Intervention, without comparison group Jadad: 1 Setting: Home health care Funding: Not reported	Sample size: 74-I, unclear -C Disease: Single disease: Heart failure Severity: Moderate Race: Not reported Gender: Not reported	Disease management, Home care.	Outcomes: Patient satisfaction, Re-hospitalization, Self-care management. Results: 35% decrease in hospitalization of patients.

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Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Heidenreich, 1999[11]	Design: Intervention, comparison group Jadad: 0 Setting: Ambulatory/outpt medical care Funding: LifeMasters Supported Self Care, AHRQ training grant 00028-10	Sample size: 68 - I, 86 - C (historical controls) Disease: Single disease: Heart failure Severity: Moderate Race: Not reported Gender: Males	Comprehensive education and telephone reporting, follow-up protocol.	Outcomes: Quality of life, Patient satisfaction, Utilization, Charges/costs. Results: Medical claims per year decreased in the intervention group, while they increased in the control group. Same was true for hospitalizations and hospital days.
Jaarsma, 1999[12]	Design: RCT/CCT Jadad: 1 Setting: Ambulatory/outpt medical care Funding: Netherlands Heart Foundation Grant 43.033	Sample size: 84 - I, 95 - C Disease: Single disease: Heart failure Severity: Advanced Race: Not reported Gender: Not reported	Intensive patient education, Telephone case management.	Outcomes: Self-care management, Self-care ability, Utilization. Results: Patients from both the intervention and control groups increased their self-care behavior within a month of discharge, but the increase in the intervention group was significantly more after one month. No significant effects on resource utilization were found.

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Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Philbin, 2000[13]	Design: RCT/CCT Jadad: 1 Setting: Ambulatory/outpt medical care Funding: VHA Empire State, Inc NY State Dept of Health grants	Sample size: 5-I, 5-C (about 1500 patients, 10 total hospitals) Disease: Single disease: Heart failure Severity: Moderate Race: Not reported Gender: Not reported	Complex hospital level program (QI).	Outcomes: Re-hospitalization, Appropriate med use, Hospital LOS, Ladder of Life, Functional status, Mortality. Results: Non-significant decreases in length of stay and hospital charges in the intervention group.
Riegel, 2002[14]	Design: RCT/CCT Jadad: 3 Setting: Ambulatory/outpt medical care Funding: Pfizer, Inc	Sample size: 281 MD's randomized, unit of analysis is patient (358 / 573 eligible participate in analysis) Disease: Single disease: Heart failure Severity: Moderate Race: Not reported Gender: Not reported	Nursing case management using decision support tool for CHF.	Outcomes: Patient satisfaction, Cost of care, Re-admission to hospital, Days of hospitalization. Results: Heart failure hospitalization rate, hospital days, multiple readmissions, and costs were all significantly lower in the intervention group. The intervention group had higher patient satisfaction.

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Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Stewart, 1999[15]	Design: RCT/CCT Jadad: 3 Setting: Home health care Funding: National Heart Foundation of Australia Postgraduate Research Scholarship	Sample size: 100 - I, 100 - C Disease: Single disease: Heart failure Severity: Moderate Race: Not reported Gender: Not reported	Post-discharge nurse focused on broad range of concerns including ensuring supportive, safe home and specific education and medical treatment of CHF, coordination of services.	Outcomes: Quality of life, Re-hospitalization, Functional status, Mortality. Results: There were fewer unplanned readmissions and associated days in the hospital among intervention group patients.
Mann, 1999[16]	Design: RCT/CCT Jadad: 2 Setting: Ambulatory/outpt medical care Funding: National Institute on Disability and Rehabilitation Research H133E60006, Administration on Aging of DHHS, and Andrus Foundation	Sample size: 52 - I, 52 - C Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	Physical therapist in home assessment, Assistive devices and modifications to home environment, Nurse and home technician assistance.	Outcomes: Functional independence, Pain, Charges/costs. Results: Pain scores increased significantly more for the control group. The control group required significantly more expenditures for institutional care.

ICU = Intensive Care Unit, I = Intervention group, C = Control group, MD = Physician, LOS = Length of Stay, RCT/CCT = Randomized Controlled Trial / Clinical Controlled Trial, DNR = Do Not Resuscitate, HRQoL = Health Related Quality of Life, ICU = Intensive Care Unit, outpt = Outpatient, QI = Quality Improvement, CHF = Chronic Heart Failure, Pt(s) = Patient(s)

Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Melin, 1992[17]	Design: RCT/CCT Jadad: 1 Setting: Ambulatory/outpt medical care Funding: Aldre Centrum Foundation, Stockholm County Council, and Central Stockholm Public Health District	Sample size: 249 randomized, 150 - I, 99 - C Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	MD / nurse home care, Interdisciplinary team management, 24- hour availability.	Outcomes: Functional status, Social contact and support, Utilization. Results: Significant improvement in instrumental activities of daily living, outdoor walking, and medical condition was found in the intervention group compared to control group.
Jerant, 2001[18]	Design: RCT/CCT Jadad: 3 Setting: Home health care Funding: UC Davis intramural grant	Sample size: 13 - I1, 12 - I2, 12 - C Disease: Single disease: Heart failure Severity: Advanced Race: Not reported Gender: Not reported	Video-based telecare, Telephone case management.	Outcomes: Re-admission to hospital, Charges/costs, Quality of life, Emergency department use. Results: Both intervention groups had significantly fewer CHF related emergency department visits and costs than the usual care group. Trends favoring both interventions were found on all other utilization outcomes; these results were not statistically significant (very small N).

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Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Stewart, 1999[19]	Design: RCT/CCT Jadad: 1 Setting: Ambulatory/outpt medical care Funding: Australian Dept of Health and Family Services, Canberra (grant 95/34956)	Sample size: 49 - I, 48 - C Disease: Single disease: Heart failure Severity: Moderate Race: Not reported Gender: Not reported	Post-discharge nurse and pharmacist follow-up focused on medication knowledge and compliance.	Outcomes: Re-admission to hospital, Mortality, Emergency department use, Charges/costs. Results: Intervention group had fewer unplanned readmissions, fewer out-of-hospital deaths, fewer days of hospitalization, and fewer total deaths.
Bruera, 1999[20]	Design: RCT/CCT Jadad: 5 Setting: Ambulatory/outpt medical care Funding: Not reported	Sample size: 60 Disease: Single disease: Mixed cancer Severity: Advanced Race: Not reported Gender: Not reported	Tape recording of consultation with MD.	Outcomes: Patient satisfaction, Pt-family communication about illness, Understanding of treatment plan and illness. Results: Addition of an audiocassette to written communications significantly increased patient satisfaction and improved recall of the information given during the consultation.

ICU = Intensive Care Unit, I = Intervention group, C = Control group, MD = Physician, LOS = Length of Stay, RCT/CCT = Randomized Controlled Trial / Clinical Controlled Trial, DNR = Do Not Resuscitate, HRQoL = Health Related Quality of Life, ICU = Intensive Care Unit, outpt = Outpatient, QI = Quality Improvement, CHF = Chronic Heart Failure, Pt(s) = Patient(s)

Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Schneiderman, 2000[21]	Design: RCT/CCT Jadad: 2 Setting: Hospital (ICU) Funding: AHCPR PAR-96-028	Sample size: 74 (35 - I, 35 - C) Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	Ethics consultation.	Outcomes: Variety of life-extending or sustaining treatments non-beneficial treatments, ICU length of stay, Family and provider perception of usefulness and stressfulness. Results: No differences in overall mortality between control and intervention groups. Intervention was associated with reductions in ICU days and life-sustaining treatments in those patients who ultimately failed to survive to discharge.
Schneiderman, 2003[22]	Design: RCT/CCT Jadad: 3 Setting: Hospital (ICU) Funding: AHRQ RO1 HS10251	Sample size: 278 - I, 273 - C Disease: Mixed disease Severity: Advanced Race: Not reported Gender: Not reported	Ethics consultation.	Outcomes: ICU length of stay, Hospital LOS, Mortality, Non-beneficial treatment (hi-tech care). Results: Ethics consultations were useful in resolving conflicts that may have inappropriately prolonged non-beneficial or unwanted treatments in the intensive care unit.
Raftery, 1996[23]	Design: RCT/CCT Jadad: 2 Setting: Home health care Funding: Medical Research Council	Sample size: 86-I, 81-C Disease: Predominately one disease: Mixed cancer Severity: Advanced Race: Not reported Gender: Not reported	Nurse coordinator.	Outcomes: Hospital LOS, Charges/costs. Results: The mean total costs incurred by the co-ordination group were significantly less than those of control group. The co-ordination groups used significantly fewer inpatient days and nurse home visits.

ICU = Intensive Care Unit, I = Intervention group, C = Control group, MD = Physician, LOS = Length of Stay, RCT/CCT = Randomized Controlled Trial / Clinical Controlled Trial, DNR = Do Not Resuscitate, HRQoL = Health Related Quality of Life, ICU = Intensive Care Unit, outpt = Outpatient, QI = Quality Improvement, CHF = Chronic Heart Failure, Pt(s) = Patient(s)

Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Selwy, 2003[24]	Design: Intervention, without comparison group Jadad: 0 Setting: Hospital (non ICU) Funding: HRSA	Sample size: 132 Disease: Single disease: HIV/AIDS Severity: Advanced Race: Not reported Gender: Not reported	Palliative care consult service.	Outcomes: Symptoms, Mortality, Survival duration, Discharge disposition, Conflict. Results: HIV palliative care services resolved the patients' problems including a mix of medical and psychosocial issues.
Stockelberg, 1997[25]	Design: Intervention, without comparison group Jadad: 0 Setting: Home health care Funding: FoU-fondation, Södra Älvsborg, Borås Bil & Traktor AB	Sample size: 17 Disease: Single disease: Other cancer Severity: Advanced Race: Not reported Gender: Not reported	Home care.	Outcomes: Utilization. Results: Supportive treatment of patients with haematological disorders, given by a nurse, is safe and well accepted. The cost for transportation and hospital care were reduced.
Goodyer, 1995[26]	Design: RCT/CCT Jadad: 1 Setting: Ambulatory/outpt medical care Funding: Not reported	Sample size: 100 (50-I, 50-C) Disease: Single disease: Heart failure Severity: Moderate Race: Not reported Gender: Not reported	Intensive medication counseling.	Outcomes: Symptoms, Functional status, Adherence. Results: Intensive medication counseling in a group of elderly patients with chronic heart failure improved exercise capacity and signs of oedema. Exercise tolerance for the patients who received no counseling worsened over the study period. No subjective benefit could be detected by VAS or the NHP.

ICU = Intensive Care Unit, I = Intervention group, C = Control group, MD = Physician, LOS = Length of Stay, RCT/CCT = Randomized Controlled Trial / Clinical Controlled Trial, DNR = Do Not Resuscitate, HRQoL = Health Related Quality of Life, ICU = Intensive Care Unit, outpt = Outpatient, QI = Quality Improvement, CHF = Chronic Heart Failure, Pt(s) = Patient(s)

Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Topp, 1998[27]	Design: Intervention, comparison group Jadad: 0 Setting: Hospital (non ICU) Funding: Not reported	Sample size: 491 (88 -I) Disease: Single disease: Heart failure Severity: Unclear Race: Not reported Gender: Not reported	Disease management.	Outcomes: Hospital LOS. Results: The patients who were case managed by the CCM/CNS demonstrated significantly shorter length of stay and lower hospital charges than the patients who were not case managed.
Roglieri, 1997[28]	Design: RCT/CCT Jadad: 0 Setting: Ambulatory/outpt medical care Funding: Not reported	Sample size: unclear - C I-149 Disease: Single disease: Heart failure Severity: Unclear Race: Not reported Gender: Females	Disease management.	Outcomes: Utilization. Results: A comprehensive congestive heart failure (CHF) disease management program significantly reduced admission and readmission rates for patients with the pure CHF diagnosis.

ICU = Intensive Care Unit, I = Intervention group, C = Control group, MD = Physician, LOS = Length of Stay, RCT/CCT = Randomized Controlled Trial / Clinical Controlled Trial, DNR = Do Not Resuscitate, HRQoL = Health Related Quality of Life, ICU = Intensive Care Unit, outpt = Outpatient, QI = Quality Improvement, CHF = Chronic Heart Failure, Pt(s) = Patient(s)

Appendix E2. IS - Continuity/Coordination Interventions Evidence Table

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Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Baker, 2000[1]	Design: RCT/CCT Jadad: 2 Setting: Hospital (non-ICU) Funding: RWJ	Sample size: 767 Disease: Mixed disease: Not reported Severity: Advanced Race: Other Gender: Not reported	Clinical nurse specialist to assist in symptom control and facilitation of communication and decision-making.	Outcomes: Family CG satisfaction with communication, Family CG satisfaction with decision-making. Results: Sub-sample of the SUPPORT study. Used prospective cohort design to examine factors associated with family satisfaction with end of life care. Larger study was an RCT. RESULTS: 16% of respondents reported dissatisfaction w/ patient comfort and 30% reported dissatisfaction w/ communication and decision-making. Factors significantly associated w/ satisfaction w/ communication & decision-making: hospital site, whether death occurred during the index hospitalization (AOR 2.2, 95% CI, 1.3-3.9), and for pts who died following discharge: whether pt. received SUPPORT intervention (AOR 2.0, 1.2-3.2). For satisfaction w/ comfort, male surrogates reported less satisfaction (0.6, 0.4-1.0), surrogates who reported patients preferences were followed moderately to not at all had less satisfaction (0.2, 0.1-0.4), and surrogates who reported the patient's illness had greater effect on family finances had less satisfaction (0.4, 0.2-0.8).
SUPPORT, 1995[2]	Design: RCT/CCT Jadad: 5 Setting: Hospital (ICU) Funding: RWJ	Sample size: 9,105 seriously ill hospitalized adults w/ 6 mo. Mortality of 47% Disease: Mixed disease: Not reported	Telephone Palliative Care: telephone advice.	Outcomes: Family CG satisfaction with communication, Family CG satisfaction with decision-making, Physical symptoms other than pain. Results: No difference in outcomes on pain, communication, DNR, CPR, decision-making, and ADs in medical record.

RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CG = Care-Giver, AOR = Adjusted Odds Ration, CI =Confidence Interval, pt(s) = Patient(s), DNR = Do Not Resuscitate, CPR = Cardiopulmonary Resuscitation, ADs = Advance Directive, PCT = Palliative Care Team, HRQoL = Health Related Quality of Life, FU = Follow Up, ADL = Activities of Daily Living, CHF = Chronic Heart Failure, COPD = Chronic obstructive pulmonary disease, T = Treatment group, HBPC = Home Based Primary Care (VA specific), C = Control group, RN = Registered Nurse, EOL = End-of-Life

Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
		Severity: Advanced Race: Other Gender: Not reported		
Hanks, 1996[3]	Design: RCT/CCT Jadad: 1 Setting: Unclear Funding: Need article	Sample size: 261 (175 allocated to FULL PCT, 86 to telephone PCT) 2:1 randomization N=191 reassessed at 1 week Disease: Unclear Severity: Advanced Race: African-American and other Gender: Not reported	Palliative care unit in hospital w/ outpatient clinic and multidisciplinary palliative care consult team, Home-based primary care program in VA pts managed by team after discharge.	Outcomes: Pain, Physical symptoms other than pain, 2, Provider satisfaction, Family satisfaction with care, Patient satisfaction with care. Results: Significant improvements in symptoms, HRQoL, mood and "emotional bother" in FULL-PCT at 1 week, maintained over the 4 week FU. A smaller effect was seen in the "Telephone PCT"; there were no significant differences between the groups. Satisfaction w/ care in both groups w/ no significant difference between groups. No difference found between the two models of palliative care delivery.

RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CG = Care-Giver, AOR = Adjusted Odds Ration, CI =Confidence Interval, pt(s) = Patient(s), DNR = Do Not Resuscitate, CPR = Cardiopulmonary Resuscitation, ADs = Advance Directive, PCT = Palliative Care Team, HRQoL = Health Related Quality of Life, FU = Follow Up, ADL = Activities of Daily Living, CHF = Chronic Heart Failure, COPD = Chronic obstructive pulmonary disease, T = Treatment group, HBPC = Home Based Primary Care (VA specific), C = Control group, RN = Registered Nurse, EOL = End-of-Life

Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Hughes, 2000[4]	Design: RCT/CCT Jadad: 2 Setting: Home Funding: HRSA and Cooperative Studies Program, Dept. of VA	Sample size: N=1966, mean age: 70 years w/ 2 or more ADL limitations or a terminal illness, CHF or COPD. T=981=HBPC in community C=985= usual post-discharge care) Disease: Mixed disease: Not reported Severity: Advanced and moderate Race: Other Gender: Males	Hospital at Home Service-RN, REACH Intervention 1.	Outcomes: Family CG satisfaction with decision-making, Mental status, Psychiatric morbidity, CG problems/unmet needs. Results: No difference in pt/cg at baseline. Terminal pts improved significantly vs. controls on 8 HR-QoL scales (emotional, social, bodily pain, mental health, vitality, general health) with greatest improvement in emotional function. No difference in terminal pt. satisfaction over study period. CG to terminal pts showed significant HR-QoL improvements (P<.05 overall) vs. controls in all but 2 dimensions (vitality, general health) with greatest improvement in emotional function (13 point gain vs. controls); CG showed significant gains in satisfaction w/ pt care (P<.001) except for personal satisfaction item. A 8% reduction in hospitalizations and mean number of hospitalizations in intervention in first 6 months but not sustained to 12 months with 22% reduction in those w/ most disability. Pt./CG benefits accompanied by a 6.8% increase in total costs of care at 6 months and 12.1% increase at 12 months.

RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CG = Care-Giver, AOR = Adjusted Odds Ration, CI =Confidence Interval, pt(s) = Patient(s), DNR = Do Not Resuscitate, CPR = Cardiopulmonary Resuscitation, ADs = Advance Directive, PCT = Palliative Care Team, HRQoL = Health Related Quality of Life, FU = Follow Up, ADL = Activities of Daily Living, CHF = Chronic Heart Failure, COPD = Chronic obstructive pulmonary disease, T = Treatment group, HBPC = Home Based Primary Care (VA specific), C = Control group, RN = Registered Nurse, EOL = End-of-Life

Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Ringdal, 2002[5]	Design: RCT/CCT Jadad: 2 Setting: Hospital (ICU) Funding: Norwegian and Swedish Cancer Society, Norwegian Medical Assn Fund for Quality Improvement	Sample size: n=180 (112 T caregivers and 68 C caregivers) Disease: Single disease: Mixed cancer diagnoses Severity: Advanced Race: African-American and other Gender: Females	Palliative care unit in hospital w/ outpatient clinic and multidisciplinary palliative care consult team.	Outcomes: Place of death, Hospital utilization, 2. Results: Satisfaction with care was measured in 49% of caregivers in the intervention group and 36% of caregivers in the control group. Reasons for refusal not recorded due to confidentiality concerns. Respondents were primarily women, median age: 56 years (57% under 60 years of age), most were spouses. No statistical significant differences between T and C at baseline. Place of death: more T pts died at home (27% vs. 14%) (not significant); most respondents reported being very satisfied or satisfied w/ care (right skewed); some lower satisfaction w/ issues related to time to diagnosis, referral to specialists, symptom management, information provided; T cg's had significantly higher satisfaction scores than C. Intervention generally improved satisfaction among close family members. Intervention stressed information on prognosis and planning ahead, pain and symptom management, family conferences, availability of physicians to family, and systematic symptom assessment (information and attention domains). Intervention allowed more pts able to die at home.

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Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Ringdal, 2004[6]	Design: Intervention, comparison group Jadad: 3 Setting: Hospital (ICU) Funding: Norwegian and Swedish Cancer Society, Norwegian Medical Assn Fund for Quality Improvement	Sample size: N=517 (285 in T 232 in C) in 2 sites Disease: Single disease: Mixed cancer diagnoses Severity: Advanced Race: African-American and other Gender: Females	Palliative care unit in hospital w/ outpatient clinic and multidisciplinary palliative care consult team.	Outcomes: Family CG satisfaction with decision-making. Results: Five of eight subscales of Health-related quality of life scores decline (RP, VT, SF, RE, & MH) to T 4 (1-2 months after patient's death) and return to baseline by the end of the study. Scores for PF, BP, & GH showed smaller and almost linear decline. Low response rates in both groups undermines the findings in this study.

RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CG = Care-Giver, AOR = Adjusted Odds Ration, CI =Confidence Interval, pt(s) = Patient(s), DNR = Do Not Resuscitate, CPR = Cardiopulmonary Resuscitation, ADs = Advance Directive, PCT = Palliative Care Team, HRQoL = Health Related Quality of Life, FU = Follow Up, ADL = Activities of Daily Living, CHF = Chronic Heart Failure, COPD = Chronic obstructive pulmonary disease, T = Treatment group, HBPC = Home Based Primary Care (VA specific), C = Control group, RN = Registered Nurse, EOL = End-of-Life

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First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Walsh, 2003[7]	Design: Intervention, comparison group Jadad: 1 Setting: Home Funding: University of Miami School of Nursing Dean's Award	Sample size: n=9 Disease: Single disease: Mixed cancer diagnoses Severity: Advanced Race: Other Gender: Not reported	RN care coordination in the community.	Outcomes: CG Burden, Depression, Social support, Reaction at EOL: panic, blame, detachment, disorganization and despair. Results: CG depression scores decreased from a mean of 20.2 +/- 9.25 to 12.8 +/-9.57. However, CG's felt more burdened (38.5 +/- 2.38 POST vs. 93.2 +/-5.93 PRE). Disorganization decreased, CGs reported less dispair. No change in panic, bloame, detachment, personal growth, or social support.

RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CG = Care-Giver, AOR = Adjusted Odds Ration, CI =Confidence Interval, pt(s) = Patient(s), DNR = Do Not Resuscitate, CPR = Cardiopulmonary Resuscitation, ADs = Advance Directive, PCT = Palliative Care Team, HRQoL = Health Related Quality of Life, FU = Follow Up, ADL = Activities of Daily Living, CHF = Chronic Heart Failure, COPD = Chronic obstructive pulmonary disease, T = Treatment group, HBPC = Home Based Primary Care (VA specific), C = Control group, RN = Registered Nurse, EOL = End-of-Life

Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Addington-Hall, 1992[8]	Design: RCT/CCT Jadad: 3 Setting: Home Funding: UK Medical Research Council	Sample size: 554 referred, (203 with evaluable outcomes), 35% (n=194) died/too ill to interview, 7% (40) moved, 39 (7%) declined to be interviewed. N=281 (51% of initial sample) at baseline 203 (72%) =1 FU. T=104, C=99. Disease: Single disease: Mixed cancer diagnoses Severity: Advanced Race: Other Gender: Not reported	REACH Intervention 1.	Outcomes: Family CG satisfaction with communication, Family satisfaction with care, Time from Final follow-up to death, Place of death, Need for more help. Results: Time between last FU and death did not differ significantly between groups. No significant difference in symptom experience (except T more likely to suffer from vomiting than C, P=.05). Few statistically significant differences in severity of symptoms, concern about symptoms, or effectiveness of treatments. No group differences in type of analgesics taken, nor in proportions of patients taking anti-emetics, laxatives, antidepressants, sedatives, or anxiolytics. A few significant differences found in CG reports of type, severity, and effectiveness of treatment of pt's symptoms in last week of life: T pts more likely to report pt symptoms (cough, constipation) and less likely to report treatment effectiveness for anxiety. No differences between groups on hospital anxiety and depression scale, social support, and quality of life, ADL assistance needs, unmet needs, financial impact, use of social services, and satisfaction w/ care. Overall, few differences found in symptoms and symptom control, service provision, coordination, and satisfaction, and social and psychological support between T and C. Intervention had no discernable impact.

RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CG = Care-Giver, AOR = Adjusted Odds Ration, CI =Confidence Interval, pt(s) = Patient(s), DNR = Do Not Resuscitate, CPR = Cardiopulmonary Resuscitation, ADs = Advance Directive, PCT = Palliative Care Team, HRQoL = Health Related Quality of Life, FU = Follow Up, ADL = Activities of Daily Living, CHF = Chronic Heart Failure, COPD = Chronic obstructive pulmonary disease, T = Treatment group, HBPC = Home Based Primary Care (VA specific), C = Control group, RN = Registered Nurse, EOL = End-of-Life

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First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Grande, 2000[9]	Design: RCT/CCT Jadad: 0 Setting: Home Funding: Elizabeth Clark Charitable Trust and NHS R&D Primary / Secondary Care Interface Programme	Sample size: N=198 (86% of 229 referred pts) and 144 CGs (73% of 198 referred CGs) Disease: Predominately one disease: Mixed cancer Severity: Advanced Race: Other Gender: Not reported	REACH Intervention 2.	Outcomes: Family CG satisfaction with communication, Family satisfaction with care, Depression, Pt functional status, Place of death. Results: There was no clear evidence that the hospital-at-home service for terminally ill patients increased the likelihood of remaining at home during the final 2 weeks of life. However, the service was associated with fewer GP out of hurs visits. All respondent groups rated CHAH favorably when compared to standard care but emphasized different aspects (GP, RN, CG respondents). RN's rated services as a better than standard care in terms of adequacy of night care and support for the carer, GPs in terms of reduction of anxiety and depression, and CGs in terms of control of pain and nausea. Overall, service provided better quality of care.

RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CG = Care-Giver, AOR = Adjusted Odds Ration, CI =Confidence Interval, pt(s) = Patient(s), DNR = Do Not Resuscitate, CPR = Cardiopulmonary Resuscitation, ADs = Advance Directive, PCT = Palliative Care Team, HRQoL = Health Related Quality of Life, FU = Follow Up, ADL = Activities of Daily Living, CHF = Chronic Heart Failure, COPD = Chronic obstructive pulmonary disease, T = Treatment group, HBPC = Home Based Primary Care (VA specific), C = Control group, RN = Registered Nurse, EOL = End-of-Life

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First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Gitlin, 2003[10]	Design: RCT/CCT Jadad: 2 Setting: Home Funding: NIA & NINR funding	Sample size: 1,222 racially & ethnically diverse cg Disease: Single disease: Dementia Severity: Other Race: Other Gender: Not reported	REACH Intervention 3.	Outcomes: Depression, CG Burden. Results: REACH designed to examine the feasibility and effectiveness of multiple intervention approaches for family caregivers to pts w/ dementia. Each site conducted as a RCT. The combined effects of active interventions vs. control at 6 months on burden and CG depression. Using meta-analysis, the pooled T effect fro burden was statistically significant p=.022, though the difference was small. Overall, CGs across REACh sites showed lower values in burden w/ behavior problems of pts vs. controls. There were no statistically significant effects for any one intervention for burden although all scores were in hypothesized direction. In contrast to burden, the pooled treatment effect for CES-D was not statistically significant. Modest intervention effect.
Smeenk, 1998[11]	Design: Intervention, comparison group Jadad: 2 Setting: Home Funding: National Committee of Chronic Diseases and the Scientific Fund of the Catharina Hospital, Eindhoven	Sample size: 45 (T=34 C=11) Disease: Single disease: Mixed cancer diagnoses Severity: Advanced Race: Not reported Gender: Not reported	Transmural home care intervention	Outcomes: Mental status. Results: The intervention contributed positively to the direct caregivers quality of life at time 2 (p=<.05) with improvements on fear, general well-being, and loneliness scales. Improvement at (p=<.05) was due to improvements on the SIP and fear scales compared with standard care.

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Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Bucher, 2001[12]	Design: Intervention, comparison group Jadad: 0 Setting: Home Funding: The Open Society Institute, Project Death in America	Sample size: 103 (49/49 Ca patients and 49/54 Ca pt. Caregivers) Disease: Single disease: Mixed cancer diagnoses Severity: Unclear Race: Other Gender: Not reported	Behavior Care.	Outcomes: Problem solving score, Problem solving ability, CG appraisal of pt behavior problems, Anxiety. Results: There was no statistically significant difference in perception of ability to provide care after the intervention for either patients or caregivers. However, a significant difference in feeling informed about community resources for both patients and caregivers was found after intervention. Caregivers significantly increased their total problem solving score (.05) after the intervention.

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Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Burgio, 2003[13]	Design: Intervention, comparison group Jadad: 3 Setting: Home Funding: NIA & NINR funding - Alabama REACH	Sample size: 118 of 140 caregivers to dementia patients (70 White 48 African-American) completed 6 mo. FU Disease: Single disease: Dementia Severity: Unclear Race: Other Gender: Females	Enhanced Care.	Outcomes: Pt behavior problems, Social support, Depression, Anxiety, Desire to institutionalize. Results: White caregivers were more likely to be older, report higher household income, and be spouses while African American caregivers more likely to be non-spouses. African American care receivers had lower educational attainment and demonstrated greater cognitive impairment than White care receivers. White caregivers showed more improvement in the minimal support control condition and African American caregivers showed the greatest improvements in the skills training condition. A significant treatment by race by relationship interaction was found with the largest decreases in the number of problem behaviors found for White spouses in the MS condition and for African American spouses in the ST condition.
Burns, 2003[14]	Design: RCT/CCT Jadad: 2 Setting: Ambulatory/outpt medical care Funding: NIA & NINR funding - Memphis REACH	Sample size: 76 of 167 caregiver-pt dyads completed 24 FU Disease: Single disease: Dementia Severity: Unclear Race: Other	Structural Ecosystems Therapy (SET), SET + Computer Telephone Integrated System (CTIS).	Outcomes: CG well-being, Depression, Pt behavior problems. Results: Significant differences in general well-being were found by group and time (p=.045). BC only had significantly worse general well-being and a trend toward increased risk of depression. Both groups improved on bother associated with care recipient. BC had significantly greater

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Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
		Gender: Females		distress at FU.
Eisdorfer, 2003[15]	Design: Intervention, comparison group Jadad: 2 Setting: Ambulatory/outpt medical care Funding: NIA & NINR funding - Miami REACH	Sample size: 225 dementia patient caregivers (114 Cuban American and 111 White American) Disease: Single disease: Dementia Severity: Unclear Race: Other Gender: Not reported	Environmental Skill-Building Program (ESP), Automated Telecare System (TLC).	Outcomes: Not reported. Results: Caregivers in the combined family therapy group (SET+CTIS) experienced a significant reduction in depressive symptoms at 6 months. The combined intervention was most effective at 18 months for Cuban American husband and daughter caregivers.
Gitlin, 2003[16]	Design: RCT/CCT Jadad: 3 Setting: Home Funding: NIA & NINR funding - Philadelphia REACH	Sample size: 190 of 255 dementia patient caregivers at 6 mo. FU Disease: Single disease: Dementia Severity: Unclear Race: African-American, Hispanic and other Gender: Not reported	The ESP (Environmental Skill-Building Program).	Outcomes: Costs, CG Depression, CG Mastery, Stress reduction, CG enhancement. Results: Intervention caregivers reported less upset with memory-related behaviors, less need for assistance from others, and better affect. Intervention spouses reported less upset with disruptive behaviors; men reported spending less time in daily oversight; women reported less need for help from others, better affect, and enhanced management ability, overall well-being, and mastery relative to controls.

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Appendix E3. IS - Family/Caregiver Concerns Interventions Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Mahoney, 2003[17]	Design: RCT/CCT Jadad: 2 Setting: Home Funding: NIA & NINR funding - Boston REACH	Sample size: 100 (49 in T, 51 in C) Disease: Single disease: Dementia Severity: Unclear Race: Other Gender: Females	A computer-mediated automated interactive voice response intervention.	Outcomes: CG well-being, CG Bother, Mastery. Results: No significant main effect of the intervention on bother, depression, or anxiety. Participants w/ low-mastery at baseline experienced a greater decline in bother scores (p=.04), depressive symptoms p=.007), and anxiety (.01). No difference for high-mastery groups.

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Appendix E5. IS - Symptoms Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Booth, 1996[1]	Design: RCT/CCT Jadad: 2 Setting: Hospice Funding: Dame Cicely Saunders Research Fund & Help the Hospices	Sample size: 45 Disease: Predominately one disease: Lung cancer Severity: Advanced Race: Other Gender: Not reported	Oxygen, Air.	Outcomes: Dyspnea rating using VAS, Modified Borg scale, SaO2 - O2 saturation. Results: Both oxygen and air had a significant effect in reducing dyspnea at rest in patients with advanced cancer.
Bruera, 1993[2]	Design: RCT/CCT Jadad: 2 Setting: Hospital (non-ICU) Funding: Not reported	Sample size: 14 Disease: Predominately one disease: Lung cancer Severity: Advanced Race: Other Gender: Not reported	Oxygen, Air.	Outcomes: Dyspnea rating using VAS. Results: Oxygen was better than air for treatment of dyspnea, as measured by visual analogue scale and patient preference.

RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, VAS = Visual Analogue Scale, ICU = Intensive Care Unit, outpt = Outpatient, TDS = Transdermal Delivery System

Appendix E5. IS - Symptoms Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Jack, 2003[3]	Design: Intervention, comparison group Jadad: 1 Setting: Hospital (non-ICU) Funding: Not reported	Sample size: 100 Disease: Mixed disease: Mixed disease Severity: Unclear Race: Other Gender: Not reported	Hospital palliative care team, Usual care.	Outcomes: Anorexia, Nausea, Insomnia, Constipation, Pain. Results: The intervention groups had a greater improvement in all their symptoms, particularly for pain and anorexia.
Latimer, 1998[4]	Design: RCT/CCT Jadad: 2 Setting: Ambulatory/outpt medical care Funding: Hamilton Civic Hospitals	Sample size: 46 Disease: Unclear: Mixed disease Severity: Unclear Race: Other Gender: Not reported	Patient Care Traveling Record.	Outcomes: Pain, Mood, Health care utilization, Patient satisfaction. Results: 21 patients completed the trial. With the exception of those aged 65+, patients using the Patient Care Traveling Record reported decreased levels of uncertainty on follow-up. There was no additional use of health care services, no differences in mood states, pain relief, or satisfaction with health care.

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Appendix E5. IS - Symptoms Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Mazzacato, 1999[5]	Design: RCT/CCT Jadad: 2 Setting: Hospital (non-ICU) Funding: Not reported	Sample size: 10 Disease: Predominately one disease: Lung cancer Severity: Advanced Race: Other Gender: Not reported	Subcutaneous morphine sulfate, Placebo.	Outcomes: Dyspnea rating using VAS, Modified Borg scale, Pain rating scale using VAS, Somnolence, Anxiety. Results: Morphine was effective for cancer dyspnea, and did not compromise respiratory function at the dose used.
Mercadante, 2002[6]	Design: RCT/CCT Jadad: 3 Setting: Home health care Funding: Not reported	Sample size: 50 Disease: Mixed disease: Mixed cancer diagnoses Severity: Advanced Race: Other Gender: Not reported	Morphine, Keterolac.	Outcomes: Pain, Nausea, Vomiting, Daytime drowsiness, Confusion, Constipation, Gastric discomfort. Results: Patients who received ketorolac in addition to morphine showed a better analgesia after a week in comparison to the group treated with morphine only. Thereafter, morphine escalation was slower and the maximum morphine dose was lower in the group treated with ketorolac. The incidence and the severity of gastric discomfort were more evident in patients treated with ketorolac, while constipation was significantly increased in patients who received morphine only.

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First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Rabow, 2004[7]	Design: Intervention, comparison group Jadad: 3 Setting: Ambulatory/outpt medical care Funding: Robert Wood Johnson Foundation	Sample size: 90 Disease: Mixed disease: Mixed disease Severity: Advanced Race: Other Gender: Not reported	Outpatient Palliative Medicine Consultation, Usual care.	Outcomes: Degree dyspnea interferes, Frequency dyspnea limits activities, Sleep, Spirituality, Health care costs, Pain, Quality of life, Anxiety, Depression, Patient satisfaction. Results: The intervention group patients had less dyspnea and anxiety, and improved sleep quality and spiritual well being, but no change in pain, depression, quality of life or satisfaction with care.
Schofield, 2003[8]	Design: RCT/CCT Jadad: 3 Setting: Hospice Funding: Wilkes Fellowship	Sample size: 26 Disease: Mixed disease: Mixed disease Severity: Advanced Race: Other Gender: Males	Snoezelen (multisensory environment), Quiet room.	Outcomes: Anxiety, Depression. Results: A significant reduction in anxiety was seen in the experimental group, but no changes were observed in any of the quality of life subscales.

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Appendix E5. IS - Symptoms Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Simmons, 2002[9]	Design: RCT/CCT Jadad: 1 Setting: Nursing home Funding: NIH/NIA, Claude Pepper OAIC	Sample size: 51 Disease: Mixed disease: Mixed disease Severity: Unclear Race: Other Gender: Females	Exercise and toileting program, Usual care.	Outcomes: Geriatric pain measure (13-item), Physical mobility. Results: No significant changes in pain reports were attributable to exercise despite significant improvements in physical performance.
Soden, 2004[10]	Design: RCT/CCT Jadad: 5 Setting: Unclear Funding: Foundation for Integrated Medicine	Sample size: 42 Disease: Mixed disease: Mixed disease Severity: Advanced Race: Other Gender: Females	Usual care, Massage with aromatherapy, Massage alone.	Outcomes: Pain rating scale using VAS, Verran and Snyder-Halpern sleep scale, Hospital Anxiety and Depression scale, Rotterdam Symptom Checklist. Results: No significant long-term benefits of aromatherapy or massage in terms of pain control, anxiety, or quality of life. However, sleep scores improved significantly in both the massage and the combined massage / aromatherapy group. Depression scores were reduced in the massage group.

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First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Wilkinson, 1999[11]	Design: RCT/CCT Jadad: 3 Setting: Hospice Funding: Not reported	Sample size: 103 Disease: Mixed disease: Mixed cancer diagnoses Severity: Advanced Race: Other Gender: Females	Massage with aromatherapy, Massage alone.	Outcomes: Rotterdam Symptom Checklist, Patient preference of treatment, Quality of life, Activity. Results: Massage with or without essential oils reduced levels of anxiety. The addition of essential oil resulted in improvement in physical and psychological symptoms, as well as quality of life.
Addingon-Hall, 1992[12]	Design: RCT/CCT Jadad: 2 Setting: Ambulatory/outpt medical care Funding: Medical Research Council	Sample size: 554 Disease: Mixed disease: Mixed cancer diagnoses Severity: Advanced Race: Other Gender: Not reported	Palliative care coordination, Usual care.	Outcomes: Time to death, Pain, Vomiting, Nausea, Constipation, Insomnia, Anxiety, Depression, Loss of appetite, Difficulty swallowing, Dyspnea, Cough, Itchy skin, Diarrhea, Incontinence/retention, Patient satisfaction, Caregiver burden, Health care utilization Results: Few differences between groups were significant. Coordination group patients were less likely to suffer from vomiting, more likely to report effective treatment for it, and less likely to be concerned about itchy skin.

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Appendix E5. IS - Symptoms Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Grande, 2000[13]	Design: RCT/CCT Jadad: 3 Setting: Home health care Funding: Elizabeth Clark Charitable Trust	Sample size: 262 Disease: Mixed disease: Mixed disease Severity: Advanced Race: Other Gender: Not reported	Usual care, Cambridge Hospital at home service.	Outcomes: Patient satisfaction, Pain, Vomiting, Nausea, Constipation, Diarrhea, Dyspnea, Anxiety, Depression, Health care utilization, Caregiver satisfaction. Results: While the Cambridge hospital at home service was not found to increase the likelihood of remaining at home during the final two weeks of life, it appeared to be associated with better quality home care.
Rogers, 1999[14]	Design: Intervention, comparison group Jadad: 0 Setting: Nursing home Funding: NINR	Sample size: 84 Disease: Mixed disease: Mixed disease Severity: Unclear Race: Other Gender: Not reported	Usual care, Skill elicitation, Habit training.	Outcomes: Functional status, Disruptive behavior. Results: Compared with usual care, during skill elicitation participants increased the proportion of time engaged in non-assisted and assisted dressing significantly and increased their overall participation in activities of daily living, with a decrease in disruptive behavior. These functional gains were demonstrated within 5 days of initiating the behavioral rehab intervention and maintained for 3 weeks during habit training.
Rovner, 1996[15]	Design: RCT/CCT Jadad: 3 Setting: Nursing home Funding: NIMH	Sample size: 118 Disease: Single disease: Dementia Severity: Unclear Race: Other Gender: Females	A.G.E. Dementia Care program, Usual care.	Outcomes: Disruptive behavior, Use of anti-psychotics, Restraints, Participation in activities. Results: Controls were more than twice as likely as intervention patients to receive anti-psychotics, to be restrained during activity times and to be restrained on nursing units.

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First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Sulzer, 2001[16]	Design: RCT/CCT Jadad: 2 Setting: Hospital (non-ICU) Funding: NIMH	Sample size: 28 Disease: Single disease: Dementia Severity: Moderate Race: Other Gender: Not reported	Haloperidol, Trazodone.	Outcomes: Delusion Scale, Hamilton Depression Rating Scale, Cohen-Mansfield Agitation Inventory. Results: Agitation scores improved in each treatment group over the 9 weeks of treatment.
Weiner, 1999[17]	Design: RCT/CCT Jadad: 2 Setting: Unclear Funding: Not reported	Sample size: 20 Disease: Single disease: Heart failure Severity: Moderate Race: Other Gender: Males	Specific inspiratory muscle training, Placebo.	Outcomes: Spirometry, Respiratory muscle strength, Inspiratory muscle endurance, 12-minute walk, Exercise tolerance test, Dyspnea index. Results: Patients in the training group showed an increase in inspiratory muscle strength, PImax, and endurance.

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Appendix E5. IS - Symptoms Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Manfredi, 2003[18]	Design: Intervention, without comparison group Jadad: 0 Setting: Nursing home Funding: New York State Dept. of Health, Bureau of Long Term Care Services Purdue Pharma	Sample size: 47 Disease: Single disease: Dementia Severity: Advanced Race: Other Gender: Females	Long-acting opioid, Placebo.	Outcomes: Cohen-Mansfield Agitation Inventory, Adverse events. Results: Among the 13 patients >=85 years old the agitation level at the end of the opioid phase was significantly lower than at the end of the placebo phase.
Sittl, 2003[19]	Design: RCT/CCT Jadad: 3 Setting: Ambulatory/outpt medical care Funding: Grunenthal GmbH	Sample size: 157 Disease: Mixed disease: Mixed disease Severity: Advanced Race: Other Gender: Not reported	Transdermal delivery system for buprenorphine, 35.0 ug/h, Transdermal delivery system for buprenorphine, 52.5 ug/h, Transdermal delivery system for buprenorphine, 70.0 ug/h, Placebo.	Outcomes: Pain, Intake of extra doses of analgesics, Pain intensity. Results: Buprenorphine TDS was associated with significantly higher response rates than was placebo at the 35.0 and 52.5 ug/h dosages, and a numerically higher response rate at 70.0 ug/h, although this difference did not reach statistical significance.

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First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Smith, 2002[20]	Design: RCT/CCT Jadad: 3 Setting: Ambulatory/outpt medical care Funding: Medtronic, Inc.	Sample size: 202 Disease: Mixed disease: Mixed disease Severity: Advanced Race: Other Gender: Not reported	Implantable intrathecal drug delivery system and comprehensive medication management, Comprehensive medication management.	Outcomes: Pain rating scale using VAS, Adverse events, Common toxicity criteria. Results: Implantable intrathecal drug delivery systems (IDDSs) improved clinical success in pain control, reduced pain, significantly relieved common drug toxicities, and improved survival.
Detmar, 2003[21]	Design: RCT/CCT Jadad: 2 Setting: Ambulatory/outpt medical care Funding: Dutch Cancer Society	Sample size: 214 Disease: Mixed disease: Mixed disease Severity: Unclear Race: Other Gender: Females	HRQL questionnaire, Usual care.	Outcomes: Patient/physician communication Results: The HRQL-related issues were discussed significantly more frequently in the intervention than in the control group. Physicians in the intervention group identified a greater percentage of patients with moderate-to-severe health problems in several HRQL domains than did those in the control group. All physicians and 87% of the patients believed that the intervention facilitated communication and expressed interest in its continued use.

