Palliative Care in Advanced Dementia

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KEYWORDS
• Dementia • Palliative care • End-of-life care • Cognitive impairment
• Skilled nursing facilities • Advance directives

KEY POINTS
• Neurodegenerative dementias are progressive and ultimately fatal diseases for which currently there is no cure. A palliative approach focusing on comfort, quality of life, and support of family and caregivers is appropriate.
• Primary care providers for patients with dementia should become proficient in the following basic discussions of prognosis and goals of care, advance care planning, avoidance of polypharmacy when possible, pain management, and initial management of behavior and mood issues.
• There is no evidence that enteral feeding improves survival or comfort in patients with advanced dementia, and it may increase the risk of pressure ulcers and aspiration pneumonia. Careful hand-feeding is the recommended alternative.
• Infections are common in advanced dementia; antibiotics may very modestly prolong life, but may decrease comfort and contribute to antibiotic resistance and burdensome care transitions at the end of life.
• Patients with advanced dementia and behavioral disturbance should be assessed for delirium and pain, and empirical treatment of pain is often warranted.

Cure sometimes, treat often, comfort always.
—Hippocrates

THE EPIDEMIOLOGY OF ADVANCED DEMENTIA

Approximately 35.6 million people worldwide are thought to be currently living with dementia, approximately 0.5% of the population, and numbers will increase as more...
individuals live into advanced age. In the United States, the number of people with dementia is estimated to increase from 4.4 million in 2010 to 11 million in 2050. Alzheimer disease (AD) is the most common type of dementia, representing 50% to 80% of cases (depending on whether “pure” or “mixed” cases are included), followed by vascular dementia (20%–30%), frontotemporal dementia (5%–10%), and dementia with Lewy bodies (<4–7.5%). These types of dementia have different neuropathologies and variable symptoms, but all are progressive and incurable. This article focuses on common issues in advanced dementia in elderly patients with AD or vascular or mixed dementia; similar principles apply to younger patients in the final stages of these and other dementing diseases.

THE RATIONALE BEHIND A PALLIATIVE APPROACH IN DEMENTIA

Many clinicians and family members of people with dementia do not consider dementia to be a progressive and ultimately fatal illness. In 2010, however, AD was noted as the sixth leading cause of death in the United States, and the fifth leading cause of death in those 65 years or older. Understanding the trajectory and prognosis of dementia are essential to people with dementia and their family members as they plan for the future. Recent research has attempted to understand the trajectory of dementia, and to identify risk factors for poorer prognosis. In a recent review, Todd and colleagues noted the median survival from dementia to range from approximately 3 to 12 years after onset and approximately 3 to 7 years after diagnosis. Increased age at diagnosis and impaired functional status are associated with greater mortality.

Unfortunately, recent reviews noted that previous studies have not found consistent factors that increase the risk of death in people with dementia. Although tools to help estimate prognosis in dementia exist, this lack of clarity on which factors increase the risk of death has prevented these tools from being widely adopted. Without good tools to estimate prognosis in dementia and with dementia progressing at different rates in different individuals, it can be difficult for clinicians to correctly estimate prognosis, and to recognize when a patient may be eligible for hospice. The occurrence of an acute illness in a patient with advanced dementia does suggest a poor prognosis, however, and can be an opportunity to readdress prognosis and goals of care. One study of nursing home residents with dementia found a 6-month mortality rate for residents with pneumonia of 47%, a febrile episode of 45%, and “an eating problem” of 38.6%.

In addition to difficulty estimating prognosis, clinicians face numerous other challenges in providing the best possible care to those living with dementia. First, there are not enough physicians trained in geriatric medicine and geriatric psychiatry to care for every patient with dementia. Palliative medicine faces similar workforce issues, and generalists will need to provide primary care, including palliative care for patients with life-limiting illnesses including dementia. Second, caring for someone with dementia can be economically and psychologically costly to families. Thus, caring for an individual with dementia should involve sensitivity to the needs of that individual’s significant others. Third, there is no cure for dementia, and available medications have modest effects at slowing dementia progression. For these reasons, a palliative approach, including identifying the patient’s goals, maximizing quality of life, aggressively managing bothersome symptoms, and focusing not only on the needs of the patient, but also the patient’s family is an optimal way to care for this population.

