

End-of-Life Care and Outcomes

Summary

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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?**

- 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).

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 death⁶⁻⁸ 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:

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 superseded 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.

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