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First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Jordoy, 2002[22]	Design: RCT/CCT Jadad: 3 Setting: Unclear Funding: Norwegian Cancer Society, Norwegian Medical Association Fund for Quality Improvement, Swedish Cancer Society	Sample size: 434 Disease: Mixed disease: Mixed disease Severity: Advanced Race: Other Gender: Not reported	Palliative Medicine Unit program, Usual care.	Outcomes: Quality of life, Impact of event scale. Results: Neither on pain, emotional and physical functioning, and psychologic distress, nor on any other HRQL dimension did the scores of patients in the intervention program show improvement in comparison with controls.
Bruera, 1994[23]	Design: Intervention, comparison group Jadad: 0 Setting: Hospital (non ICU) Funding: Not reported	Sample size: 10 Disease: Mixed disease: Mixed disease Severity: Advanced Race: Other Gender: Not reported	Morphine, Placebo.	Outcomes: Dyspnea, SaO2 - O2 saturation, Respiratory rate, Pain. Results: Intermittent injections of morphine are safe and effective for the management of dyspnea in terminal cancer.
Gottlieb, 1999[24]	Design: RCT/CCT Jadad: 2 Setting: Ambulatory/outpt medical care Funding: National Institute on Aging, Claude D. Pepper Older Americans Independence Center	Sample size: 33 Disease: Single disease: Heart failure Severity: Advanced and moderate Race: Other Gender: Males	Usual care, Exercise.	Outcomes: Six-minute walk, Depression, Quality of life, Peak VO2, Activities of daily living. Results: Elderly patients with severe heart failure can safely exercise, with an improvement in peak exercise tolerance. However, not all patients will benefit, and daily energy expenditure and quality of life do not improve to the same extent as peak exercise.

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Appendix E5. IS - Symptoms Evidence Table

First Author Year ID	Study Characteristics	Population	Interventions	Outcomes Results
Sarna, 1998[25]	Design: RCT/CCT Jadad: 2 Setting: Ambulatory/outpt medical care Funding: American Cancer Society	Sample size: 48 Disease: Single disease: Lung cancer Severity: Advanced Race: Other Gender: Not reported	Usual care, Structured symptom assessment.	Outcomes: Nausea, Dyspnea, Pain frequency, Pain severity, Bowel function, Sleep, Fatique. Result: High score in depression and more functional limitation were related to higher levels of overall distress. Subjects with more depression and greater functional limitations had greater symptom distress.
Stephenson, 2000[26]	Design: Intervention, comparison group Jadad: 1 Setting: Hospital (non ICU) Funding: Not reported	Sample size: 23 Disease: Mixed disease: Mixed disease Severity: Unclear Race: Other Gender: Not reported	Foot reflexology, Usual care.	Outcomes: Pain, Anxiety. Results: Following the foot relexology intervention, patients with breast and lung cancer experienced a significant decrease in anxiety.Patients with breast cancer experienced a significant decrease in pain on one of three measures.
Abernethy, 2003[27]	Design: RCT/CCT Jadad: 5 Setting: Ambulatory/outpt medical care Funding: Flinders Medical Centre Foundation, Doris Duke Charitable Foundation	Sample size: 48 Disease: Predominately one disease: Advanced chronic lung disease Severity: Advanced Race: Other Gender: Not reported	Morphine, Placebo.	Outcomes: Dyspnea rating using VAS, Side effects, Sleep, Performance on physical exertion. Results: In a community setting, sustained release morphine (oral) at low dosage provided significant improvement in refractory dyspnea.

RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, VAS = Visual Analogue Scale, ICU = Intensive Care Unit, outpt = Outpatient, TDS = Transdermal Delivery System

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Appendix F

Table F1. Technical Expert Panel members

Name	Institution
Kathleen Folye, M.D	Memorial Sloan-Kettering Cancer Center
Irene Higginson, M.D.	Kings College London
Margaret Heitkemper, PhD, RN, FAAN	University of Washington
Marianne Matzo, PhD, APRN, BC, GNP, FAAN	University of Massachusetts-Worcester
Diane Meier, M.D.	Mount Sinai School of Medicine
Richard Payne, M.D.	Duke University Divinity School
Joan Teno, M.D., M.S.	Brown Medical School

Table F2. Peer Reviewers

Name	Institution
Robert Arnold, M.D.	University of Pittsburgh
Eduardo Bruera, M.D.	University of Texas
Betty Rolling Ferrell, PhD, RN	City of Hope National Medical Center and Beckman Research Institute
Rolfe Sean Morrison, M.D.	Mount Sinai School of Medicine
Virginia P. Tilden, DNSc, RN	University of Nebraska Medical Center
Susan W. Tolle, M.D.	Oregon Health Sciences University

Appendix G. Cambridge Ballot

Southern California Evidence-based Practice Center End of Life Care and Outcomes Project

Matrix for Prioritizing Outcomes

We have developed a matrix of principles vs. outcomes to help us in our decision making process about which outcomes to prioritize. To score this modified Cambridge Ballot, first score each "cell" (0-10,10 being the most important), and then give a summary hierarchical ranking of each item.

When you have completed it, please fax to Cony Rolon, RAND (fax: 310-451-6930).

	1. Relative Importance at EOL (0-10)	2. Relationship to Patient Experience (0-10)	3. Feasibility (0-10)	4. Relevance to care and policy (0-10)	5. Recent Reviews (0-10)	6. Differences by Selected Diseases (0-10)	7. Modifiability (0-10)	**Total [Col 1-7] (0-70)**	**Overall Rank* (1-11)**
Pain									
Affective Symptoms									
Other symptoms									
QOL / HRQOL									
Spiritual / existential wellbeing									
Caregiver/ family well-being and satisfaction									
Provider communication									
Advance care planning									
Continuity and coordination									
Utilization of Services									
Site of Death									

*Rank each outcome hierarchically where 1 is the most important outcome and 11 is the least important.

Appendix H1. Methodological Issues in Measurement

Our literature review also identified a number of articles that dealt with specific methodological issues that are prominent in end-of-life care research. Our search strategy captured challenges to measurement in end-of-life care during the undertaking of identifying validated measures. Two recently published expert opinion compilations provide additional data: a series of 6 articles in the Journal of Palliative Medicine [1-6] and 3 articles in a special issue of the Gerontologist.[7-9] Also, an on-line symptom research text provides an review of methodological challenges and research approaches in this field.(Interactive Textbook on Clinical Symptom Research. Eds. Max MB and Lynn J. http://symptomresearch.nih.gov/tablecontents.htm)

Ten articles looked at the concordance between raters or proxy determinations. One study found that inter-rater kappa values were poor for pain, anxiety, and depression. A number of articles reported that current patient-proxy ratings had higher agreement with each other than with relatives' retrospective ratings, and that knowledge ratings were better matched; overall agreement of family proxy evaluations to patient evaluation is moderate. [10,11, 12]An examination of patient-caregiver congruence in QOL assessment in newly-diagnosed lung cancer patients reported large differences. Low congruence was related to low patient-related self-efficacy, high patient psychological distress, and caregiver strain.[13] Another study reported that family members were better proxies than staff for symptoms.[14] A study of patient-proxy perception of the quality of care found that agreement was best when both lived together and shared everyday experiences.[15] A comparison of patient and surrogate satisfaction ratings found low correlation.[16] A study between patients, physicians, and proxy demonstrated that significant others and physicians had poor agreement on symptoms experience in the last week of life with kappa values across multiple symptoms <= 0.4.[17] Sulmasy, et. al. explored the accuracy of substituted judgments by proxy compared to patients with terminal diseases with hypthetical scenarios and explored associations that affected the congruence.[18] On average, agreement was 66% and was increased if patient and surrogate had spoken about end-of-life issues (OR 1.9), if patient had private insurance (OR 1.5), and if the patient was more educated (OR 1.7). Clipp and George explored the reliability of spouse informants finding that caregivers agreed with patients on objective but not subjective measures of functioning and viewed patients' functioning more negatively than patients in domains such as depression and fear of the future.[19]

Agreement between professional health care providers and patients revealed similar shortcomings. A comparison of patient and nurse assessments reported good agreement for symptom control but differences for anxiety, personal thoughts, practical matters, and information received.[20] Another comparison of patients and nurses found low correlations between patients and providers and symptoms; nurses tended to rate patients' symptoms more highly than patients rated their own symptoms.[21] An article evaluating the number of symptom ratings needed for reliability found that 3 raters on 1 occasion or 2 raters on 2 occasions were needed.[22] An evaluation of patient-physician concordance reported that patients and clinicians disagreed in 26% of cases about whether end-of-life communication had occurred.[23] Agreement for symptoms assessed by the Rotterdam

Symptom Checklist in over 33,000 cases between physician and patients showed 78% agreement with the highest discordance in severity assessment where providers demonstrated a consistent bias toward underestimation.[24] Fatigue showed marked omissions by nurse recognition.[25] Another study documented that proxy and physician reports agree with patient self-reports for prevalence of chronic diseases but that proxy respondents missed certain diagnoses in after-death interviews.[17] Three articles compared the usefulness of different tools. A comparison of FACT-G, Spitzer QLI, ECOG-PS, VAS, and a 5 point word anchor categorical scale concluded that a single-item global measure of quality of life was as effective as the multidimensional ones (although QOL didn't change much during the study).[26] One study evaluated the content validity of EORTC QLQ-C30, ESAS, POS, MQOL, and MSAS by comparing the content of each to the symptoms and problems noted in records of admitted palliative cancer patients. They found that the EORTC QLQ-C30 covered 10 and the MSAS 11 of the 12 most frequent problems.[27] One article described a surgical palliative workgroup that identified validated measures which were potentially applicable to the palliative population.[28]

One article evaluated the use of instruments designed for healthier populations for use at the end of life. An evaluation of a needs assessment found that some items did not apply for hospice patients (such as work issues).[29]

Cassarett, et. al. compared 2-week post-death survey to 6-week post-death survey timing and found no differences in response rates or self-report of distress.[30]

Two articles compared thresholds with different instruments. A study evaluating the impact of measuring somatic symptoms when diagnosing depression in the terminally ill reported that this inflated the rate of diagnosis only with a low-threshold approach to diagnosing depression.[31] Another study comparing pain intensity markers, the pain relief scale, a pain satisfaction scale, and 3 pain management indices reported that the proportion of inadequately treated patients ranged from 16-91% depending on the measure.[32]

Five studies evaluated feasibility issues in assessing patients near the end of life. One study using a number of scales reported that 66% of eligible palliative care patients were able to participate with significant help, although much data was incomplete.[33] One group devised a 3-word choice to use instead of a numerical scale.[14] One study reported that missing data was an indicator of more severe illness.[34] One study described methods for increasing sample size for proxy reports in after death studies with extensive case-finding strategies.[35] Hopwood, et. al. report limitations in QOL questionnaires in lung and head and neck cancer trials including logistical problems with patients being too ill to complete evaluations, organizational problems administering questionnaires, and differential quality in administration of measures between type of staff member.[36]

A number of articles looked at potential sources of bias introduced by methodology in end-of-life and palliative care research. One study reported an assessment bias that pain was much more likely to be documented on the MDS in nursing home residents enrolled in hospice.[37] Another study examined selection bias with cluster randomization as is often done when comparing different programs or centers of care and reported differences in demographic characteristics and diseases representations that were attributable to the specialty mix of the groups.[38]

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Appendix H2. VERSION
TABLE H-2. Reliability and Validity Data for Measures Identified

Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Agitation Distress Scale[1] Domain(s): Emotional symptoms	Mixed cancer 6-item; clinician-rating scale	Principal components analysis reveal only 1 component; significantly correlated with agitation items on MDAS & DRS (0.61) but scale was not correlated with cognitive items Cronbach's 0.91; inter-rater kappa 0.72-1.0
Anticipatory Grief Scale[2 Toolkit] Domain(s): Grief and bereavement	Mixed diseases 27 items; interviewer or self-administered	See Toolkit for details See Toolkit for details
"Are you depressed?[3]" Domain(s): Emotional symptoms	Mixed diseases Single-item screening for depression	Correctly identified diagnosis of depression in all patients Kappa=0.76 between interviewers and observers
Barthel Index [2 Toolkit] Domain(s): Functional status	Mixed diseases 10 item; self-administered and a 15 item version that is medical professional administered	see Toolkit for details see Toolkit for details
Bereavement Phenomenology Questionnaire (BPQ)[4] Domain(s): Grief and bereavement	Mixed diseases 22-items, 4 point Likert scale	Discriminate MANOVA showed decreasing scores over time; factor analysis reveals only one factor despite being designed to assess four dimensions Cronbach's alpha 0.93
Bereavement Risk Index (BRI)[5] Domain(s): Grief and bereavement	Mixed diseases Uses an adapted 8-item version	Significant differences were found between low and high-risk groups in the Brief Symptom Inventory; results persisted 25 months after death. NR
Brief Hospice Inventory[6] Domain(s): Quality of life; Physical symptoms; Emotional symptoms	Mixed diseases NR	Factor analysis reveals 2 factors Cronbach's alpha 0.84-0.94
Brief scale[7] Domain(s): Quality of life	Lung cancer patients of mixed severity (uses 2 of 5 items from Spitzer Quality of Life index); consists of 2 separate implicit scores on 3 tier scale for mood/outlook (based on 3 structured questions) and social support (based on 2 questions); clinician assessment	Reported against HADS (outlook correlation 0.61, support 0.43) and RSCL (outlook 0.64, support 0.18); correlation to corresponding Spitzer QL-Index (outlook 0.55, support 0.53) NR

Appendix H2. VERSION
TABLE H-2. Reliability and Validity Data for Measures Identified

Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Cambridge Palliative Assessment Schedule (CAMPAS-R)[8] Domain(s): Physical symptoms	Mixed diseases Patient physical and psychological symptoms; patients-rated caregiver psychological symptoms; VAS	Correlated with EORTC & HADS items and scales for some symptoms but not others; significant differences between patients who did and who didn't survive Cronbach's alpha 0.77-0.8
Cancer Patient Need Survey[9] Domain(s): Needs assessment (Quality of care)	Mixed cancer 51 items, 5 categories - coping needs, help needs, information needs, work needs, cancer shock needs	Discriminate validity with different scores for hospice and clinic patients - may need different instrument for hospice patients Cronbach's alpha 0.91
Caregiver Reaction Assessment[2] Toolkit Domain(s): Caregiver well-being	Mixed diseases 24 items; interviewer administered	See Toolkit for details See Toolkit for details
Caregiver Strain Index[2] Toolkit Domain(s): Caregiver well-being	Mixed diseases 13 items; interviewer administered	See Toolkit for details See Toolkit for details
Center for Epidemilogic Studies (CES-D)[2] Toolkit Domain(s): Emotional symptoms	Mixed diseases 20 items; interviewer or self-administered	See Toolkit for details See Toolkit for details
Chao Patient Perception[2] Toolkit Domain(s): Continuity of care	Mixed diseases 23 items; self-administered mailed survey and medical record review	See Toolkit for details See Toolkit for details
Comfort Assessment in Dying with Dementia (CAD-EOLD)[10] Domain(s): Physical symptoms, Emotional symptoms	Single disease -advanced dementia 14 items; 4 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)
Communication Capacity Scale[1] Domain(s): Emotional symptoms	Mixed cancer 5 item; clinician-rating scale	Principal components analysis show only 1 component; highly associated with cognitive items on MDAS and Delirium Rating Scale (0.83); not correlated with agitation items Cronbach's 0.96; inter-rater kappa 0.78-0.95

Appendix H2. VERSION
TABLE H-2. Reliability and Validity Data for Measures Identified

Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Concept of a Good Death measure[11] Domain(s): Multidimensional measure (Palliative Outcomes)	Mixed diseases; not used with patients 17 descriptive statements of components that might be related to concept of good death; 3 subscales: closure, personal control, clinical criteria	Factor analysis - 3 subscales; small-to moderate association with other measures suggesting that these are distinct but related constructs; some items with low variability Test-retest: ICC 0.66-0.83.
Core Bereavement Items (CBI)[12] Domain(s): Grief and bereavement	Mixed diseases 17 items, 3 subscales, measuring bereavement phenomena (developed from Bereavement Phenomenology Questionnaire)	Factor analysis to develop subscales; face validity examines - kept subscales that described key components of bereavement; discriminant validity to time and group effects Cronbach's alpha 0.91
Cornell Scale for Depression in Dementia (CSDD)[13] Domain(s): Emotional symptoms	Single disease - dementia; elderly nursing home residents 19 items (16 items retained in 4 domains), 3 level scale; 2 steps - clinician interview of caregiver, brief patient interview and clinical observation	Oblique rotation 4-factor matrix with eigenvalues >1.0 account 50% variance; inter-factor correlation 0.30 for depression and disturbed sleep, others <0.181; criterion-validity done; no testing with external scales Internal consistency 0.76 total 16 item, depression subscale 0.75, somatic 0.72; Cronbach's 0.76
Cost and Reciprocity Index (CRI)[14] Domain(s): Caregiver well-being	NR 25 items(modified), 4 subscales, face-to face for hospice caregivers; concepts of social support, reciprocity, cost, and conflict	Testing was done of the original instrument in healthy populations - relations between subscales are consistent with theoretical framework. Cronbach's alpha 0.68-0.83
Death Attitude Profile[2 Toolkit] Domain(s): Spirituality	Mixed diseases 21 items; self-administered	See Toolkit for details See Toolkit for details
Death Transcendence Scale[2 Toolkit] Domain(s): Spirituality	Mixed diseases 25 items; self-administered	See Toolkit for details See Toolkit for details
Decisional Conflict Scale (DCS)[15] Domain(s): Advance care planning (Treatment decisions)	Mixed diseases; applied scale to cancer patients 16 items, 5 point Likert scales; 3 subscales (uncertainty, factors contributing, and effective decision making)	Construct validity among subscales 0.58 - 0.76; criterion validity significant between certain vs. uncertain groups; 3 factor model rejected (4 factor suggested in exploratory work) Prior testing - internal consistency 0.78-0.89; test-retest >0.80; in combined subscales in this study - uncertainty 0.75, factor contributing 0.82, and decision making 0.82

Appendix H2. VERSION
TABLE H-2. Reliability and Validity Data for Measures Identified

Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Duke-UNC Social Support Scale[16] Domain(s): Quality of life	Single disease - lung cancer NR	NR Cronbach's overall 0.94, subscales 0.88 to 0.92
Dyspnea Descriptor Questionnaire[17] Domain(s): Physical symptoms (dyspnea)	Single disease -heart failure; study done as convenience sample at single emergency department 13 descriptors asked retrospectively (derived from literature search)	Factor analysis done - 4 factor 71% Cronbach's 0.95; inter-item correlation 0.60
Edmonton Functional Assessment Tool (EFAT-2)[18,19,20] Domain(s): Functional status	Mixed diseases 10 items (revised version); professional grading and evaluation scale describing symptoms and functions, one summary functional assessment; 0-4 scale	Concurrent validity shows it to be highly correlated with KPS and ECOG; total score highly correlated with global scale. Construct validity distinguished between inpatients and home palliative care patients. EFAT -2 (revision of EFAT)[19] not correlated with pain; significantly different in different groups based on discharge location; factor analysis: 2 components - physical & cognitive/affective Inter-rater, ICC 0.71; Cronbach's alpha 0.86; Interrater ICC 0.97 for self trained clinicians (n = 2) and 0.95 for formal trained (n = 2); kappa on items ranged from 0.25 to 0.96 for self trained clinician pair and 0.17 to 0.95 for formal trained

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Edmonton Symptom Assessment Scale (ESAS)[2, Toolkit, 21] Domain(s): Physical Symptoms	Mixed diseases 9 items on 100mm visual analogue scale; self-administered or proxy	See Toolkit for additional details Correlation to MSAS Global Distress r = 0.73; concurrent validity ESAS summary distress score to MSAS demonstrated; TMSAS scale (0.72), GDI (0.73), physical symptom subscale (0.74), and psychologic 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 2 days and 0.45 at 1 week; all items significantly correlated at 2 days (r = 0.43 to 0.86) but at 1 week only pain (0.75), activity (0.65), depression (0.54), shortness of breath (0.53) and distress (0.45) were significantly correlated;
European Organization for Research and Treatment Core Quality of Life Questionnaire, version 3.0 (EORTC QLQ-C30)[22, Toolkit,2, 16] Domain(s): Quality of life	Mixed diseases 30 items; self-administered	See Toolkit for additional details; Inter-scale correlations were moderate in general, statistically significant - weak correlations where they should have been weak; discriminative by functional status (p=0.01); responsiveness to changes in health status over time - significant difference (p<0.001) for pre & post treatment; construct - exploratory factor analysis - 6 factors. Cronbach's overall 0.93, subscales 0.69 to 0.89 (7 or 12 subscales > 0.80); in palliative population Cronbach's 0.56-0.79
FACT/FACIT (Fact-G)[23,2 Toolkit] Domain(s): Quality of life	Mixed diseases 27 items; self-administered	See Toolkit for details See Toolkit for details