The National Consensus Project for Quality Palliative Care’s Clinical Practice Guidelines identify that palliative care is appropriate for “patients at all ages living with a persistent or recurring medical condition that adversely affects their daily functioning or will predictably reduce life expectancy,” including “people living with progressive
chronic conditions."" Although palliative care has been a growing field and a palliative approach is now more accepted for many patients with advanced illness, the palliative approach is not uniformly applied near the end of life for patients with dementia, especially those in nursing homes. Patients with dementia in nursing homes often have burdensome symptoms and are subjected to nonbeneficial interventions, including artificial nutrition, diagnostic procedures, and hospitalizations. They are referred to hospice much less frequently than patients dying from cancer.

Applying a palliative approach more uniformly to patients with advanced dementia has potential benefit for individual patients, families, and the health system. Hospice and palliative care can improve symptoms and support families while reducing the cost of care by reducing hospitalizations and nonbeneficial interventions, and by allowing patients to die at home rather than in an institution if that is their preference. Fortunately, the use of a palliative approach is gaining support, with access to hospice and palliative care for patients with dementia improving in the past 2 decades. A study using the Minimum Data Set (MDS) and Medicare claims showed an increase in hospice use from approximately 15% of those with advanced and 13% of those with mild-moderate dementia in 1999 to approximately 43% and 38%, respectively, in 2006. Mean length of stay in hospice also increased significantly. Guidelines for optimal palliative care in patients with dementia were recently released by the European Association for Palliative Care (see Box 1 for a list of palliative care domains). In the United States, the National Hospice and Palliative Care Organization provides a set of care guidelines.

What follows is a discussion of the aspects of dementia that may be amenable to a palliative approach. Because of the workforce issues discussed previously, primary care providers caring for elderly patients will need to become comfortable providing primary palliative care for patients with dementia at all stages. See Fig. 1 for a list of relevant issues for primary care providers to address with patients with dementia and their families.

THE END OF LIFE IN DEMENTIA

Although dementias may present with different symptoms and progress at different rates, the terminal stage of all dementias is similar. People with dementia develop apraxia, dysphagia, decreased mobility, and decreased ability to report early symptoms that lead to infection, malnutrition, and other adverse outcomes. The main causes of death in patients with advanced dementia are pneumonia, other infections, and cardiovascular and cerebrovascular events; the latter are more common in patients with vascular or mixed dementia. See Box 2 for a summary of contributing factors to death from dementia, common causes of death, and common end-of-life symptoms.

