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 acknowledging 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. 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. 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. Measured 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.
Reference List