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
FAMCARE[2, Toolkit, 24, 25] Domain(s): Satisfaction	Mixed diseases 20 items; interviewer administered	See Toolkit for details Inter-item correlations met criterion (minimum 50% with r = 0.3 to 0.7) for 18 of 20 items; item correlation to total score 0.4 to 0.75 for 12 of 12 items; Cronbach's alpha 0.93
Family Assessment Device (FAD)[24] Domain(s): Satisfaction, Caregiver well-being	Mixed disease 12 items; assess family functioning	NR Inter-item correlations met criterion (minimum 50% with r = 0.3 to 0.7) for 18 of 20 items; item correlation to total score 0.4 to 0.75 for 12 of 12 items; Cronbach's alpha 0.88
Family Caregiver Medication Administration Hassles Scale[26] Domain(s): Caregiver well-being	Community study (details of patients not given) - looks at problems caregivers experience with assisting elderly with medications 24 items paper survey; 4 subscales (Information, Safety Issues, Scheduling, & Polypharmacy); scale 0-5 for each item	Principal components and factor analysis done (66.5% cumulative variance; construct validity to Medication Complexity Index (r=0.19) & modified Caregiver Strain Index (r=0.44) Test-Retest at 2 weeks (n=53) 0.84 (0.78-0.85 Pearson correlation across subscales); internal consistency 0.95; Cronbach's alpha (0.80-0.92 across subscales)
F-Care Expectations Scale[24] Domain(s): Satisfaction	Mixed diseases 16 items; assess family care expectations	NR Inter-item correlations met criterion (minimum 50% with r = 0.3 to 0.7) for 13 of 16 items; item correlation to total score 0.4 to 0.72 for 12 of 16 items; Cronbach's alpha 0.88
F-Care Perceptions Scale[24] Domain(s): Satisfaction	Mixed diseases 21 items; sssess family members care perceptions	NR Inter-item correlations met criterion (minimum 50% with r = 0.3 to 0.7) for 18 of 21 items; item correlation to total score 0.4 to 0.72 for 13 of 21 items; Cronbach's alpha 0.86
FIM™ Instrument[2,Toolkit] Domain(s): Functional status	Mixed diseases 18 items; interviewer administered	See Toolkit for details See Toolkit for details
Frail Elderly Functional Assessment Questionnaire (FEFA)[27] Domain(s): Functional status	Mixed diseases; age > 65 years; homebound and nursing home 19 items; assess function in elderly at very low activity level; interviewer administered	Correlation to direct observation (r=0.90); also Katz's ADL index (r=0.86), Barthel index (r=0.91), Lawton's IADL index (r=0.67) Test-retest in n = 29 at 2 week interval - kappa 0.82 overall, all items > 0.40 (0.45-0.91)

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TABLE H-2. Reliability and Validity Data for Measures Identified

Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Grief Experience Inventory (GEI)[28] Domain(s): Grief and bereavement	NR 102 statement self-administered inventory scaled yes/no; nine composite scales including 3 validity and 6 domains	Discriminate validity bereaved versus non-bereaved reported significant at 0.001 level on all subscales Test-retest coefficients 0.53-0.87; Cronbach's alpha 0.52-0.84 on bereavements scales
Grief Resolution Index[2,Toolkit] Domain(s): Grief and bereavement	Mixed diseases 7 items; interviewer or self-administered	See Toolkit for details See Toolkit for details
Hebrew Rehabilitation Center for Aged index (HRCA-QL)[29] Domain(s): Quality of life	Adapted for patients with advanced cancer Version of the Spitzer Quality of Life index	Scores declined as patients became closer to death; sensitive to change in status; criterion validity correlated with KPS and IADL index Cronbach's alpha 0.7-0.78; test-retest: 0.89; inter-rater 0.67
Herth Hope Index[2 ,Toolkit] Domain(s): Spirituality	Mixed diseases 12 items; interviewer administered;	See Toolkit for details See Toolkit for details
Hogan Grief Reaction Checklist (HGRC)[30] Domain(s): Grief and bereavement	Mixed diseases 61 items; six constructs, (despair, panic behavior, blame and anger, disorganization, detachment, and personal growth)	Convergent validity to TRIG, GEI and IES 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 (illness, accident, suicide, or homicide) revealed differences in blame and anger; discriminate validity with subset of mothers with deaths <or>3 years in past revealed difference in intensity of grief and personal growth; factor analysis reported Cronbach's alpha overall 0.90 (despair 0.89, panic behavior 0.90, blame and anger 0.79, disorganization 0.84, detachment 0.87, and personal growth 0.82); test-retest over 4 week interval significant at p<0.001 (despair r = 0.79, blame and anger r = 0.56, disorganization r = 0.85, detachment r = 0.77 and personal growth r = 0.81)

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Hospice Pressure Ulcer Risk Assessment Scale (HoRT)[31] Domain(s): Clinical assessment tool	Mixed diseases assess physical activity, age, mobility	discriminant validity with statistically significant differences between patients with and without ulcers. PPV 50%, NPV 100%. NR
Hospital Anxiety and Depression Scale (HADS)[32] Domain(s): Emotional symptoms	Breast cancer self-report, 7-items depression, 7-items anxiety; tries to discriminate between anxiety and depression	Using cutoff value of tool, sensitivity/specificity (depression) 75%, 75%, misclassification rate 25%; (anxiety) 75%, 90%, 12% NR
Index of Independence in ADLs[2] Domain(s): Functional status	Mixed diseases 6 items; medical professional rating	See Toolkit for details See Toolkit for details
Index of support; done as part of Canadian Study of Health and Aging (CSHA)[33] Domain(s): Instrumental support available to older Canadian community residents	Community study of elderly 6 items; 4 level scales; interview	4 phases: factor analysis (item correlations 0.26 to 0.83), item response theory analysis, external (construct and predictive validity on 2nd half of study population), and IRT(r=0.53 to network size)/classical (r=0.61) comparison Cronbach's alpha 0.76; IRT marginal reliability 0.85
Kansas City Cardiomyopathy Questionnaire[34] Domain(s): Quality of life; Physical symptoms; Functional status	Single disease - CHF Self-administered, 23-items, HRQOL in CHF	Convergent validity 0.46 - 0.74 across 7 domains; physical limitation to 6-minute walk (r=0.48), SF-36 (r=0.84), LiHFe (0.65); responsiveness higher than LiHFe and SF-36 for admission with CHF exacerbation Cronbach's alpha 0.62-0.95 across 7 domains; test-retest at 3 months without exacerbation 0.8 to 4 point changes in 1-100 point scale
Life Closure Scale (LCS)[35] Domain(s): Spirituality	Mixed cancer diagnoses 45 items; assess psychological adaptation in dying	Content validity with interviews and experts evaluation Cronbach's alpha 0.80

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Life Evaluation Questionnaire (LEQ)[36] Domain(s): Quality of life	Mixed diseases 121 items, 0-60 scale; self-administered; five subscales (freedom, appreciation of life, contentment, resentment, social integration)	Convergent validity to RSCL ranged from 0.01 to 0.62 (sufficient only for freedom, resentment, and social integration); convergent to MacAdam and Smith Support scale factor ranged from 0.02 to 0.62 and similarly sufficient only for freedom, resentment, and social integration; analysis with five components reported. Cronbach's alpha (freedom 0.70, appreciation of life 0.76, contentment 0.76, resentment 0.85, social integration 0.78); test-retest n=40, at 2-3 days (freedom r=0.80, appreciation of life r=0.91, contentment r=0.77, resentment r=0.92, social integration r=0.84)
Linear Analogue Scale (LAS) for quality of life in cancer patients[37] Domain(s): Quality of life	Mixed cancer 5 questions, linear analogue scale, self-assessment	Correlation between LAS and performance status (r=0.46); questionnaire and performance status (r=0.38) - overall poor performance noted Cronbach's alpha 0.75; subgroup LAS (alpha 0.58) compared to questionnaire (0.93); n=41 test-retest LAS (29.3% of cases judged reliable), questionnaire (82.9%)

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TABLE H-2. Reliability and Validity Data for Measures Identified

Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Lung Cancer Symptom Scale (LCCS)[38,39,40] Domain(s): Quality of life; Physical symptoms; Emotional symptoms; Functional status	Single disease - lung cancer 2 scales; patient - 9 items visual scale (100mm) and observer - 6 items (4 point or none scale)	Construct validity with KPS 0.15-0.63 across items (symptomatic distress 0.49, effect on activities 0.63, QOL 0.43); criterion validity (patient scale / observer scale respectively) - KPS (r=0.63, NA), SIP(0.40, 0.56), POMS(0.67,0.54), ATS 29 cough (0.56, 0.65) and dyspnea (0.46, 0.64), SF-MPQ (items range 0.51 - 0.67); content validity (high agreement noted without specific data); construct validity between scales: cough (r=0.74), dyspnea (r=0.66), hemoptysis (r=0.71), pain (r=0.71), wt loss (r=0.61); criterion validity to Karnofsky r=0.59 Cronbach's alpha 0.82 (patient scale) and 0.75 (observer); internal consistency to BSI (r=0.93), SIP (r=0.94), POMS (r=0.94), SF-MPQ (r=0.91, r=0.64-0.74 for 3 components); test-retest r>0.75 for all items; interobserver r>0.75 for all items except cough (r=0.65) and weakness (r=0.54); note weakness has subsequently been dropped
McCusker Scale[2,Toolkit] Domain(s): Continuity of care	Mixed diseases 4 items; interviewer administered	See Toolkit for details See Toolkit for details
McGill Pain Questionnaire[2,Toolkit] Domain(s): Physical symptoms	Mixed diseases 11 items; interviewer or self-administered	See Toolkit for details See Toolkit for details
McGill QOL Questionnaire[2 ,Toolkit] Domain(s): Quality of life	Mixed diseases 17 items, 0-10 scale; self-administered	See Toolkit for details See Toolkit for details
McMaster Quality of Life Scale[41] Domain(s): Quality of life	Mixed cancer Administered to proxies or patients; responsive to perceptions of change in clinical status (p=0.01)	Concurrent validity as correlated well with Spitzer QOL (r=0.7); those able to rate it themselves rated QOL higher than those who needed to have it read to them (p-0.04); days until death explained 7% of the variance in QOL Interobserver r = 0.83-0.95; intrarater 1 week 0.63 (lower than on same day); Cronbach's 0.8

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Meaning in Life Scale[2] Domain(s): Spirituality	Mixed diseases 15 items; interviewer administered	See Toolkit for details See Toolkit for details
Measure of patients' assessment of the quality of communication about end-of-life care[42] Domain(s): Advance care planning	Single disease - HIV/AIDS 4 items	Correlated with overall satisfaction with medical care (0.76); those with higher-rated communication had clinicians more likely to know if the had a DPOA Cronbach's alpha 0.81
Medical Outcome Study Satisfaction Survey[2,Toolkit] Domain(s): Satisfaction	Mixed diseases; 21 items; self-administered;	See Toolkit for details See Toolkit for details
Memorial Pain Assessment Card[2] Domain(s): Quality of life	Mixed diseases 8 descriptors and 3 visual analogue scales; self-administered;	See Toolkit for details See Toolkit for details
Memorial Symptom Assessment Scale[2, Toolkit , 43, 44] Domain(s): Physical symptoms, Emotional symptoms	Mixed diseases 32 items; interviewer or self-administered;	See Toolkit for additional details. 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 noncancer patients[43] (best for behavioral and sensory subscales of the PFS); factor analysis yielded one psychological factor and one physical symptom with 3 subgroups; separate study [44] showed univariate correlations to MHI well being -0.60 (-0.53 to 0.66 for 3 subscales), MHI distress 0.65 (0.48 to 0.80), 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 Cronbach's alpha 0.85 in cancer patients (n = 66) and 0.77 in noncancer end-stage group (n = 69);
Missoula-VITAS QOL Index[2,Toolkit] Domain(s): Quality of life	Mixed diseases 27 items; self-administered	See Toolkit for details See Toolkit for details

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Pain Assessment in Advanced Dementia (PAINAD)[45] Domain(s): Physical symptoms	Single disease - advanced dementia patients in nursing home 5 items with 5 subdomains of pain each with scale 3 levels (29 choices); overall additive score 0-10	Factor analysis done; convergent analysis to DS-DAT & DS-VAS (r=0.76, n=19) and PAIN-VAS (r=0.75, n=18) - note also done in different conditions (r>=0.82 in activity) Multiple observations across 44 patients; Cronbach's alpha 0.57 - 0.83 in multiple phases
Palliative Care Outcome Scale (POS)[46] Domain(s): Quality of life; Physical symptoms; Functional status; Continuity of care; Multidimensional measure	Mixed diseases 2 parts - patient & staff; each 12 items, most 0-4 scale; general audit designed as a palliative care outcome measure, eight site study	Construct validity r=0.43-0.80 against ETORTC QLC-C30 AND STAS (n=29 patients, 43 staff); change over time not statistically significant; face validity by patient survey (n=12 - qualitative) Test-retest for seven items kappa - 0.08-0.62 with % agreement 74-100%; Cronbach's alpha patient part (0.65) & staff part (0.70); Kappa > 0.3 staff compared to patient responses for 8 out of 10 items
Palliative Care Quality of Life Instrument (PQLI)[47] Domain(s): Quality of life	Mixed cancer 28 items, 6 scales	Face validity: expert review, patients asked to pick most important issues, rate scales; compared patients with better & worse ECOG performance status (significant); responsiveness before and after treatment; factor analysis; construct - correlated with AQEL (correlation coefficients 0.44-0.94) and EORTC - QLQ-C30 (0.79-0.97); criterion: ability to predict independent criterion variables (p<0.001); convergent & discriminative: related to corresponding & not to non-corresponding variables on interview (p<0.001) Cronbach's alpha 0.79; test-retest coefficients of agreement 0.82
Physical Disability Index (PDI)[48] Domain(s): Functional status	NR 54 items, for use with frail individuals; requires calibrated specialized performance measuring equipment	Discriminate validity against Folstein Mini-Mental State Exam (r=0.11); convergent validity Physical Self-Maintenance Scale (r=-0.71) and Sickness Impact Profile (r=-0.59); Test-retest in n = 36 at 2-5 days 0.97 overall, 4 subscales 0.92-0.96; interrater reliability 0.81-0.99 (mobility scale -0.02-0.70)

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Physical Self-Maintenance Scale[2], Toolkit Domain(s): Functional status	Mixed diseases 6 items; interviewer or self-administered	See Toolkit for details See Toolkit for details
Picker-Commonwealth Surve[y2,] Toolkit Domain(s): Continuity of care, Satisfaction	Mixed diseases 62 items; self-administered	See Toolkit for details See Toolkit for details
Postal questionnaire to examine career satisfaction with palliative care[49] Domain(s): Satisfaction	Mixed diseases 89 question; after-death postal survey of caregivers	Discriminant validity tested with 36 attitudinal questions when health problems identified - only 4 were significant by Chi square; convergent testing reported in tabular form in reference Cronbach's alpha 0.68 to 0.84 across 7 subsets
Profile of Mood States[2, Toolkit] Domain(s): Emotional symptoms	Mixed diseases 11 items; interviewer administered	See Toolkit for details See Toolkit for details
Quality of Dying and Death (QODD)[50-53] Domain(s): Quality of life, Functional status, Survival time and aggressiveness of care, Advance care planning, Spirituality, Grief and bereavement, Caregiver well-being, Multidimensional	Mixed diseases 31 item family after-death interview across 6 domains; separate 23-item ICU version; 2 parts assess frequency and quality ratings; also 14-item nurse caregiver measure	Measure development included qualitative data from multiple focus groups and interviews. QODD 31-item family after-death measure: construct validity r=-0.52 against MSAS, r=-0.47 MSAS psychological sub-score, r=-0.42 MSAS physical sub-score; 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 7 days of life r=0.55, moment of death r=0.51 (two factors explaining 38% of QODD variance) Overall 31-items QODD Cronbach's alpha 0.89; Cronbach's alpha 0.96 for 14 item RN version; interobserver reliability 0.44 for overall QODD (23-item ICU version) after-death survey; components ranged from 0.15 to 1.0 for frequency components (mean 0.54), 0.16 to 0.59 for quality rating component (mean 0.32)

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Quality of End-of-Life Care and Satisfaction with Treatment (QUEST)[54] Domain(s): Satisfaction	Mixed diseases 4 scales (MD care, MD satisfaction, RN care, RN satisfaction); patients & surrogates, rate RNs & MDs	Reviewed by experts; construct - correlate with PSI (Patient Satisfaction Index) 0.38-0.47; subscales correlated with each other (0.47-0.69); not correlated with unrelated constructs; positive skew distribution for many items; negative correlation with symptoms; patients scores were lower for patients with DNR orders Test-retest: kappa 0.43-0.86 (1-2 days); Cronbach's 0.83-0.95
QUAL-E (Quality of Life at End of Life)[55] Domain(s): Quality of life	Mixed diseases 24 items	Factor analysis reveals 5 domains: life completion, relationships with the health care system, preparation/anticipatory concerns, symptom impact, connectedness and affective social support. Cronbach's alpha 0.6-0.84
RAND Mental Health Inventory (MHI-5)[2 ,Toolkit] Domain(s): Emotional symptoms	Mixed diseases 5 items; self-administered	See Toolkit for details See Toolkit for details
Rapid Disability Rating Scale[2 ,Toolkit] Domain(s): Functional status	Mixed diseases 18 items; medical professional rating	See Toolkit for details See Toolkit for details
Relatives' patient management questionnaire[56] Domain(s): Advance care planning; Satisfaction	Mixed cancer 21 items, 5 scales in final version: families' attitudes, perceptions, and patterns of choice in management of terminal cancer patients	Construct validity inter-scale correlations 0.6-0.86; discriminant low correlation with unrelated items Cronbach's alpha 0.5-0.69
Resident Assessment Instrument for Palliative Care (RAI-PC)[57] Domain(s): Physical symptoms; Emotional symptoms; Functional status; Advance care planning; Spirituality; Palliative Outcomes	NR Builds on RAI for NH resident assessment; 9 domains; for clinician assessment in NH	NR Interobserver - kappa 0.77-0.9
Rotterdam Symptom Checklist (RSCL)[32] Domain(s): Physical symptoms; Emotional symptoms; Functional status	Single disease - breast cancer Self-report; 3 subscales: physical (22 items), psychological (8 items), ADL (8 items); 4 point scale	Using cutoff value of tool, sensitivity/specificity 75%, 80%; misclassification rate 21% NR

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Santa Clara Strength of Religious Faith Questionnaire (SCSORF)[58] Domain(s): Spirituality	Mixed cancer 10-items developed to evaluate links with psychological health	Convergent: strongly correlated with intrinsic religiosity, moderately correlated with religious practice, perception of self as spiritual, comfort derived from religion. Test-retest: 0.82; Cronbach's alpha 0.95.
Satisfaction With Care at the End of Life in Dementia (SWC-EOLD)[10] Domain(s): Satisfaction	Single disease - dementia 10 items; 4-point scale; one-factor	Item-total correlations range 0.33 to 0.79 Cronbach's alpha 0.90
Smith-Falvo Paitent-Doctor Interaction Scale[2 ,Toolkit] Domain(s): Continuity of care	Mixed diseases 17 items; self-administered	See Toolkit for details See Toolkit for details
Spiritual Perspective Scale[2 ,Toolkit] Domain(s): Spirituality	Mixed disease; 10 items; self-administered	See Toolkit for details See Toolkit for details
Spiritual Well-Being Scale[2 ,Toolkit] Domain(s): Spirituality	Mixed diseases 20 items; self-administered	See Toolkit for details See Toolkit for details
Stanford Health Assessment Questionnaire[2 ,Toolkit] Domain(s): Functional status	Mixed diseases 20 items; interviewer/telephone or self-administered	See Toolkit for details See Toolkit for details
Support Team Assessment Schedule (STAS)[59,60] Domain(s): Physical symptoms; Multidimensional measure	Mixed diseases - broadly across hospice patients; one study[60] applied to acute care oncology unit and a palliative care unit 17 items, scale 0-4; 7 items grouped into a) patient and family items (4) and b) service items (3); interview administered	Validity by comparison of type of rater: kappa for patient to staff (n=62-78) ranged from 0.12-0.78, total score Spearman rho 0.66; kappa for family to staff (n=58-67) ranged from -0.06-0.51, total score Spearman rho 0.44. Validity by comparison to patient rating - overall r=-0.09 palliative care and r=0.28 oncology (p>0.05); to family rating overall r=0.38 palliative care and r=0.37 oncology (p>0.05); item kappa 0.00 - 0.61. Interobserver reliability mostly r=0.4-0.6 (range 0.27-1.0) ; intraobserver reliability (r=-0.33-0.88) for overall score and range 0.1-1.0 for items; test-retest 0.50 for palliative care team and 0.71 for oncology team

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Measure name **Domain(s)**	**Population Setting** **Brief description**	**Validity Testing** **Reliability Data**
Symptom Distress Scale (SDS)[61] Domain(s): Physical symptoms	Mixed diseases – applied to symptoms in females with lung cancer 10 items, self-report; modified to 13 items for lung cancer in 1980s	Factor analysis with principal components and varimax rotation - 5 factor 65% variance; also correlation of certain items to parts of Karnofsky Performance Status (r= -0.27 to -0.48) overall r=-0.58 NR
Symptom Management at the End of Life in Dementia (SM-EOLD)[10] Domain(s): Physical symptoms, Emotional symptoms	Single disease - dementia 9 items; frequency ratings of multiple symptoms	Item-total correlations range 0.18 to 0.66; correlations for symptom items on CAD-EOLD r = 0.475 to 0.559 Cronbach's alpha 0.78
Symptom Monitor[62] Domain(s): Physical symptoms	Mixed diseases 10-item diary for physical symptoms	NR Inter-rater ICCs > 0.75
Toolkit After-Death Bereaved Family Member Interview[63,2 ,Toolkit] Domain(s): Satisfaction	Mixed diseases (hospice, nursing homes, & hospital) 8 domains, telephone survey with family member 3-6 months after death; up to 133 items	See Toolkit for additional details; scales moderately correlated with overall satisfaction and with corresponding individual rating question for the construct; families of those who died in hospice reported better care - significant for three of the eight scores Cronbach's >0.7 for >3 item scales, 0.58 for 3-item scales; test-retest: 34 items had Kappa/ICC <0.4 - low ICC question dropped.
Willingness to Accept Life-sustaining Treatment instrument (WALT)[64] Domain(s): Advance care planning	Mixed diseases; associated with age, ethnicity, & functional impairment No description provided	face: reviewed by patients & experts; correlated with simpler measure of preference inter-rater 0.73-0.95; test-retest 0.49-0.93
Wisconsin Brief Pain Questionnaire[2 ,Toolkit] Domain(s): Physical symptoms	Mixed diseases 17 items; self-administered	See Toolkit for details See Toolkit for details

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Group	Section	Comment	Response
Peer	Overall	...the economic cost of caregiving at end-of-life is not given a full discussion.	Due to limited time and resources, economic issues were beyond the scope of this report.
Peer	Overall	About midway through the document, it seemed to me that a great deal of content seems to be written from a geriatrician's perspective. …some of the text is more appropriate for a review of chronic illness care or geriatric care.	The end of life will certainly have a geriatric tone, since most dying now is in older persons, and since we did not address dying of children at all. We did not take up the special issues of aging or of younger and mid-life adults who face fatal illness. The age-related issues would deserve special attention in an ensuing project.
Peer	Overall	I don't believe that such a negative interpretation of the data is either beneficial or scientifically accurate.	We hope you will mention this at the State of the Science Conference. It may be that one should accept as evidence some insights arising from other study designs, or that one should call for funding of stronger designs.
Peer	Overall	The document reads as if it is written by several different people with very inconsistent format and quality.	We have tried now to impose more stylistic control.
TEP	Overall	..you refer to an unpublished systematic review—the review has been published by the National Institute of Clinical Excellence. It was published in 2004.	We have updated the citation.
TEP	Overall	… you should explain up front the need to be narrowly focused and address some issues and not all	The revised history of the project in Chapter 1 makes more clear just how much we did not get to address.
TEP	Overall	…as long as we refer to palliative care as end of life care, no one will be in our denominator for research studies. Palliative care should be need- and complexity-based, not prognosis-based.	We did use "end of life" in that broad sense, focused upon serious and eventually fatal illness. We did not include palliative care for stable but serious conditions. Since the task order specified "end of life care," we did feel that we were obliged to stay with that term and scope.
Peer	Overall	…the Evidence Report seems to lack attention to race/ethnicity and culture.	We have added summaries of observational studies which address these issues.
TEP	Overall	…there seems to be little attention given to end of life issues that may be ethnically or culturally specific.	We have added summaries of observational studies which address these issues.
Peer	Overall	…use the more inclusive language of palliative care. By continuing to refer to our field as end-of-life care, I think that we are sending the wrong message….	We have struggled with this recent change in the field. The task order is given in terms of "end of life care." We mostly have to stay allegiant to the task as written. We have used "palliative" when that is not misleading, and we have used the broadest definition of the field of "end-of-life," that of serious and eventually fatal chronic illness.