Recent studies have described the experience of dying from dementia, including symptom prevalence and the nature and frequency of transitions of care near the end of life. In a study of 323 nursing home residents with advanced dementia in the United States, Mitchell found high symptom prevalence in the last 18 months of life. She also found increased prevalence of pain, dyspnea, agitation, aspiration, and pressure ulcers in the last 3 months of life, with prevalence between 25% and 35% for each symptom. Hospital transfers of nursing home residents with advanced dementia are frequent in the United States, but may not be beneficial. Gozalo and colleagues examined MDS data from nearly 475,000 US nursing home residents with advanced dementia. They found that 19% of the population had at least one transfer in the last 120 days of life. Risk factors for hospital transfer included nonwhite race, male
<table>
<thead>
<tr>
<th>Box 1</th>
<th>Eleven domains of optimal palliative care, with selected recommendations from the European Association for Palliative Care (all domains included; recommendations selected from the full list of 57)</th>
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</thead>
<tbody>
<tr>
<td>1. Applicability of palliative care</td>
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<tr>
<td>1. Improving quality of life, maintaining function, and maximizing comfort, which also are goals of palliative care, can be considered appropriate in dementia throughout the disease trajectory, with the emphasis on particular goals changing over time.</td>
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<td>2. Person-centered care, communication, and shared decision making</td>
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<td>3. Setting care goals and advance planning</td>
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<td>3.2. Anticipating progression of the disease, advance care planning is proactive. This implies it should start as soon as the diagnosis is made, when the patient can still be actively involved and patient preferences, values, needs, and beliefs can be elicited.</td>
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<td>4. Continuity of care</td>
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<td>4.4. Transfers between settings require communication on care plans between former and new professional caregivers and patients and families.</td>
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<td>5. Prognostication and timely recognition of dying</td>
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<td>5.2. Prognostication in dementia is challenging and mortality cannot be predicted accurately. However, combining clinical judgment and tools for mortality predictions can provide an indication that may facilitate discussion of prognosis.</td>
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<td>6. Avoiding overly aggressive, burdensome, or futile treatment</td>
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<td>6.4. Hydration, preferably subcutaneous, may be provided if appropriate, such as in the case of infection; it is inappropriate in the dying phase (only moderate consensus).</td>
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<td>6.6. Antibiotics may be appropriate in treating infections with the goal of increasing comfort by alleviating the symptoms of infection. Life-prolonging effects need to be considered, especially in the case of treatment decisions around pneumonia.</td>
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<td>7. Optimal treatment of symptoms and providing comfort</td>
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<td>7.3. Tools to assess pain, discomfort, and behavior should be used for screening and monitoring of patients with moderate and severe dementia, evaluating effectiveness of interventions.</td>
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<td>8. Psychosocial and spiritual support</td>
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<td>8.3. Religious activities, such as rituals, songs, and services, may help the patient because these may be recognized even in severe dementia.</td>
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<td>9. Family care and involvement</td>
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<td>10. Education of the health care team</td>
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<td>11. Societal and ethical issues</td>
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<td>11.6. Economic and systemic incentives should encourage excellent end-of-life care for patients with dementia.</td>
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sex, lack of an advance directive, lack of a do not resuscitate order, and lack of a do not hospitalize order. Givens and colleagues examined emergency room and hospital transfers of 323 nursing home residents with advanced dementia. In this population, 16% were hospitalized and 10% visited an emergency room over an 18-month
Element

Communicating the diagnosis
Communicating prognosis
Helping patient and family with anticipatory grief
Assessing decisional capacity
Helping patient assign a surrogate decision maker
Discussing goals of care
Discussing the role of artificial nutrition
Discussing the role of antibiotics
Helping patient and surrogate complete advance directives
Planning for transitions in living situation if necessary
Assessing medication appropriateness
Assessing for comorbid depression
Assessing and treating pain
Assessing and treating delirium
Reassessing goals of care and appropriateness of hospital transfer
Making hospice referral when appropriate
Managing terminal pain and delirium
Responding to family's grief after patient death
Expressing condolences
Referring to community resources for grief counseling

Stage of dementia

Mild dementia

Moderate dementia

Severe dementia

Fig. 1. Essential elements of primary palliative care in patients with dementia.

Box 2
Contributing factors, causes of death, and common symptoms at the end of life

Contributing factors
Apraxia
Dysphagia
Malnutrition
Decreased mobility
Decreased ability to report symptoms

Common symptoms
Pain
Agitation
Shortness of breath
Aspiration
Pressure ulcers

Causes of death
Pneumonia
Cardiac events
Cerebrovascular events
Other infections

Data from Refs. 9,15,116
period. The most frequent reason for hospitalization was suspected infection and the most frequent reason for emergency room transfer was feeding tube problems. Clinicians, patients, and caregivers should consider discussing likely future causes of death, common end-of-life symptoms, and the possibility of end-of-life transfers between facilities. As will be discussed in subsequent sections, burdensome end-of-life transitions can often be avoided with clear advance directives and thoughtful management of symptoms and acute events.

**MANAGEMENT DECISIONS RELATED TO CARE OF PATIENTS WITH ADVANCED DEMENTIA**

The Role of Artificial Nutrition at the End of Life

Up to one-third of nursing home residents with advanced dementia had feeding tubes, based on 1999 MDS data. There is wide geographic and socioeconomic variation in the prevalence of this practice. Placement of percutaneous endoscopic gastrostomy (PEG) tubes in elderly hospitalized patients increased between 1993 and 2003, and placement in hospitalized patients with Alzheimer dementia doubled from 5% to 10%. The intention of PEG placement is to improve nutritional status, reduce aspiration, and improve patient comfort and longevity. Financial incentives to both skilled nursing facilities and hospitals favor placement of PEG tubes. Placement of a new feeding tube qualifies a patient for skilled nursing services under Medicare, and patients with advanced dementia who are hand-fed require more staff time than those with feeding tubes. Although weight loss is part of dementia progression, this may be mistaken for negligence or mistreatment by nursing homes.