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Federal	Overall	Having been a Joanne Lynn employee, I know she has done a substantive amount of quality improvement work. What can be learned from this literature? If there is "no high quality evidence" what evidence of supposed less quality is there?	In the way that evidence is assessed, evidence arising from quality improvement is not generally taken to be very reliable. In this project, we addressed only prospective cohort and case-control designs among descriptive studies. No quality improvement work would have qualified.
Peer	Overall	Suggest you have a final reader who reviews for acronyms.	Acronyms are now defined upon first use.
Peer	Overall	The conclusions reached in almost every section (there is not evidence) are just not consistent with my reading of the report and my perception of the evidence.	The structure of the evidence review requires looking first at intervention trials, then at the strongest designs of descriptive studies. We stretched that some to include some thoroughly retrospective and uncontrolled studies, but still, the summary of the sections regarding the stronger designs is often going to be fairly disappointing in tone.
TEP	Overall	The document also pays little attention to issues surrounding age.	That is true. More than three-quarters of all deaths are now past age 65, so most studies of the end of life are among persons commonly considered to be elderly. However, only a few differentiate between the older elderly and the younger elderly. Indeed, many studies are biased by having median ages well under 65 - especially studies of cancer and heart disease. Obviously, studies of frailty would emphasize the older patient. Lubitz et al and Shugarman et al have shown that age is a strong determinant of medical care costs in the last year of life, with a progressive decline with age. However, no study comes to mind that associates age itself with better and worse dying. Surely that would be a good area for study *and we mention it now in the chapter on recommendations* .
Peer	Overall	The outline seems to fall apart as the report moves along.	We have tightened up the explanation of the progress and the outline.
Federal	Overall	The reader's confidence is undermined when they learn (repeatedly) that the research team had "limited time." How significant was the lack of time?	This report was given sustantially less time and had substantially more literature to review than a typical EPC project. The report is very straightforward about the strategies that we used in order to complete the most useful work possible in the time allowed. Undoubtedly, another project with more time and resources, would address more topics and seek broader literature.

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Peer	Overall	The tone and voice of the paper changes multiple times….because it was written by a number of different individuals….in some places it is less of a review and more of a personal interpretation of the data.	We have revised toward a settled style and a straightforward reporting of findings and recommendations.
Peer	Overall	There is a lack of consistency in the details in which the evidence was reviewed.	After review and revision, there is much more consistency.
Peer	Overall	This reviewer generally agrees with the great majority of the findings and above all with the conclusions with the authors regarding the state of the art of research in this area.	Thank you.
Peer	Overall	Throughout the draft the term "medicine" is used, and while the meaning is not clear….It is a major concern that there is not more interdisciplinary focus and also that literature from other fields is not recognized.	We checked the text for "medicine" and "medical" and corrected to a broader and more inclusive term wherever possible. It is still the case that literature from social sciences and nursing are under-represented with our search strategy.
Peer	Introduction	..it is useful to add cancer as one of the major causes of dyspnea.	This has been noted.
Peer	Introduction	It may help to – in the first chapter—lay out your definitions that inform the review.	The introduction has been revised to address this issue.
Federal	Introduction	Last full sentence is very clumsy.	This sentence has been rewritten.
Federal	Introduction	Last paragraph - "Other mean a large..." needs re-write.	This paragraph has been rewritten.
Peer	Methods	I worry that by limiting the data to “end-of-life care” that you have missed a large number of relevant articles…in cancer pain and dyspnea topics, which I have reviewed recently there are important references you have left out.	That is undoubtedly true. In some ways, a comprehensive review would have had to have addressed the serious end of every fatal condition, and to have looked at the literature on that point. We could not accomplish that task. Those who work in one or another segment of this field will be able to rely upon our stated search and winnowing strategies, but they will undoubtedly find other sources that we did not find.
Peer	Methods	It is also possible that media also contributes to variation in populations. Some studies and interventions receive much more media attention and draw greater localized efforts at system change and collaboration in some regions than others.	This seems likely to be true. However, evaluating the media response to research is well beyond the scope of this project.
Peer	Methods	It would be important to explain the JADAD scores to the reader and use them consistently.	There is now a summary explanation in Chapter 2.

TEP	Methods	...in the discussion of symptoms, I do think that it would be worthwhile to list all of the symptoms that have been described in patients in the last year of life and then discuss why you have chosen to address only those included here	The introductory chapters do give the methodological details of how the selection was made. Listing all symptoms and their rates is not directly responsive to the task order, though we recognize the importance of a wide array of symptoms (especially in considering the course to death from all diseases).
Peer	Methods	...the authors address a number of "core considerations". …it may be more appropriate to address these issues within the context of a narrative review or a systematic review of very selected areas.	That would be very useful to do. Perhaps there will be an opportunity to do much more focused reviews, building upon this base.
Peer	Methods	I am surprised that the topic of withdrawal of life-support was excluded.	It would be a good topic for a future, focused, review. Perhaps the NHLBI would be interested, or NIDDK.
Peer	Methods	It seems appropriate to add a disclaimer acknowledging that the synergistic impact of multiple or sequential interventions is not considered with this methodology. I recommend this disclaimer be included in Section H, p.76 which has not yet been written. This section explores outcome variations among populations.	This is an important point which has been added to our discussion.
TEP	Methods	Regarding measures, I would use the term palliative outcomes	In many contexts, that seems to be a better term. We did not change the term in this report, since we aimed to stay close to the language and categories of the Task Order
Peer	Methods	Suggest you make clear what you mean by “grey literature”	This is now defined.
TEP	Methods	The attached review from our group indicates in detail some of the difficulties with measuring satisfaction.	We have added text addressing these measurement issues.
Peer	Methods	The authors characterize their clinical trials using the JADAD score. There is considerable controversy about the appropriateness of this score for the judgment of the quality of clinical trials particularly when non-pharmacological interventions are involved.	We recognize the controversy, but still claim that it helps demonstrate the rigor and merit of research design. Furthermore, it is a requirement of the sponsor (OMAR) to use this scale.

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Peer	Methods	The authors have missed a very considerable contribution made during the 1980s and 1990s. It would have been desirable to start the search in 1980.	We agree. However, we have done all we could in the shortened time frame allowed. Either someone might get to go back and fill in older work, or it will become less important to do over time. Insofar as the existing systematic reviews mostly go back into older literature, our use of them will bring in insights from that work.
Peer	Methods	The authors once again make emphasis to a very limited number of symptoms and this needs to be addressed	Have done, see above.
Peer	Methods	The draft suffers from a lack of core definition of terms.	The introduction has been revised to address this issue.
Peer	Methods	The exclusion of clinical trials about chemotherapy, radiotherapy, stent, laser, etc., is concerning. The authors need to discuss the fact that there may be need for more in depth review of this area in the future.	As for many of our restrictions, this one also would be well worth doing. As Irene Higginson noted in explaining why her reviews used the same restriction, these treatments are not ordinarily at the heart of the palliative care enterprise. Of course, there are exceptions, but we simply had to follow suit in order to have any opportunity to deal with over twenty thousand articles.
TEP	Methods	The review and ranking process makes sense and is well described.	Thank you.
Peer	Methods	There are a number of devastating symptoms that have not been part of this review. It is important to emphasize that delirium, cachexia, and chronic emesis are all much more frequent than depression and anxiety, both in the cancer and a large percentage of the non-cancer populations. Fatigue is an almost universal symptom and there has been no review of this major symptom complex. The authors need to emphasize that they have conducted a very partial review of the symptom distress experience.	We have now stated the limitation early on and in the section reporting results.
Peer	Methods	There are also large gaps in the literature review regarding bereavement.	Due to limited time and resources, bereavement issues were beyond the scope of this report.
Peer	Methods	There is a lack of a clear, concise framework to guide this entire analysis.	The rewriting of Chapter 2 and the clarifications throughout should make this less of a problem.

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Peer	Methods	Throughout the text there are weak definitions in use of the term "qualitative". There is confusion about qualitative methods versus qualitative analysis.	Most qualitative studies involved focus groups or unstructured interviews of individuals. We have added this information.
Federal	Methods	Were issues of reimbursement / pay for performance / quality considered under question 2c?	No. We did not address economic issues.
TEP	Methods	You discuss alternative pain interventions….perhaps it would be useful to say why/how the interventions that are reported were chosen for inclusion.	We have tried to make the Cambridge balloting more clear, including it in the text as well as in an Appendix.
TEP	Methods	Your search methods and rationale are clearly stated and defended.	Thank you.
Peer	Methods	Your use of unpublished literature (the two systematic reviews) worries me. …your justification for use of unpublished sources should be stronger.	Indeed, the strongest unpublished review has now been published, so this is less of a concern.
Peer	Results	A major problem for me is the lack of consistency in the details in which the evidence was reviewed.	There is much more consistency now in the degree to which studies are characterized.
Peer	Results	For some studies that I know well, the interpretation and the reanalysis of them are nihilistic.	The revisions will address some of the problems of tone, but it is still true that the typical EPC report focuses heavily upon "quality of research design," which values randomization, large study populations, blinding, etc. The literature in end-of-life care does not have much strength in that sort of study.
Peer	Results	I would think that the draft would benefit greatly by...having each major section with a very clear, defined summary.	We have added such paragraphs to the results section.
TEP	Results	..randomized controlled trial of hospice at home conducted by Todd and colleagues – do you have a reference from the BMJ from 1999?	This intervention study is now discussed under topics caregiver concerns and symptoms.
Peer	Results	…report would benefit greatly from some summary paragraphs to synthesize the key findings.	We have added such summaries at the end of the results section.
Peer	Results	I would like to see more information on symptoms.	Due to limited time and resources, our review was limited to the following symptoms: pain, dyspnea, depression, and behavioral symptoms.

Peer	Results	In the healthcare system issues, I thought there were some studies of case management and RN homecare practices, that in fact did show positive results in heart failure.	The literature for heart failure is fairly positive, and the reviews of that literature are now clearly laid out in the paragraphs on heart failure in Chapter 3 section on continuity.
Peer	Results	It would be helpful if you gave more data about the methods used in the qualitative studies….	Most qualitative studies involved focus groups or unstructured interviews of individuals. We have added this information.
Peer	Results	The authors have not reported on the randomized controlled trials on the administration of prompt sheets. A significant number of studies have been conducted [see Butol P, et al, Bruera E, et all]. It is not clear why these papers were not captured by the review.	We were unable to obtain the Butol article in time to include in our report.
Peer	Results	The summaries seem unduly short and not particularly helpful.	We have tried to balance the page limit with the extensive literature. The summaries are short, though mostly in line with the style in evidence reports. At the least, we hope that they are enough to point the reader to the useful literature for the reader's interests.
Peer	Results	There are many places through the text in which summary comments are made without citing the particular study.	These have been eliminated from the first three chapters. The summary perspectives of the working team are restricted to Chapter 4 on recommendations.
TEP	Results	there is a very large amount of literature which has examined the effectiveness of rehabilitation type interventions….it might well be worth you making a reference to this literature.	We now reference the sample that comes up with our search strategy. This does not reflect the large literature that is not particularly focused upon end-of-life.
TEP	Results - ACP	Although you include in the references the data from Emmanuel, I don't see a discussion of that paper as to caregiver burden from the particular issue of the stress on the caregiver, which appears to be multifaceted and related to high burden of disease. You do reference the paper.	The new version of the report spells out much more about this paper, including this point.
TEP	Results - ACP	It is extremely difficult to engage in meaningful communication regarding advance directives if professionals cannot communicate well with patients and families.	That is true, but we did not include general issues of communication in this review.
Federal	Results - ACP	No summary for section G on advance care planning.	This section has been completed.

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Peer	Results - ACP	Nowhere in the document is the Physician Orders for Life-Sustaining Treatment (POLST) program described. …that might most effectively be listed at the top of page 67 under "Information/Record Continuity."	Because we address all intervention trials and most prospective cohorts, we did not include many descriptive reports with other designs. Nevertheless, we agree with the reviewer that this work is important and have included it in the paragraph concerning especially important descriptive articles in the section on advance care planning.
Federal	Results - ACP	Regarding advance care planning... let's admit it, they are a conceit and secondly ethically suspect.	We are glad to point out that an evidence report requires that we report the data. Strong conclusions may be taken by others.
Federal	Results - ACP	Section G needs a summary / Section H sounds very promising	These sections have been completed.
Peer	Results - ACP	The section on advance care planning seemed extremely weak for me. This entire section reads as if it is the professional's plan, not the patient's.	This section has been revised extensively.
TEP	Results - Continuity	...on the discussion of advanced directives again are there any published papers in the national database and whether that has had any impact of a use of a national database.	The literature on advance directives and advance care planning was remarkable for the diversity of small studies with a variety of interventions or situations that were neither sustainable or generalizable. A national database of any sort would undoubtedly be helpful in building a more useful literature.
Federal	Results - Continuity	Expand the Continuity section if possible. An important topic that gets little attention.	This section has been expanded.
TEP	Results - Continuity	The discussion of continuity and coordination of care doesn't get into the issue of transfer orders	There is now some attention to these issues. There was not much evidence base with regard to transfers in end-of-life or palliative care.
Peer	Results - Family & Caregiver	…why is the section on caregiver burden placed under the Key Questions 2a and 3a (pg. 54)?	We have revised the section headings so this is no longer the case.
TEP	Results - Family & Caregiver	In the Caregiving section (perhaps this is already implied), I think we need to point out that there is great variability in cultural expectations of care, and very little research to understand this in a systematic way.	This has been added to the Discussion section of the report.
Peer	Results - Measures	Ultimately the value of these tools is related to their ability to be used effectively in the clinical setting.	See response just above.

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Peer	Results - Measures	…it is of concern that the "validity" of clinical indicators continues to be defined by their psychometric properties rather than by the results of application in the clinical setting.	This is probably true. There are very few rigorous reports of usefulness of measurement strategies in clinical medicine.
TEP	Results - Measures	Farsides B, Dunlop RJ. Measuring quality of life: Is there such a thing as a life not worth living? BMJ 2001;322:1481-3. Could you include?	This is indeed an important conceptual piece. Because it did not include original research it was not captured by our original search. We have now cited it.
TEP	Results - Measures	Have you reviewed George LK, Research design in end-of-life research: state of science. The Gerontologist 2002;42:86-98.	Yes - we cite her early in the work on the point of the scope of the field, for example.
Federal	Results - Measures	I have always had severe reservations about whether measures used to determine "successful" EOL are valid. As you note at various points in the review, quality of life, quality of care, satisfaction, etc. is almost entirely dependent on who you ask and when	That would be a potential springboard for an influential editorial, perhaps. The Task Order specified "satisfaction" and "better and worse outcomes." Our work was tied to the reports that addressed those concepts. Obviously, one of the outcomes of our work is to note that, as the reviewer says, there is no settled understanding of the merits of various ways to come to the end of life.
TEP	Results - Measures	The Support Team Assessment Schedule is widely used. STAS is a unique tool that assesses the clinical outcomes and intermediate outcomes of palliative care	We have included a description of this instrument in our measures section.
Federal	Results - Measures	waiting 6 months after the patient has died is probably too long for an accurate measurement of certain experiences. I am not sure if this is important to this report - but I would love to have the issue raised as a potential problem	We did not provide a review of the methodological issues in end of life care, of which this is one of the more troubling. That would be a good topic for future work.
TEP	Results - Satisfaction	...satisfaction is such a weak measure, your recommendations seem to support ongoing measurement for it. Would you be bold enough to suggest that it is not the approach that should be used?	We have added some language suggesting that broader constructs are needed - for example, "… the overall measures of a desirable care system may require constructs other than satisfaction". We have also suggested that satisfaction alone is not sufficient - but must be linked to processes of care.
Federal	Results - Satisfaction	First full paragraph - "..although that interventions..." needs re-write	This paragraph has been rewritten.
TEP	Results - Symptoms	…there has been a Cochrane review examining the control of breathlessness	We agree that this is an important review. We included it in our final report under discussion of dyspnea.

TEP	Results - Symptoms	I am of the opinion that there is an expanding literature on the treatment of depression in the elderly, which would be coded in that fashion not specifically disease related	We agree that this is a limitation of our report.
TEP	Results - Symptoms	... it's not exactly clear to me whether it is useful for you to refer to the previous State of the Science meetings that have focused on some aspects of these symptoms, particularly pain and emotional symptoms. I may be opening up a Pandora's box but there is a literature of recommendations that exist that are not captured anywhere in this report .	These were included because they were systematic reviews - this is the EPC methodology. We recognize that there is a large non-systematic literature that hasn't been included, especially clinical practice guidelines, and have added language to note this.
TEP	Results - Symptoms	A study by DuPen of a pain intervention demonstrated that the existing medical oncology pain approaches are not as good as pain expertise.	Since the DuPen study used a pre-post evaluation of a quality improvement endeavor, we did not include it as a priority research design.
TEP	Results - Symptoms	I couldn't help but wonder if the behavioral issues described under AD are in fact 'end of life' issues.	As the broader understandings of "end of life" would have it, serious chronic illness that worsens through to death would count - thus advanced dementia is in the category. This comports with the work of the national hospice organizations to reach out to serve dementia patients, too.
Peer	Results - Symptoms	It is worth emphasizing more strongly, the need for effective ways to quantify and compare distressing symptoms other than pain over time.	This has been added to the recommendations.
Peer	Results - Symptoms	The authors have missed a study on the role of oxygen versus air in patients with lung cancer subjected to exercise [Bruera E, et al, Palliative Medicine 2003] and a randomized control trial between morphine and placebo conducted before the study by Mazzocato et al [Bruera E, et al, 1993].	We were unable to access these articles in time to include in our report.
Peer	Results - Symptoms	The discussion of complementary and/or alternative medicine treatments is troublesome to me. For example, very broad terms such as "behavioral therapy" or "relaxation" are used. But one has no sense of what particular modalities were being evaluated in a given study.	We have tried to give a little description when citing a study of CAM. Reviews of CAM include a variety of approaches and the reader will have to go to the source to follow up on the specific modalities.

Peer	Results - Symptoms	The information regarding anxiety and depression reads as if it is being taken from some other polished document.	The writer in this section was better at drafting. This was not copied from some other document.
Peer	Results - Symptoms	The whole paragraph on pain is vague. The first sentence is inappropriate since there is no need for "high quality evidence" to support the palliation of pain at the end of life in conditions other than cancer.	We have removed that sentence and revised the paragraph. We do believe more studies of pain in conditions other than cancer are warranted.
Peer	Results - Symptoms	Under "Pharmaceutical Interventions" the authors have not captured a large number of studies on different opiod formulations….	We agree. We captured some, but not all of this literature. Due to the quantity of literature on this topic and limited time frame, we relied on systematic reviews.
TEP	Results - Symptoms	We should emphasize that key aspects of the "basic epidemiology" of pain and other symptoms in cancer and non-cancer populations is not only the prevalence, but the incidence or rate at which these symptoms occur. This point was emphasized in the NIH symptom conference last year.	This has been added to the research recommendations.
TEP	Results - Symptoms	Your analysis of the Smith reference doesn't really capture the importance of that study. There are two important features of that study that are not mentioned. First, patients were cared for in a standard oncology practice and when they received a pain assessment for potential participation in the trial, they received pain expertise management. This evaluation had a clear impact on their pain before they even entered the trial. Secondly, those patients who had the intervention with improved pain management lived longer than those who did not.	We have incorporated these important modifications to our interpretation of the study.
TEP	Results- Family & Caregiver	I am not sure if you are aware of the review on carer interventions with Harding and I conducted….	This systematic review went to the measures section.
TEP	Recommendations	…recommendation that should come out of this work is to undertake cross state and cross country studies	This is a very important recommendation that does not arise naturally from the examination of existing data. Since the reviewer will have the opportunity to present a good case for this at the conference in her session, we will be supportive without rewriting to make the case in the evidence report.

Appendix K. REVIEWER COMMENTS
"Evidence Report on End-of-Life Care and Outcomes"

Peer	Recommendations	I am unsure why in your final recommendations you talk about the neural basis of dyspnea. This was not a focus of the review.	We agree. Reference to the neural basis of dyspnea has been removed.
Peer	Recommendations	I'd suggest putting much of the summary information that is currently contained in recommendations into your section summaries.	We have revised the document accordingly.
Peer	Recommendations	In the recommendation section it might be easier if you used a consistent style – summarizing first what was known and then what is not known.	Recommendations have been extensively re-written.
Peer	Recommendations	These final sections become less of a review and more of a personal narrative and evaluation by the reviewer of the literature and interpretation of implications.	We have revised toward a settled style and a straightforward reporting of findings and recommendations.
TEP	Recommendations	...one is left with the impression that there is so little evidence of any value that there is not much basis for the existence of the field. It is a glass half full versus glass half empty disagreement. I hope you will reconsider the negative tone of the summary comments. The difference is subtle but important for this audience.	Thank you. The recommendations have been revised extensively.
TEP	Recommendations	…there is no clear executive summary that contextualizes the state of the science in an overall manner and that gives clear recommendations for the types of studies, designs and methodological approaches that will be required to answer the priority/key questions in the field.	An executive summary is now provided.
Federal	Recommendations	Chapter 4 needs a wrap-up section/paragraph	This section has been completed.
Federal	Recommendations	From a policy perspective, it would be good if you would summarize (using bullets) the research recommendations after each section in Chapter 4. That way policy makers can quickly identify what are the research needs.	This has been done.
TEP	Recommendations	I don't understand what the phrase "research estimation" means (about line 7 from the top).	This has been changed to "further research".
Federal	Recommendations	I found the recommendations weak considering again all that is not known.	These have been strengthened.

Appendix K. REVIEWER COMMENTS
"Evidence Report on End-of-Life Care and Outcomes"

TEP	Recommendations	It is probably worth stating that not only do we need to understand the use of non-pharmacological therapies, but we also need to understand the sequencing and combining of pharmacological and non-pharmacological therapies--apparently there is nothing in the literature on this very important clinical issue.	This has been added to the Discussion section.
Federal	Recommendations	Satisfaction section needs work	This section has been revised.
Peer	Recommendations	The conclusion reads like a very polished editorial or a lecture given by a palliative care leader to inspire future work, but it is not consistent with the remainder of the document or in scientific terms.	The concluding section has been entirely replaced and rewritten.
Peer	Recommendations	The recommendations section presently lacks much luster and seems oddly organized.	Recommendations have been extensively re-written.
Federal	Recommendations	The recommendations should be formatted as bolded statements and following by discussion.	We have revised accordingly.
TEP	Recommendations	There are two further references that might be very helpful for your research: [1] Chapter 13 in the NICE guidance manual deals specifically with a review of the evidence and the future directions for research. [2] Similarly, the recent World Health Organization guidance on Palliative Care for Older People and Palliative Care: The Solid Facts deals with research recommendations.	We read both documents and agree with many of the suggestions. This is reflected in the revised Discussion section.
Peer	References	This draft report has not yet undergone professional copyediting and has a number of typographical errors….reference 50 and 52 are both the same reference.	These errors have been corrected and we have undertaken much more copyediting.

First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Desbiens, 1998[1]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: Robert Wood Johnson Foundation	Sample size: 9105 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Hospitalization Outcomes: Pain, preferences of care Duration: 10 days Withdrawals: 6437	Results: Preference of care does not affect patients' overall pain experience in later stages of disease.
Gagnon, 2000[2]	Design: Prospective Cohort Quality: Fair Setting: Hospital (non ICU) Funding: NCI of Canada	Sample size: 94 Disease: Single disease: Cancer Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Delirium Outcomes: Delirium Duration: Not reported Withdrawals: 5	Results: Delirium as an outcome may not be as poor as previously considered in cancer.
Goodwin, 2003[3]	Design: Prospective Cohort Quality: Good Setting: Ambulatory/outpt medical care Funding: London Region NHS Research and Development Program	Sample size: 173 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Palliative Day Care Outcomes: Pain, symptom control, palliative day care, QOL Duration: 18 weeks Withdrawals: 56	Results: Palliative day care was not found to improve health related quality of life relative to usual care.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Lammi, 2001[4]	Design: Prospective Cohort Quality: Fair Setting: Hospice Funding: Europe Against Cancer Program of the European Union	Sample size: 100 Disease: Single disease: Cancer Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Palliative care Outcomes: Anxiety, depression Duration: >180 days Withdrawals: 28	Results: Awaresness of the multidimensional needs of hospice patients in primary health care centers is needed.
van der Steen, 2002[5]	Design: Prospective Cohort Quality: Fair Setting: Nursing home Funding: Dutch Ministry of Public Health	Sample size: 706 Disease: Unclear Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Antibiotic treatment for pneumonia Outcomes: Discomfort associated with pneumonia Duration: 3 months Withdrawals: 44	Results: Level of comfort is generally higher in demented patients who are not receiving antibiotics.
de Wit, 1999[6]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: Ducth Cancer Society	Sample size: 383 Disease: Single disease: Cancer Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Pain treatment Outcomes: Pain management Duration: 20 months Withdrawals: 77	Results: Structural resoruces were not the major cause of suboptimal pain management rather, the major cause was the process component.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Friedman, 2001[7]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: American Heart Association	Sample size: 212 Disease: Single disease: CHF Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Depression Outcomes: Physical symptoms, functioning, depression Duration: 6 weeks Withdrawals: 142	Results: High levels of physical symptoms and poor functioning patients reported higher levels of depression.
Fulop, 2003[8]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: NIMH Grant	Sample size: 263 Disease: Single disease: CHF Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Depression Outcomes: Hospitalization, health services utilization Duration: 6 months Withdrawals: 42	Results: High prevalence of depression in CHF patients at discharge depressed patients utilized more medical services.
Goldberg, 1997[9]	Design: Prospective Cohort Quality: Fair Setting: Nursing home Funding: Not reported	Sample size: 109 Disease: Single disease: Dementia Severity: Unclear Race: Not reported Gender: Not reported	Exposure: Risperidone Outcomes: Dementia-related bahavioral disturbances Duration: 6 months Withdrawals: 46	Results: Risperidone was well tolerated overall among nursing home residents and deemed helpful in 38% of sample, moderately helpful in 26% of sample, slightly helpful in 17% of sample and not helpful in 19% of sample.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Payne, 2002[10]	Design: Prospective Cohort Quality: Good Setting: Nursing home Funding: R-01 The depression in Alzheimer Disease Study	Sample size: 201 Disease: Single disease: Dementia Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Depression Outcomes: Depression Duration: One year Withdrawals: Not reported	Results: Incidence and prevalence of dementia is high in long term care facility residents incidence of depression seems to decrease within a year of admission is appropriate diagnosis and treatment were initiated.
Rumsfeld, 2003[11]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: Pharmacia Corporation	Sample size: 460 Disease: Single disease: CHF Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Depression Outcomes: Heart failure health status Duration: 6 weeks Withdrawals: Not reported	Results: Depressive symptoms are strong predictors of short term worsening HF specific health status.
Keene, 2002[12]	Design: Prospective Cohort Quality: Good Setting: Home health care Funding: Medical Research Council, Eli Lilly	Sample size: 100 Disease: Single disease: Dementia Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Behavioral symptoms Outcomes: Symptom experience, behavior, causes of death Duration: 11 years Withdrawals: 9	Results: Family members might benefit from prognostic information in terms of caregiving concerns.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Jiang, 2002[13]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: National Institute of Aging	Sample size: 374 Disease: Single disease: CHF Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Depression Outcomes: Depression, mortality, re-hospitalization Duration: One year Withdrawals: 43	Results: Major depression common in hospitalized patients and is associated with poor prognosis.
Breitbart, 2002[14]	Design: Prospective Cohort Quality: Fair Setting: Hospital (non ICU) Funding: Not reported	Sample size: 83 Disease: Single disease: Cancer Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Olanzapine Outcomes: Delirium Duration: 7 days Withdrawals: 4	Results: Olanzapine effective and safe for treatment of delirium in cancer patients.

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Evtab1. OS Continuity and Coordination Evidence Table

First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Bradley, 2001[1]	Design: Cross sectional Quality: N/A Setting: Hospital (ICU and non-ICU) Funding: Not reported	Sample size: 223 Disease: Single disease: Cancer Severity: Advanced Race: White, Hispanic, Black Gender: Males and females	Exposure: Demographic, clinical factors, hospice enrollment Outcomes: Chart documentation of a discussion about prognosis Duration: N/A Withdrawals: 232 / 325 approached agreed to medical record review	Results: Only 38% of charts included a documented discussion about prognosis, 29-45% of charts included discussions related to advance care planning. Non-physicians directed such discussion in 20/89 cases. Only emergency admission and length of stay, and hospital death were associated with increased odds of prognostic discussion in adjusted models.
Burge, 2003[2]	Design: Retrospective cohort secondary data analysis Quality: N/A Setting: Unclear Funding: Cancer Research and Education Nova Scotia (CaRE)	Sample size: 8702 Disease: Single disease: Cancer Severity: Advanced Race: Not reported Gender: Males and females	Exposure: MMCI as measured by family physician care - number of visits adjusted by number of physicians involved Outcomes: Emergency department use Duration: 6 months Withdrawals: N/A	Results: Patients with low continuity, MMCI < 0.5, made more emergency department visits (rate ratio 3.93) and those with intermediate continuity, MMCI 0.5-0.8 made more emergency visits (rate ratio 2.28) compared with those experiencing high continuity (MMCI > 0.8). Absolute number of visits approximately 2 in the lowest continuity group. Women and older patients less likely, and rural lower income, not enrolled in palliative care, receiving specialty treatment patients more likely to have emergency visits.

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Burge, 2003[3]	Design: Retrospective cohort secondary data analysis Quality: N/A Setting: Unclear Funding: Cancer Research and Education Nova Scotia (CaRE)	Sample size: 8702 Disease: Single disease: Cancer Severity: Advanced Race: Not reported Gender: Males and females	Exposure: MMCI as measured by family physician care - number of visits adjusted by number of physicians involved Outcomes: Emergency department use Duration: 6 months Withdrawals: N/A	Results: Patients with low continuity, MMCI < 0.5, made more emergency department visits (rate ratio 3.93) and those with intermediate continuity, MMCI 0.5-0.8 made more emergency visits (rate ratio 2.28) compared with those experiencing high continuity (MMCI > 0.8). Absolute number of visits approximately 2 in the lowest continuity group. Women and older patients less likely, and rural lower income, not enrolled in palliative care, receiving specialty treatment patients more likely to have emergency visits.
Tang, 2003[4]	Design: Prospective Cohort Quality: Good Setting: Home health care Funding: Roxane Laboratories	Sample size: 127 Disease: Single disease: mixed cancer Severity: Advanced Race: Not reported Gender: Males and females	Exposure: Not reported Outcomes: hospice home care use Duration: 2-293 days Withdrawals: Not reported	Results: 50% used hospice home care. Use of home care predicted use of hospice. Number and length of re-hospitalizations were higher for hospice home care group.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Tang, 2003[5]	Design: Prospective Cohort Quality: Fair Setting: Unclear Funding: Not reported	Sample size: 180 Disease: Single disease: Cancer Severity: Advanced Race: Non-hispanic white, other Gender: Males and females	Exposure: Demographic and clinical characteristics, social support, health system factors Outcomes: Site of death Duration: median of 36 days Withdrawals: 127 / 180 enrollees (207 approached) were eligible for analysis of site of death	Results: Only 30% of patients died at the site they preferred to die. In a limited model developed using variables selected for significance, re-hospitalization was significantly associated with a lower likelihood, hospice and perceived family support associated with a higher likelihood of achieving death in preferred site.
Wennberg, 2004 [6]	Design: Retrospective cohort secondary data analysis Quality: N/A Setting: Hospice and Hospital (ICU & non ICU) Funding: RWJF, NIA 1PO1AG19783-01	Sample size: 115089 Disease: Mixed Disease Severity: Advanced Race: Black, non-black Gender: Males and females	Exposure: High quality geriatric, cardiovascular, cancer, or pulmonary disease as indicated by US News and World Report rankings. Outcomes: Healthcare resource use, number of days spent in hospital or ICU, % of patients seeing 10 or more physicians, % enrolled in hospice - in last 6 months of life. Duration: 6 months Withdrawals: N/A	Results: On average, 37% of the cohort saw more than 10 physicians in the last 6 months of life, 40% died in hospital and 27% were admitted to hospice. There was widespread variation in the use of resources and intensity of care over the last 6 months of life in hospitals with high quality perceived care.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Townsend, 1990[7]	Design: Prospective Cohort Quality: Poor Setting: Home health care Funding: Harrow Health Authority, Rehabilitation Research Fund	Sample size: 84 Disease: Single disease: mixed cancer Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Not reported Outcomes: congruence between preference for location of death and actual site of death Duration: 5-18 mos (or until death) Withdrawals: 6	Results: Preference for site of death on initial interview: 58% at home, 20% in hospital, 20% in hospice, 2% other. Preference at final interview: 49% at home, 24% hospital, 25% in hospice. Of 32 who died in hospital, 63% had stated preference to die elsewhere.
Hutt, 2002[8]	Design: Retrospective cohort secondary data analysis Quality: N/A Setting: Nursing home Funding: CMS Contract No. 94-058	Sample size: 636 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Males and females	Exposure: Demographic, clinical factors, advance directives Outcomes: Hospitalization vs. no hospitalization during acute illness in the nursing home Duration: N/A Withdrawals: N/A	Results: For three tracer conditions (UTI, CHF, and pneumonia), hospitalization varied greatly during acute illness in the nursing home (UTI 11%, pneumonia 46%, CHF 58%). Older age decreased and male gender increased odds of hospitalization for CHF, male gender increased and DNR decreased odds of hospitalization for pneumonia. Weekend and night / evening shifts increased odds of hospitalization for UTI.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Burns, 2003[9]	Design: Prospective Cohort Quality: Poor Setting: Ambulatory/outpt medical care Funding: Australian Commonwealth Department of Health and Community Services	Sample size: 136 caregivers Disease: Single disease: mixed cancer Severity: Mixed Race: Not reported Gender: Males and females	Exposure: time Outcomes: Caregiver's knowledge of treatment intent Duration: 12 weeks Withdrawals: 51 (unclear)	Results: There was little change over time in caregiver's knowledge of treatment intent. 40% at week 1 vs 48% at week 12 understood that treatment would not cure. However, patient prognosis was associated with knowledge: only 10% of caregivers of patients with less than six months to live believed that the treatment intent was curative. IN bivariate analyses at baseline, multiple factors were statistically significantly associated with the view that treatment intent was curative, including male caregiver gender, older caregiver age, those who were still working, retired or unemployed (compared to those who had stopped work to care for the patient). Patient clinical characteristics associated with lack of caregiver understanding included breast or ovarian cancer and recruitment through radiation oncology.
Chin, 1997[10]	Design: Prospective Cohort Quality: Good Setting: Ambulatory/outpt medical care Funding: Not reported	Sample size: 257 Disease: Single disease: CHF Severity: Moderate Race: Not reported Gender: Not reported	Exposure: Not reported Outcomes: hospitalization Duration: 60 days Withdrawals: None	Results: 31% were re-hospitalized within 60 days. In multivariate analysis, neither race nor gender predicted re-hospitalization.

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Evtab1. OS Continuity and Coordination Evidence Table

First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Chin, 1997[10]	Design: Prospective Cohort Quality: Fair Setting: Ambulatory/outpt medical care and Hospital (non ICU) Funding: NIA K12-AG-00488 award	Sample size: 257 Disease: Single disease: CHF Severity: Moderate Race: White, non-white Gender: Males and females	Exposure: Demographic, clinical, and social characteristics Outcomes: Readmission Duration: 60 days Withdrawals: Not reported	Results: Single marital status, comorbidity, and other clinical variables were independently associated with risk of readmission. Risk of re-admission was 31% at 60 days.
Fried, 1997[11]	Design: Retrospective cohort secondary data analysis Quality: N/A Setting: Nursing home Funding: Not reported	Sample size: 3782 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Males and females	Exposure: Demographic, clinical, functional factors, advance directives. Outcomes: Hospitalization vs. no hospitalization during a six month period Duration: N/A Withdrawals: N/A	Results: Older, female residents hospitalized less frequently. Stage 2 or greater pressure ulcer, feeding tube, recent medication prescription associated with higher risk of hospitalization. Advance directives not associated with hospitalization. Moderate to severe cognitive impairment associated with lower risk and severe functional impairment a higher risk of hospitalization.

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Evtab1. OS Continuity and Coordination Evidence Table

First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Kane, 2003[12]	Design: Prospective Cohort Quality: Good Setting: Nursing home Funding: CMS	Sample size: ~4800 Disease: Mixed Disease Severity: Moderate Race: Not reported Gender: Not reported	Exposure: Evercare Outcomes: resource utilization: hospital, ER, physician, and psychotherapy use Duration: 15 months Withdrawals: 3% disenrollment in Evercare per month, "almost all due to death"	Results: Evercare is a capitated HMO for ong-stay nursing home residents. The model seeks to increase primary care intensity by employing nurse practitioners in contracted nursing homes to supplement the care of the primary care physicians and train nursing home staff. They enrolled 44 Evercare and control facilities and compared 3 groups: Evercare patients, patients in Evercare-contracted nursing homes not receiving Evercare, and patients in non-Evercare-contracted nursing homes. Patients were matched by admission date. Multivariate analyses controlling for multiple patient variables (but not accounting for clustering by facility) found fewer hospitalizations and less hospital use in the Evercare group, mainly by substituting nursing home care for hospital care. Preventable hospitalizations were also reduced. Patient attention was more than twice as high. No information is given on the terminally ill or those who died.

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Evtab1. OS Continuity and Coordination Evidence Table

First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Knol, 2003[13]	Design: Prospective Cohort Quality: Good Setting: Home health care Funding: Dutch government, University of Groningen, Faculty of Medical Sciences, Dutch Cancer Foundation, Netherlands Organization for Scientific Research	Sample size: 555 Disease: Mixed Disease Severity: Moderate Race: Not reported Gender: Not reported	Exposure: time Outcomes: utilization of professional home care Duration: 2 years Withdrawals: 555 are of an original sample of 753.	Results: Patients who died or couldn't participate in interviews due to illness were excluded. 25% were receiving home care initially, compared to 35% 2 years later. The best predictors of new home care use were high chronic morbidity, older age, and a high level of mastery. Lower income and less self-efficacy had borderline statistical significance. Disability and the amount of informal help did not play a role in prospectively determining home care use.
Heller, 2000[14]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU and non-ICU) Funding: Not reported	Sample size: 4981 Disease: Predominately one disease: Cardiovascular disease Severity: Moderate Race: Not reported Gender: Males and females	Exposure: Disease group (post-MI, other heart disease, CHF, or stroke), Demographic and clinical characteristics Outcomes: Death and readmission to a hospital the year after discharge for an index condition Duration: 1 year post-index discharge Withdrawals: None	Results: Patients with CHF had the highest risk for re-admission or death (49%) the year after index hospitalization. Stroke had a low re-admission rate of about 11%. Age was the most important consistent prognostic indicators.

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Evtab1. OS Continuity and Coordination Evidence Table

First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Holtzman, 1998[15]	Design: Prospective Cohort Quality: Good Setting: Home health care Funding: HCFA, Assistant Secretary for Planning and Evaluation	Sample size: 970 Disease: Mixed Disease Severity: Moderate Race: Not reported Gender: Not reported	Exposure: HMO care Outcomes: ADL function, hospital readmission Duration: 6 months Withdrawals: None in 6 weeks	Results: This study compared Medicare patients discharged after a CVA, COPD, CHF, hip replacement, or hip fracture repair. Information on end-of-life issues (such as mortality rate) is not reported. In multivariate analyses, there were no significant differences in hospital readmissions or ADL status by HMO or fee-for-service status.
Nourhashemi, 2001[16]	Design: Cross sectional Quality: N/A Setting: Hospital (non ICU) Funding: Not reported	Sample size: 118 Disease: Single disease: Dementia Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Not reported Outcomes: Emergency hospital admission Duration: N/A Withdrawals: 118 / 118 cases described	Results: Behavioral problems followed by falls.

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Evtab1. OS Continuity and Coordination Evidence Table

First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Stewart, 2002[17]	Design: Prospective Cohort Quality: Fair Setting: Home health care Funding: National Heart Foundation of Australia	Sample size: 90 Disease: Single disease: CHF Severity: Moderate Race: Not reported Gender: Not reported	Exposure: Not reported Outcomes: Early Clinical Deterioration hospital utilization Duration: 6 months Withdrawals: None	Results: Among 90 patients with chronic heart failure assigned to a multidisciplinary, home-based intervention and followed for 14 days, 2 died, 5 had an unplanned readmission, and 28 were clinically unstable at a planned home visit. The outcome of Early Clinical Deterioration (ECD) was defined as the combination of these 3 outcomes. In multivariate analysis, greater age and greater comorbidity were associated with ECD. ECD was associated with greatly reduced event-free survival (death or hospitalization) in the next six months.
Zweig, 2004[18]	Design: Prospective Cohort Quality: Good Setting: Nursing home Funding: AHRQ, HRSA, RWJ	Sample size: 1031 Disease: Mixed Disease Severity: Unclear Race: White, Black Gender: Males and females	Exposure: Evaluation for a lower respiratory tract infection Outcomes: Hospitalization Duration: 30 days Withdrawals: 21	Results: In logistic regression model, there was no significant difference in the adjusted odds of hospitalization within 30 days of evaluation for a lower respiratory infection for African-Americans. The adjusted odds ratio for males was borderline significant (1.42 (0.99-2.03). DNR orders decreased the odds of hospitalization (0.69 (0.49-0.97)).