There is no evidence that enteral feeding improves patient outcomes, and there is significant evidence that feeding tubes may be harmful. A 2009 Cochrane review found no evidence that enteral feeding prolongs survival, improves quality of life, improves nutrition, or decreases the risk of pressure sores. Some evidence suggests that enteral feeding increases the risk of aspiration pneumonia in patients with dementia. A prospective cohort study of more than 30,000 nursing home residents with advanced dementia and eating problems found no survival benefit with feeding tubes. A second cohort study of nursing home residents with advanced dementia and eating difficulties found that residents with a PEG tube were 2.27 times more likely to develop a new pressure ulcer (95% confidence interval 1.95–2.65), and less likely to have an existing ulcer heal. Decreased mobility and increased diarrhea with artificial nutrition are the likely mechanisms for this association. Both the American Geriatrics Society and the American Academy of Hospice and Palliative Medicine recommend against placement of percutaneous feeding tubes in patients with advanced dementia. The practice was recently included on both organizations’ lists of “Five Things Physicians and Patients Should Question” as part of the national Choosing Wisely campaign. Please see Box 3 for more information.

The recommended approach in patients with advanced dementia and dysphagia is careful hand-feeding for comfort. A paradigm of “Comfort Feeding Only” has been suggested for discussions with families and nursing home staff, emphasizing the importance of focusing on the patient’s comfort in all interactions around nutrition. Optimal hand-feeding in patients with advanced dementia includes upright positioning, use of preferred foods and foods with strong flavors, offering smaller boluses, and frequent reminders to swallow. A systematic review of oral feeding options in patients with dementia concluded that high-calorie supplements help people with dementia and feeding problems gain weight; one study found better pressure ulcer healing with supplementation, but no study showed improvements in function, cognition, or mortality with high-calorie supplements.
Box 3
The case against artificial nutrition in advanced dementia

Feeding tubes in patients with advanced dementia:

- Are risky and associated with morbidity, mortality, and frequent hospitalization.
- Periprocedural mortality of patients with dementia is estimated at 6% to 28%.\textsuperscript{113}
- 64% mortality in the year after placement with a median survival of 56 days.\textsuperscript{114}
- Approximately 20% require replacement or repositioning, within a median of 145 days after placement.\textsuperscript{114}
- Nursing home residents with dementia and feeding tubes have an average of 9 hospitalized days per patient in the year after placement.\textsuperscript{114}
- Do not improve survival, nutrition, quality of life, or the risk of aspiration pneumonia.
- Meaningful improvement in nutritional parameters has not been proven.\textsuperscript{113}
- Tube feeding does not improve survival or the risk of aspiration pneumonia.\textsuperscript{25}
- No evidence that tube feeding improves quality of life.\textsuperscript{25,31}
- Cause harm and suffering.
  - Increase social isolation by removing the necessity for patients to participate in mealtime
  - Are associated with increased use of physical and chemical restraints.\textsuperscript{115}
  - Are associated with an increased risk of developing a new pressure ulcer.\textsuperscript{27}
  - Respondents whose loved ones died with a feeding tube were less likely to report excellent end-of-life care than those whose loved ones did not have a feeding tube.\textsuperscript{31}

There is room for improvement in shared decision making with families about PEG tube placement in patients with advanced dementia. In a mortality follow-back survey of 486 family members whose loved one died of dementia, approximately one-third of those whose loved one died with a feeding tube did not recall discussing risks associated with feeding tube insertion, and approximately half felt the health care provider was strongly in favor of feeding tube insertion.\textsuperscript{31} A written or audio decision aid was tested in a randomized controlled trial of nursing home residents with advanced dementia and feeding problems and their surrogate decision makers. Surrogates who used the decision aid reported less decisional conflict, more certainty in their preference for oral feeding, decreased expectations of benefits from tube feeding, and more discussion of feeding options with a health care provider.\textsuperscript{22}