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Collins, 1994[1]	Design: Prospective Cohort Quality: Good Setting: Nursing home and home Funding: NIMH	Sample size: N=142 (46 residential CGs vs. 49 CGs of institutionalized vs. 47 bereaved CGs) Disease: Single disease: Dementia Severity: Unclear Race: Caucasian (98%), African-American (2%) Gender: Males and females	Exposure: Three 60-90 minute interviews and complete a self-administered booklet (Intake, 22 months, 37 months) Outcomes: Depression . Duration: 3 years Withdrawals: Not reported	Results: No statistically significant differences were found among residential, institution, and bereaved caregivers on demographic characteristics. No statistically significant differences were found between the three groups on depression. Female bereaved caregivers experienced a pattern of decreasing depression following their relative's death while male bereaved caregivers experienced an increase.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Emanuel, 1999[2]	Design: Survey Quality: Good Setting: Home, nursing home, hospital (ICU) and hospice Funding: Commonwealth Fund & Nathan Cummings Foundation	Sample size: 988 terminally ill patients and 893 caregivers in 6 randomly selected areas of the US. 59% were over the age of 65 years and 51.5% were women (cancer 52%, heart disease-18%, and chronic obstructive pulmonary disease-11%). 4% were in a nursing home, hos Disease: Mixed Disease Severity: Advanced Race: White (79%), Black (14%), Hispanic (3%), Other (4%) Gender: Not reported	Exposure: Once Outcomes: Type of assistance needed. Duration: None Withdrawals: Not reported	Results: A need for assistance was reported by 87% of the patients, including help with transportation (reported by 62%), homemaking services (55%), nursing care (29%), and personal care (26%). Seventy-two percent of caregivers were women and 96% of caregivers were family members. Most patients relied completely on family members and friends for assistance. Only 15.5% of patients relied totally on paid assistance for more than half of the care they needed. Volunteers (unpaid helpers who were not family members) provided less than 3% of all care. In addition to medical care, dying patients often need many types of assistance. Family members, primarily women, provided the majority of assistance with non-medical care.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Grant, 2002[3]	Design: Prospective Cohort Quality: Good Setting: Nursing home and home Funding: NIA	Sample size: N=167 (119 CG and 48 non-caregiving comparison CG) Disease: Single disease: Alzheimer's Disease Severity: Mixed Race: Not reported Gender: Females	Exposure: baseline, 6 months, 12 months, 18 months Outcomes: CG physical and mental health. Duration: 18 months Withdrawals: Not reported	Results: CG who placed the care recipient in a NH or whose care recipient died showed improvement in depressive and physical symptoms compared to CG who continued to provide care and non-caregiving comparisons. Both placement and death of pt associated with higher blood pressure during transitions. However, there were continued symptoms long term after transtions.
Hays, 1994[4]	Design: Prospective Cohort Quality: Good Setting: Not reported Funding: NIMH & NIA	Sample size: N=1,112 caregivers Disease: Mixed Disease Severity: Advanced and moderate Race: White (91%), African American (8.5%), Hispanic (.5%) Gender: Females	Exposure: Baseline, 2 mo., 6 mo., 13 mo., and 25 mo. After enrollment Outcomes: Depression, General Anxiety, Feelings of Helplessness and Hopelessness. Duration: 2 years Withdrawals: 371 (25% of eligible respondents)	Results: Distress was related to the severity of the patient's illness, the actuality and timing of the bereavement, as well as the gender and age of the respondent.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Hodgson, 1997[5]	Design: Prospective Cohort Quality: Good Setting: Home health care Funding: Cancer Society, Europe Against Cancer	Sample size: N=757 pts (508 died while in HH) and 747 caregivers Disease: Single disease: Cancer Severity: Advanced Race: White (100%) Gender: Females	Exposure: Baseline, 2 weeks, week of death Outcomes: Cg function and ability to self-care, patient and family physical symptoms, psychological functioning, and communication. Duration: 6 months Withdrawals: Not reported	Results: 75% of patients died at home. 32% of families had severe or overwhelming anxiety. During the last week of care, anxiety remained severe for 26% of CGs. Patient and family well-being were inter-related and there were significant interactions between family anxiety and patient physical and psychological symptoms and communication. Family anxiety at referral strongly predicts family anxiety at last week of life. Excluding family anxiety at referral, other predictors for family anxiety were patient symptom control, sex of patient, diagnosis, and patient age.
Martikainen, 1998[6]	Design: Prospective Cohort Quality: Good Setting: Not reported Funding: Social Science Research Council, Academy of Finland	Sample size: N=5,500 widowed decedents Disease: Mixed Disease Severity: Advanced Race: Caucasian (100%) Gender: Not reported	Exposure: Baseline, 5 years later Outcomes: Mortality. Duration: 5 year Withdrawals: Not reported	Results: Results indicated that both men and women experience excess mortality after the death of a spouse and that the relative excess mortality among the bereaved is broadly similar in all education and income subgroups analyzed. The absolute mortality difference between widowed and married persons, however, tends to be larger among less educated and, especially, low-income persons.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Schulz, 2001[7]	Design: Prospective Cohort Quality: Good Setting: Unclear Funding: NIMH	Sample size: N=129 caregivers Disease: Single disease: Cardiovascular Disease Severity: Advanced and moderate Race: White (90%) Gender: Males and females	Exposure: Baseline, 3 annual in-person interviews, 2 years after Outcomes: Depressive symptoms, anitdepressant medication use, 6 health risk behaviors, weight. Duration: 4 years Withdrawals: 103	Results: CES-D scores remained high but did not change among strained caregivers (p=.76)while CES-D scores increased for both non-caregivers (p=<.001) and non-strained caregivers (p=.04). Non-caregivers signifcantly more likely to be using antidepressant medications following the death than non-strained group (p=.05). The strained CG group experienced significant improvement in health reisk behaviors following the death of their spouse (P<.001) while the non-caregiver and non-strained CG groups showed little change. Non-caregivers expereinced significant weight loss following the death while the strianed and non-strained CG groups did not. The impact of losing one's spouse among older persons varies as a function of the caregiving experiences that precede the death. Among individuals who are already strained prior to the death, the death itself does not increase their level of distress.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Schulz, 2003[8]	Design: Prospective Cohort Quality: Good Setting: Home Funding: NIMH	Sample size: N=217 caregivers Disease: Single disease: Alzheimer's Disease Severity: Advanced and moderate Race: White (66%), Black (20%), Hispanic (14%) Gender: Females	Exposure: Baseline, 6 months, 12 months, 18 months Outcomes: Number of hours/wk spent helping pt, type of assistance provided patient, CG burden and depression, medication use, impact of caregiving on employment, formal health service use, CG response to death of patient. Duration: 18 months Withdrawals: 48	Results: Overall, caregivers exhibited high levels of depressive symptoms while providing care to the relative with dementia (mean CES-D score: 15.8+ 11.7; median, 13). Forty-three percent of caregivers had scores above 15. At the death of the relative, depressive symptom scores spike to 22. However, within three months of the death of the relative, caregivers had clinically significant declines in the level of depressive symptoms, declining to a level similar to pre-bereavement levels 9mean, 16.2+12.3; median, 14). Within one year the levels of symptoms were substantially lower than at baseline (mean 11.5+9.4; median, 9) (P=0.03). Caregivers who cared for and then placed their relative in a nursing home had mean scores for depression of 17.1+11.9 (median, 15) before placement and mean depression scores of 18.1+13.0 (median, 15) after placement. One year after placement, depression scores remained high among and were significantly higher among caregivers of patients who had been institutionalized than among those caregivers of patients who had died (mean, 16.2 vs. 11.5; median, 14 vs. 9; P=0.02). Use of antidepressant medication and anxiolytic drugs increased after the death of the relative (16.6% and 19.4% before the death, 21% and 18% after the death). While the death of a close relative is generally viewed as a powerful source of psychological stress, the caregivers in this study showed remarkable resilience in adapting to the death of their relatives.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Teno, 2004[9]	Design: Telephone Survey Quality: Good Setting: Home, hospice, nursing home, and hospital (ICU and non-ICU) Funding: RWJ	Sample size: N=1578 respondents Disease: Mixed Disease Severity: Advanced Race: White (83%), Black (12%), Hispanic (3%) Gender: Males and females	Exposure: Survey Outcomes: Patient and family centered end of life care. Duration: None Withdrawals: 1697	Results: 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 1 or more concerns with family emotional support, compared with about 1/5 of those receiving home hospice services. Nursing home residents were less likely than those care for in a hospital or by home hospice services to always 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.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Tilden, 2004[10]	Design: Telephone Survey Quality: Good Setting: Home, nursing home, hospice and other Funding: NINR and RWJ	Sample size: N=1,089 widowed caregivers Disease: Mixed Disease Severity: Advanced Race: White (83%), Black (4.4%), Hispanic (3.9%), Asian-Pacific Islander (4.3%), American Indian (4.1%) Gender: Males and females	Exposure: Once Outcomes: Advance directives, hospice enrollment, use of life-sustaining treatments, perceived decedent symptom distress, financial hardship, out-of-pocket costs, family caregiver strain. Duration: None Withdrawals: 471	Results: 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.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Volicer, 2003[11]	Design: Mail Survey Quality: Good Setting: Home, nursing home, hospital (ICU and non-ICU) Funding: Alzheimer's Association and Dept. of Veterans Affairs	Sample size: n=156 Caregivers Disease: Single disease: Alzheimer's Disease Severity: Advanced Race: Caucasian (97%) Gender: Males and females	Exposure: Once Outcomes: Severity of dementia, Place of death, CG burden, CG satisfaction with care, enrollment in hospice, amount and type of help received by CG. Duration: None Withdrawals: Not reported	Results: 22% of pts died at home. Results suggest that end of life experiences of individuals with dementia differ according to setting of care. Patients cared for at home and receiving hospice care during last 90 days had fewer symptoms vs. other groups and fewer signs of physical distress during the dying process. Hospice use did not affect caregiver burden but these patients stayed at home 23 days longer and were twice as likely to die at home than in an institution. Caregivers of patients dying at home had increased time dependence burden but other burden scores were similar among all groups. Caregivers with patients dying both at home and in an institution were less satisfied with care than those cared for in only one setting. No effect on burden was found for use of formal or informal assistance. Psychiatric symptoms in the patient increased caregiver burden and were the most common cause of institutionalization. Receipt of psychiatric care was associated with longer stay at home. Presence of advance directive decreased hospital stays and increased the likelihood of dying in a nursing home. These results indicate that quality end of life dementia care can be provided at home by hospice and psychiatric care.

I = Intervention group, C = Control group, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive, MD = Physician, ACP = Advance Care Planning, AD/DPA = Advance Directive/Durable Power of Attorney,HRQoL = Health Related Quality of Life, T = Treatment group, DPA = Durable Power of Attorney

First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
McCarthy, 1997[12]	Design: Telephone Survey Quality: Good Setting: Hospital (ICU and non-ICU), home and other Funding: North East Thames Regional Health Authority, East Anglia Regional Health Authority, South East Thames Regional Health Authority, The Care Foundation, Tunbridge Wells, the Stanley Luff Bequest Fund	Sample size: 600 Caregivers Disease: Single disease: Cardiovascular Disease Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Once Outcomes: Information about illness, Knowledge of prognosis, Learning about dying, Support in dying, Place of death, Time to death. Duration: None Withdrawals: 75	Results: Just under half (47%) of caregivers felt they had not been able to get all the information regarding the deceased's illness that they had wanted or when they had wanted it. Thirty-seven percent of caregivers said they had known the deceased was likely to die and 26% said they had "half-known," whereas 26% of deceased patients were reported to have known and 25% were reported to have "probably" known that they were likely to die. Of those deceased patients who were reported to have known or probably known they were likely to die, most were reported to have had to work this out for themselves: only 8% were said to have been told by a GP or hospital doctor. Moreover, only 44% of caregivers were told of the terminal prognosis. Half of the patients (54%) died in hospitals, 30% at home, and 4% in other places. Patients under age 75 were less likely to die in an institution and more likely to die at home than patients 75 or older. Women aged 75 or older more frequently died in residential or nursing homes than males. A quarter of the deceased were reported to have expressed a wish to die sooner; more women than men were said to have expressed such a wish (30% vs. 17%, P<0.01). Moreover, decedents who were aged 75 or older were 2.6 times more likely to have expressed a wish to die sooner; those with four or more symptoms perceived as "very distressing" were 2.3 times more likely; and those who had a poor quality of life wee 1.9 times more likely to expressed such a wish.

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Evangelista, 2002[13]	Design: Prospective Cohort Quality: Good Setting: Home Funding: American Heart Association Western Division and the UCSF School of Nursing	Sample size: 103 CG/PT dyads Disease: Single disease: Cardiovascular Disease Severity: Advanced Race: White (77%), Black (6%), Other (17%) Gender: Males and females	Exposure: Once Outcomes: Emotional well-being. Duration: None Withdrawals: Not reported	Results: Caregivers were predominantly female (71%) and spouses of patients with HF (83%). Patients had significantly lower (poorer) emotional well-being scores than caregivers. Both gender and age were associated with patients' emotional well-being; male and younger respondents had higher (better) scores than female and older patients (P<.05). Patient's age, gender, and caregivers' emotional well-being accounted for 54% of the variance in patients' emotional well-being. Findings suggest that caregiver emotional well-being is associated with HF patient well-being. A focus on supporting caregivers and providing them with methods to support their loved ones would be beneficial to patients.

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Covinsky, 1994[14]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU & non ICU) Funding: RWJ	Sample size: N=2,129 caregivers Disease: Mixed Disease Severity: Advanced Race: White (81%), Black (16%), Other (3%) Gender: Males and females	Exposure: Baseline, 2 months, 6 months Outcomes: Frequency of adverse caregiving and economic burdens, patient functional status. Duration: 6 months Withdrawals: Not reported	Results: One third (34%) of patients required considerable caregiving assistance from a family member. In 20% of cases, a family member had to quit work or make another major life change to provide care for the patient. Loss of most or all of the family savings was reported by 31% of families, whereas 29% reported the loss of the major source of income. Patient factors independently associated with loss of the family's savings included poor functional status (OR 1.40; 95% CI 1.10 to 1.78), lower family income (OR 1.74; 95% CI 1.37 to 2.21 for those with annual incomes below $25,000_, and young age (OR, 2.85; 95% CI 2.13 to 3.82 for those younger than 45 years of age compared to those 65 or older). Families of younger, poorer, and more functionally dependent patients are the most likely to report loss of most or all of the family's savings to a serious or fatal illness.
Brazil, 2003[15]	Design: Interview Survey Quality: Fair Setting: Home, nursing home, hospital (ICU) and nursing home Funding: N/R	Sample size: N=151 caregivers Disease: Predominately one disease: Cancer Severity: Advanced Race: Not reported Gender: Males and females	Exposure: Once Outcomes: Physical restrictions, need for assistance, CG burden. Duration: None Withdrawals: Not reported	Results: The majority of respondents were the female spouses (79%) of the patient. The numbers of caregivers providing assistance in specific functional activities were: bathing (88%); mobility 81%); dressing and undressing (76%); TOILETING (67%); and assistance at night (64%). 41% reported that they had been providing some form of care for over 1 year. CGs reported that physical demands in caregiving increased substantially during the last three months of the care recipient's life. As family caregivers provided more assistance in ADLs, they were at greater risk of reporting high caregiver burden.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Emanuel, 2000[16]	Design: Interview Survey Quality: Good Setting: Home, nursing home, hospital (ICU) and hospice Funding: Commonwealth Fund & Nathan Cummings Foundation	Sample size: 988 terminally ill patients and 893 caregivers in 6 randomly selected areas of the US. 59% were over the age of 65 years and 51.5% were women (cancer 52%, heart disease-18%, and chronic obstructive pulmonary disease-11%). 4% were in a nursing home, hos Disease: Mixed Disease Severity: Advanced Race: White (79%), Black (14%), Hispanic (3%), Other (4%) Gender: Not reported	Exposure: Once Outcomes: Economic and non-economic burdens of caregiving. Duration: None Withdrawals: Not reported	Results: 35% of the sample had substantial care needs and that those with substantial care needs were more likely to report that they had a subjective sense of economic burden (44.9% vs. 35.3%; difference 9.6 percentage points [95% CI, 3.1 to 16.1]; P=0.005). In addition, 10% of these families household income was spent on health care (28% vs. 17%; difference, 11 percentage points [CI 4.8 to 17.1]; P<0.001) and that they or their families had to take out a loan or mortgage spend their savings, or obtain an additional job (16.3% vs. 10.2%; difference, 6.1 percentage points [CI 1.4 to 10.6]; P=0.004). Patients with substantial care needs were more likely to consider euthanasia or physician-assisted suicide (P=0.001). Caregivers of thee patients were more likely to have depressive symptoms (P=0.01) and to report that caring for the patients interfered with their lives (P=0.001). Caregivers of patients whose physicians listened to patients' and caregivers' needs had fewer burdens.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Markowitz, 2003[17]	Design: Interview Survey Quality: Good Setting: Nursing home and home Funding: Janssen Pharmaceutica Products, L.P.	Sample size: 2,477 dementia caregivers Disease: Single disease: Alzheimer's Disease Severity: Advanced and moderate Race: Not reported Gender: Males and females	Exposure: Once Outcomes: Health related quality of life, difficulty of caregiving, patient functioning level, IADLs, health care use. Duration: None Withdrawals: Not reported	Results: Compared with a normative, age-adjusted sample, the dementia caregivers had lower mental and physical scores (for the latter, only those 54 years of age or older). Increased caregiver mental functioning was associated with caregiver support and perceived quality of patient medical care, fewer hus of caregiving, and fewer patient behavioral symptoms.

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Steinhauser, 2000[18]	Design: Telephone Survey Quality: Good Setting: Hospital (ICU and non-ICU) Funding: VA Health Services Research and Development award	Sample size: N=1,462 (340 seriously ill patients, 332 recently bereaved family members, 361 physicians and 429 other health care providers = nurses, social workers, chaplains, and hospice volunteers) Disease: Other: Severity: Other Race: White (82%), African American (7.4%), Asian American (3.6%), Latino (2.2%), Native American (3.4%), Other (1.9%) Gender: Males and females	Exposure: Once Outcomes: End of Life factors considered important by patients, families, physicians and other health care providers. Duration: None Withdrawals: Not reported	Results: 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.” Additionally, respondents expressed a strong preference for human development at the end of life. 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 4 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 9 major attributes. Thus, although pain and symptom management, communication with one’s physician, preparation for death, and the opportunity to achieve a sense of completion are important to most, other factors important to quality at the end of life differ by role and by individual.

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Baker, 2000[1]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU and non-ICU) Funding: RWJF	Sample size: 726 Disease: Mixed Disease Severity: Advanced Race: White, non-white Gender: Males and females	Exposure: pain, disease category, functional status, use of life sustaining treatment, circumstances of death Outcomes: Satisfaction with communication and comfort pain, disease category, functional status, use of life sustaining treatment, circumstances of death. Duration: up to 6 months Withdrawals: 216 / 983 deaths	Results: Gender of surrogate (male) associated with lower and death and intervention status associated with higher satisfaction with comfort. Not following preferences, and great and moderate impact on family finances associated with lower satisfaction with communication.
Correa-Velez, 2003[2]	Design: Prospective Cohort Quality: Good Setting: Ambulatory/outpt medical care Funding: National Health and Medical Research Council #991215	Sample size: 111 Disease: Single disease: Cancer Severity: Advanced Race: Not reported Gender: Not reported	Exposure: physical symptoms, psychological symptoms, satisfaction with conventional medical care, Outcomes: Physical symptoms, psychological symptoms, satisfaction with conventional medical care, complementary and alternative medicine (CAM) use. Duration: 12 months Withdrawals: 11/111 too ill to participate in longitudinal phase	Results: Complementary and alternative medicine (CAM) use was associated with lower satisfaction with conventional medical (e.g. oncology) care, non-users of CAM were even more dissatisfied in last 3 months of life.

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Curtisa, 1999[3]	Design: Prospective Cohort Quality: Good Setting: Ambulatory/outpt medical care Funding: University of Washington Intramural funds	Sample size: 57 Disease: Single disease: AIDS Severity: Advanced Race: Not reported Gender: Not reported	Exposure: degree of MD-patient communication about end of life care Outcomes: Presence and quality of patient-physician communication about end of life care, preferences for life-sustaining treatment, satisfaction with care. Duration: 6 months Withdrawals: 5 / 57 (baseline only)	Results: Lower income patients noted lower quality of communication, higher quality of communication associated with higher overall satisfaction with care.
Fakhoury, 1996[4]	Design: Retrospective cohort Quality: N/A Setting: Unclear Funding: Hariri Foundation, ORS award, UK regional health authorities, Care Foundation Tunbridge Wells	Sample size: 1858 Disease: Single disease: Cancer Severity: Advanced Race: White, non-white Gender: Males and females	Exposure: service characteristics of end of life care Outcomes: satisfaction with district nurse, general practitioner, and hospital physician care multiple sociodemographic, informal caregiver, and service characteristics. Duration: N/A Withdrawals: N/A	Results: High level of satisfaction for nurses, GP's, and hospital MDs noted. Stepwise procedures used to select from expansive regressor set.

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Fakhoury, 1997[5]	Design: Retrospective cohort Quality: N/A Setting: Unclear Funding: Hariri Foundation, ORS award, UK regional health authorities, Care Foundation Tunbridge Wells	Sample size: 1858 Disease: Single disease: Cancer Severity: Advanced Race: White, non-white Gender: Males and females	Exposure: service characteristics of end of life care Outcomes: Satisfaction with district nurse, general practitioner, and hospital physician care multiple sociodemographic, informal caregiver, and service characteristics. Duration: N/A Withdrawals: N/A	Results: Owner-occupiers, older patients, spouses vs non spouses, those with short duration of several symptoms somewhat higher satisfaction measures. Multiple comparisons.
Fisher, 2003[6]	Design: Retrospective cohort secondary data analysis Quality: N/A Setting: Unclear Funding: RWJF, NIH CA52192, NIA 1PO1 AG19783-01	Sample size: ~1,000,000 Disease: Predominately one disease: 3 cohorts (hip fracture, colorectal cancer, acute myocardial infarction) Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Clinical and demographic characteristics, End of Life Exposure Index (EOL-EI) Outcomes: Mortality, functional status change, and satisfaction with care. Duration: N/A Withdrawals: N/A	Results: Higher spending at the end of life not associated with reducted mortality, improved functional status, or greater satisfaction with care in any cohort.

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Heyland, 2003[7]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU) Funding: Canadian ICU Foundation, Queen Elizabeth II Hleath Sciences Center Research Foundation	Sample size: 256 Disease: Mixed Disease Severity: Advanced Race: N/A Gender: Not reported	Exposure: overall experience related to death of a loved one, communication Outcomes: Overall death experience, communication, overall satisfaction. Duration: 4 weeks Withdrawals: 256 / 413 responded	Results: Higher percieved courtesy and compassion, satisfaction with overall level of care, completeness of information provided were all associated with higher overall satisfaction with ICU care.
Higginson, 2002[8]	Design: Prospective Cohort Quality: Good Setting: Hospice Funding: European Commission, International Union Against Cancer for the International Cancer Fellowship	Sample size: 1326 Disease: Mixed Disease Severity: Advanced Race: N/A Gender: Males and females	Exposure: enrollment in palliative care service Outcomes: Quality of life including communication. Duration: median, approximately 30 days Withdrawals: Not reported	Results: No gender differences in communication (trend toward lower difficulties in professional / pt / family communication among women, but not significant (p=0.09)), nor differences in interprofessional or professional / pt / family communication by site of death were observed.
Kristjanson, 1997[9]	Design: Cross sectional cohort Quality: N/A Setting: Home health care and hospice Funding: NCI Canada, Manitoba Health Research Council	Sample size: 72 Disease: Mixed Disease Severity: Advanced Race: N/A Gender: Not reported	Exposure: family expectations and functioning Outcomes: Family care expectations, family functioning, satisfaction. Duration: N/A Withdrawals: 72 / 82 responded	Results: Satisfaction differed by geographic province, higher among younger families, discrepancy score between expectations and perception of care was significantly related to satisfaction, site of care unrelated.

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Larsson, 2004[10]	Design: Cross sectional cohort Quality: N/A Setting: Home health care Funding: Not reported	Sample size: 67 Disease: Unclear Severity: Advanced Race: N/A Gender: Not reported	Exposure: gender, age, and status (spouse, child, other) of family member, frequency of contact Outcomes: Patient and family perceptions of care. Duration: N/A Withdrawals: 67 / 100 responded	Results: Family members with more frequent contact both perceived better care and rated the perceived importance of those aspects of care to the patient's wellbeing higher than family members with less frequent contact.
Malacrida, 1998[11]	Design: Retrospective cohort Quality: N/A Setting: Hospital (ICU) Funding: 125th Jubileum Basle Insurance Company	Sample size: 123 Disease: Mixed Disease Severity: Advanced Race: N/A Gender: Males and females	Exposure: quality of the ICU experience Outcomes: Family members perceptions of care delivered in the ICU. Duration: N/A Withdrawals: 123 / 390 respondents	Results: Multiple bivariate comparisons up to eight years after death.

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Sulmasy, 2002[12]	Design: Cross sectional cohort Quality: N/A Setting: Hospital (non ICU) Funding: Altman Foundation	Sample size: 84 Disease: Mixed Disease Severity: Advanced Race: White, non-white Gender: Males and females	Exposure: pain, depression, nature of nursing and physician care Outcomes: Symptoms severity, anxiety and depression, perceptions and satisfaction with physicians and nurses. Duration: N/A Withdrawals: 110 /367 refused 84 / 88 remaining eligibles for current survey	Results: Only +DNR status, house-staff vs. private physician service status, and depression significant in multivariate models. All were associated with lower satisfaction with physician and nursing care.
Teno, 2004[13]	Design: Retrospective cohort Quality: N/A Setting: Hospice, nursing home and Hospital Funding: RWJF	Sample size: 1578 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Not reported	Exposure: services and setting of care at the end of life Outcomes: Family perceptions of end of life care. Duration: N/A Withdrawals: 1578 / 3275 deaths	Results: Death in home hospice associated with improved satisfaction by all unadjusted measures, and improved emotional support, family emotional support, perceptions of treating patient respectfully, and overall quality compared to home care, nursing home, and hospital dying. Inadequate physician involvement, coordination noted in hospital and nursing home settings in particular.

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Tierney, 1998[14]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: AHRQ (RO1 - HS07632, 07763, 09083	Sample size: 42 (26 witth 2 measurements) Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Not reported	Exposure: inpatient hospice treatment Outcomes: Satisfaction, quality of life, symptoms. Duration: 3-4 days Withdrawals: 16/42 (baseline only)	Results: Higher satisfaction highly correlated with better quality of life on admission, and also with better symptom control at follow-up.
Tolle, 2000[15]	Design: Retrospective cohort Quality: N/A Setting: Hospice, nursing home and Hospital Funding: Proejct on Death in American, Meyer Memorial Trust, RWJF, Nathan Cummings Foundation	Sample size: 475 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Not reported	Exposure: services and setting of care at the end of life Outcomes: Family perceptions of end of life care. Duration: N/A Withdrawals: 475 / 1,458 deaths	Results: Transfers in care settings associated with respecting treatment preferences, pain management. Neither advance care planning and respect for treatment preferences, nor satisfaction with support from clinicians differed by setting of care. Report of pain comparable to Teno et.al., worse in hospital. Most difficulties in management of pain associated with home death. Difficulties with respect for treatment preferences and support from clinicians associated wtih worse pain management.
Volicer, 2001[16]	Design: Retrospective cohort Quality: N/A Setting: Unclear Funding: Alzheimer's Association, USPHS P30 AG13846	Sample size: 156 Disease: Single disease: Dementia Severity: Advanced Race: Not reported Gender: Not reported	Exposure: services and setting of care at the end of life Outcomes: Family perceptions of end of life care. Duration: N/A Withdrawals: 156 / 572 surveys returned	Results: Unclear sampling frame. Symptom scale and comfort scales modestly (~0.30) correlated with scale assessing aspects of health care and decision making.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Zhukovsky, 1995[17]	Design: Cross sectional cohort Quality: N/A Setting: Hospital (non ICU) Funding: Not reported	Sample size: 101 Disease: Single disease: Cancer Severity: Unclear Race: Not reported Gender: Not reported	Exposure: pain and physician management of pain Outcomes: Pain, satisfaction with pain control. Duration: N/A Withdrawals: 101 / 171 approached	Results: Worse pain, belief that physician not adequately concerned about pain, and desire for more control in pain regimen associated with dissatisfaction with pain management.
Dawson, 1991[18]	Design: Retrospective cohort Quality: N/A Setting: Home health care, hospice and hospital Funding: Not reported	Sample size: 100 Disease: Unclear Severity: Advanced Race: Not reported Gender: Not reported	Exposure: site of care and death Outcomes: Emotional needs of patient and family, satisfaction with psycho-social support of nurse caregivers, overall satisfaction with medical care. Duration: N/A Withdrawals: 100 / 179 surveys returned	Results: Hospice users who died at home more satisfied by all measures than hospice users who died in other settings or non-hospice users who died in hospital.
Jacoby, 1999[19]	Design: Retrospective cohort Quality: N/A Setting: Hospice, nursing home and Hospital Funding: Not reported	Sample size: 156 Disease: Unclear Severity: Advanced Race: Not reported Gender: Not reported	Exposure: service quality and site of care Outcomes: Family perceptions of end of life care. Duration: N/A Withdrawals: 156 / 355 surveys returned	Results: Satisfaction with different practitioners and settings of care correlated with perceived efforts to relieve symptoms and communication.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Kane, 2002[20]	Design: Cross sectional cohort Quality: N/A Setting: Ambulatory/outpt medical care Funding: HCFA #500-96-0008	Sample size: 1161 Disease: Mixed Disease Severity: Moderate Race: Not reported Gender: Not reported	Exposure: Wisconsin Partnership Program participation Outcomes: Functional status, caregiver burden, advance directives, service attributes and satisfaction. Duration: N/A Withdrawals: 1161 / 1372	Results: WPP participants demonstrated much higher levels of advance care planning and preference for limiting care compared with in-area controls. Satisfaction with care was largely no different, although in-area and out-of-area controls were more likely to report that their doctor treats them with respect, and that their care is well coordinated. Few to no differences in care-giving burden.
Steinhauser, 2000[21]	Design: Cross sectional cohort Quality: N/A Setting: Unclear Funding: VA HSR&D IIR 96-066	Sample size: 1462 Disease: Mixed Disease Severity: Advanced Race: White, African-American, Asian-American, Latino, Native American, Other Gender: Males and females	Exposure: N/A Outcomes: Ratings of attributes of experiences at the end of life. Duration: N/A Withdrawals: 1462 / 2000	Results: Areas of concordance and discordance identified in the relative importance of 44 items related to symptoms or personal care, preparation for end of life, achieving a sense of completion, care planning, being treated as a 'whole person', and relationships with health professionals as noted by patients, physicians, family, and other providers. Race / gender, religiousness / spirituality, and relationship to deceased all related to various items or groups of items.

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Evtab5. OS Advance Care Planning

First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Curtis, 1999[1]	Design: Prospective Cohort Quality: Good Setting: Not reported Funding: 1) Pickner/ Commonwealth Scholars Program, 2) University of Washington Royalty Research Fund, 3) University of Washington Center for AIDS Research	Sample size: 57 Disease: Single disease: AIDS Severity: Moderate Race: Not reported Gender: Not reported	Exposure: Initial interview. Outcomes: Quality of patient-clinician communication about EOL care. Duration: 6 months Withdrawals: 4 pts.	Results: Occurrence of concordance on the presence of a LW associated with EOL communication. Better communication with higher patient income and non-Hispanic whites.
Curtis, 2000[2]	Design: Prospective Cohort Quality: Fair Setting: Ambulatory/outpt medical care Funding: 1) Project on Death in America, 2) Parker B. Francis Fellowship Program, 3) University of Washington Royalty Research Fund	Sample size: 57 Disease: Single disease: AIDS Severity: Moderate Race: Not reported Gender: Males and females	Exposure: One-time. Outcomes: Barriers and facilitators of patient-clinician communication about EOL. Duration: Unclear Withdrawals: Not reported	Results: Patients identified barriers associated with EOL education, EOL counseling, health care system changes. Clinicians identified more barriers than patients. Nonwhite patients reported more barriers: fear of talking about death and its impact on available care and unwillingness to talk about future health status.

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Golin, 2000[3]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU & non ICU) Funding: RWJ (SUPPORT)	Sample size: 1288 Disease: Mixed disease: Cancer, Chronic disease Severity: Advanced Race: Black, Other Gender: Males	Exposure: Pts enrolled in SUPPORT. Outcomes: Communication of pts resuscitation preferences with their physicians. Duration: 2 month follow up Withdrawals: Not reported	Results: 30% of pts communicated resuscitation preferences to physicians. Pts wanting to forgo CPR and whose preferences changed from desiring to forge CPR were more likely to communicate their preference than pts who continued to prefer to receive CPR. 50% of pts maintain preference to forgo CPR communicated their preferences over the study period. Having an AD and remaining in hospital associated with communication.
Higginson, 2002[4]	Design: Prospective Cohort Quality: Good Setting: Hospice and Home Funding: 1) European Commission & 2) International Union Against Cancer for the International Cancer Fellowship	Sample size: 1326 Disease: Single disease: Cancer (Digestive, Respiratory, Breast, Genitourinary, Other) Severity: Advanced Race: Not reported Gender: Males and females	Exposure: Time between first visit and death. Outcomes: Responsiveness to clinically important changes, correlation with other measures, correlation between patient self-assessment, family assessment, and team assessment. Duration: Data collected over a 6-month period Withdrawals: Not reported	Results: 40% of EOL patients had severe communication. Communication problems associated with respiratory & breast cancers, shorter time in care, and hospice death.

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Lockhart, 2001[5]	Design: Prospective Cohort Quality: Fair Setting: Community Funding: AHRQ-HS08180	Sample size: 50 Disease: 8: Severity: Unclear Race: Not reported Gender: Not reported	Exposure: Initial interview - pts asked to imagine 7 different states. Outcomes: Participant rating of 7 states better/worse than death. Duration: Sub sample of 50 participants re-contacted, 5-16 months, asked same questions Withdrawals: 0	Results: Moderate stability in ratings of state that were better or worse than death.
Rose, 2000[6]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU & non ICU) Funding: RWJF (SUPPORT)	Sample size: 642 Disease: Single disease: Cancer Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Beginning of SUPPORT. Outcomes: Compare 844 oncologist pts. to 449 generalist pts. Duration: 6 months or pt. death Withdrawals: Not reported	Results: Generalists more pessimistic than specialists in prognostication. Similar LOS, discharge with supportive care, and hosp. readmission. Proportionally, more hospital deaths with generalists.
Tierney, 2001[7]	Design: Prospective Cohort Quality: Good Setting: Ambulatory/outpt medical care Funding: AHRQ Grant-Ro1-HS07632	Sample size: 686 Disease: Mixed Disease Severity: Unclear Race: African American Gender: Males	Exposure: Pt. visit when physician received computer reminder - part of the Dexter RCT. Outcomes: Level of patient satisfaction. Duration: Interview in waiting room following visit Withdrawals: 74	Results: Discussing advance directives associated with greater satisfaction with primary care physician. Elderly, chronically ill patients are more satisfied when they discuss ADs with their primary care physician.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Weeks, 1998[8]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: 1) RWJF (SUPPORT) & 2) American Society of Clinical Oncology	Sample size: 917 Disease: Predominately one disease: Lung cancer or colon cancer metastatic to liver Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Pts enrolled in SUPPORT. Outcomes: Relationship between pts prognostic estimates and their treatment preferences. Duration: After enrollment in SUPPORT Withdrawals: Not reported	Results: Pts estimating at least 6-month survival favored life-extending therapy over comfort care. Pts overestimated survival time.
Wenger, 2000[9]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU & non ICU) Funding: RWJF (SUPPORT)+C191	Sample size: 5055 Disease: Not reported Severity: Advanced Race: White Gender: Males	Exposure: Pts enrolled in SUPPORT. Outcomes: Physician understanding of pts CPR preferences. Duration: Between second to sixth day after study enrollment Withdrawals: Not reported	Results: Physicians did not know of pts CPR preferences.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
McCarthy, 1997[10]	Design: Prospective Cohort Quality: Good Setting: Unclear Funding: 1) North East Thames, South East Thames, and East Anglia Regional Health Authorities, 2) South East Thames Regional Health Authority, 3) Care Foundation Tunbridge Wells, 4) Stanley Luff Bequest Found, 5) Other participating districts	Sample size: 600 Disease: Single disease: Heart disease Severity: Advanced Race: Not reported Gender: Males and females	Exposure: Pt Death. Outcomes: Information about illness, knowledge of prognosis, learning about dying, support in dying, place of death, and timing of death. Duration: Follow-up with spouse, another relative, friend or neighbor, or formal carers. Withdrawals: Not reported	Results: Despite recognizing they were going to die, clinical staff rarely discussed the pts. Likelihood of death. Lack of discussion with pt on preferred place of death.
Townsend, 1990[11]	Design: Prospective Cohort Quality: Good Setting: Hospital (non-ICU) and community Funding: 1) Harrow Health Authority & 2) Rehabilitation Research Fund	Sample size: 100 Disease: Single disease: Cancer Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Cancer pts expected to live less than 1 year. Outcomes: Place of death, care before death. Duration: Pts interviewed at 2 week intervals if expected to live less than 2 months Withdrawals: 34	Results: Pts knew diagnosis and prognosis. Most pts admitted for investigation or treatment, but often stayed for respite and symptom control. 63% of pts who died in hospital, would prefer to die at home.

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Danis, 1991[12]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: AHRQ - HS06655	Sample size: 244 Disease: Mixed Disease Severity: Advanced Race: White, Black Gender: Males and females	Exposure: Pts. With short life expectancy due to end-stage heart, lung, or liver disease, metastic cancer, or lymphoma. Outcomes: Life-sustaining treatment utilization & cost of hospital care. Duration: Followed for 6 months Withdrawals: 258	Results: Majority of pts wanted to receive life-sustaining treatment to prolong life. Chemotherapy and intensive are were the most frequent treatments. CPR and mechanical ventilation were the most frequently withheld. Pts decising life-sustaining treatment to prolong life were no more likely to receive treatments than pts who desired limited treatment.
Hakim, 1996[13]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU & non ICU) Funding: RWJF (SUPPORT)+C210	Sample size: 8836 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Pts enrolled in SUPPORT. Outcomes: Association between pts resuscitation preferences and frequency and timing of DNR orders. Duration: Third day after study enrollment Withdrawals: Not reported	Results: DNR orders written earlier for pts older than 75 years of age, regardless of prognosis. Pt preferences associated with timing of DNR orders.

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First Author Year ID	Study Characteristics	Population	Exposure, Outcomes Duration, Dropouts	Results
Junod Perron, 2002[14]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: Not reported	Sample size: 255 Disease: Predominately one disease: Cancer (Metastatic) Cardiac disease, Other Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Pts who stayed more than 24 hours in hospital, and were provided with a DNR order. Outcomes: Agreement between physicians and DNR pts. Perception of quality of life. Duration: 5 days following DNR order implementation Withdrawals: Not reported	Results: Quality of life was considered in more than 70% of DNR decisions. Physicians underrate their DNR pts. quality of life. Severe depression, social isolation and physical dependence negatively influenced patient's perception of their quality of life.
McParland, 2003[15]	Design: Prospective Cohort Quality: Good Setting: Nursing home Funding: American Federation for Aging Research/John A. Harford Foundation Fellowship	Sample size: 65 Disease: Unclear Severity: Unclear Race: Not reported Gender: Not reported	Exposure: Nursing home residents. Outcomes: CPR and hydration and nutrition preferences. Duration: 12 and 24 months Withdrawals: 21	Results: Change in cognitive status related to changes in decision. Preferences changed at 12 and 24 months.

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Azoulay, 2000[16]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU) Funding: Not reported	Sample size: 102 Disease: Unclear Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Representatives of pts visited by at least one person during their ICU stay. Outcomes: Representatives' comprehension of the diagnosis, prognosis, and treatment of the pt. Duration: 2 days after ICU admission. Withdrawals: 124	Results: Families poor comprehension related to the age, unemployment, and referral from hematology or oncology ward, admission for acute respiratory failure or coma, and favorable prognosis. Family-related factors were foreign descent, not French speaking, not the spouse, and no healthcare professional in family.
Butow, 1997[17]	Design: Prospective Cohort Quality: Good Setting: Ambulatory/outpt medical care Funding: Not reported	Sample size: 80 Disease: Predominately one disease: Cancer (Breast, Genitourinary, Colon, Lung, Other) Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Pts seeing oncologists in outpatient clinic, completed a questionnaire before a directly after one consultation. Outcomes: Differences in general information and involvement preferences before and after consultation. Duration: Pts complete questionnaire before their next consultation. Withdrawals: 38	Results: Females wanted more detailed information than males. Those whose follow-up visit encompassed a significant change in their condition were more likely to prefer having the doctor make decisions. General information and involvement preferences were relatively stable in the short term despite medical intervention. By the time of their next consultation, pts preferences had shifted considerably.

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Phillips, 2000[18]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU & non ICU) Funding: RWJF (SUPPORT)	Sample size: 9105 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Females	Exposure: Pts enrolled in SUPPORT. Outcomes: Timing of decisions to withold or withdraw ventilator support and dialysis, and decisions to withhold surgery. Duration: Between hospital days 3 and 6 after enrollment Withdrawals: Not reported	Results: Decisions to withhold or withdraw ventilatory support or dialysis, or withhold surgery, varied by race. African American pts more likely to prefer life-extending treatments.
Teno, 1997[19]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU & non ICU) Funding: RWJF (SUPPORT)	Sample size: 4804 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Time of study enrollment in SUPPORT. Outcomes: Relationship between AD in record and hospital utilization. Duration: 6 months follow up or death. Withdrawals: Not reported	Results: ADs in medical records did not guide medical decision-making. Despite specific instructions, care was inconsistent in half of the cases.

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Teno, 1998[20]	Design: Prospective Cohort Quality: Good Setting: Hospital (ICU & non ICU) Funding: RWJF (SUPPORT)	Sample size: 14 Disease: Mixed Disease Severity: Advanced Race: Not reported Gender: Not reported	Exposure: Patient receives patient-specific information on prognosis and specially trained nurse to facilitate decision-making. Pt has AD. Outcomes: Role of AD in decision-making. Duration: Timeline of communication and decision-making. Withdrawals: Not reported	Results: Pt had a period of diminished capacity when AD should have been invoked. AD used in 5 of 14 cases. Complex interaction of several factors associated with AD having a limited role.
Wenger, 2000[21]	Design: Prospective Cohort Quality: Good Setting: Hospital (non ICU) Funding: Not reported (SUPPORT)	Sample size: 565 Disease: Single disease: Kidney Disease Severity: Advanced Race: White Gender: Males	Exposure: Pts enrolled in SUPPORT. Outcomes: Predictors of decisions to withhold or withdraw dialysis. Duration: Between 2 and 7 days after study enrollment Withdrawals: Not reported	Results: Dialysis withheld associated with older men with a cancer diagnosis.

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I = Intervention group, C = Control group, RCT/CCT = Randomized Controlled Trial/Clinical Controlled Trial, ICU = Intensive Care Unit, CPR = Cardiopulmonary Resuscitation, RN = Registered Nurse, DNR = Do Not Resuscitate, outpt = Outpatient, AD = Advance Directive, MD = Physician, ACP = Advance Care Planning, AD/DPA = Advance Directive/Durable Power of Attorney,HRQoL = Health Related Quality of Life, T = Treatment group, DPA = Durable Power of Attorney