Infections and the Role of Antibiotics in Advanced Dementia

Infections are a common cause of death in patients with advanced dementia, and unexplained febrile episodes are also common. Antimicrobials are given often in this setting, but evidence suggests that although antimicrobials in patients with advanced dementia may modestly prolong life, even oral antibiotics are associated with decreased comfort. One prospective cohort study of 214 nursing home residents with advanced dementia found that 66% received at least one course of antibiotics, with a mean number of 4 courses per resident during an average of 322 days of follow-up. Quinolones and third-generation cephalosporins were the most commonly prescribed antimicrobials in this study. Among the 99 patients who died during the study period, approximately 42% received antimicrobials during the 2 weeks preceding death, and nearly 42% were parenteral.\textsuperscript{33} Another study found that severity of dementia was the most important predictor of mortality from pneumonia, rather than type
of treatment of pneumonia. A study of fever in institutionalized patients with AD showed no difference in survival between patients with the most advanced dementia given antibiotics and those treated with comfort measures. A retrospective cohort study of patients with severe dementia and gram-negative bacteremia showed that patients with decubitus ulcers and bacteremia who received appropriate antibiotics did not survive longer than those given inappropriate antimicrobials.

Studies of patients with advanced dementia and pneumonia have suggested a survival benefit from antibiotics, but no improvement in comfort. In a prospective study of nursing home residents with advanced dementia, 56% to 64% of those treated with oral, intramuscular, or intravenous antibiotics were alive 90 days after the episode of pneumonia, as compared with 33% not treated with antimicrobials. Notably, intravenous antibiotics did not confer a survival benefit over oral antibiotics in this cohort. Comfort levels, as measured by a standardized scale completed by a nurse, were inversely associated with aggressiveness of treatment. Those not receiving antibiotics had the highest comfort levels, and those receiving intravenous antibiotics had the lowest. A similar study of nursing home residents with advanced dementia and pneumonia found an association between antibiotics and decreased 10-day mortality, but no association between antibiotic use and 6-month mortality.

Polypharmacy and Medication Appropriateness

Most patients with dementia have multiple comorbidities and are on multiple medications, and medications may be added for symptom management as dementia progresses. In one study of nursing home residents with advanced dementia, patients were prescribed a mean of approximately 15 medications during the 6 months before study enrollment. In patients who died, the total number of medications did not decrease as illness progressed. Some medications were stopped as others were added for symptom management. Adding medications increases the likelihood of adverse drug reactions, drug-drug reactions, and drug-disease interactions. In a small study of patients with advanced dementia enrolled in a palliative care program who underwent medication review by 12 geriatricians using a modified Delphi process, patients were taking an average of 6.5 medications. Ten (29%) of the 34 patients were taking a medication considered inappropriate in patients with advanced dementia. Clinicians caring for patients with dementia should be familiar with the Beers Criteria for potentially inappropriate medication use in older adults, the shorter list of medications frequently associated with adverse drug events requiring hospitalization, and lists of medications that may be inappropriate in patients with advanced dementia. In addition, beneficial medications in patients with longer life expectancy should be readdressed as patients enter the more advanced stages of dementia. See Box 4 for a list of medications that are potentially inappropriate in patients with advanced dementia.

Management of Pain in Advanced Dementia

Patients with advanced dementia may have painful comorbid conditions, such as osteoarthritis, and some common infectious complications of advanced dementia, such as decubitus ulcers, pneumonia, or urinary tract infections, can be painful. Assessment and management of pain in patients with dementia can be challenging. Patients often
### Box 4
Medications that may be inappropriate in patients with advanced dementia

- Lipid-lowering medications
- Cytotoxic chemotherapy
- Antiplatelet agents, excluding aspirin
- Immunomodulators
- Sex hormones
- Hydralazine
- Sulfonylureas
- Bisphosphonates
- Insulin
- Warfarin
- Appetite stimulants
- Digoxin
- Clonidine
- Alpha-blockers

*Data from Refs.* [42-45]

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cannot report pain, and often manifest pain as nonspecific symptoms such as agitation or decreased oral intake. Pharmacologic management of pain in patients with dementia also can be challenging because patients cannot report side effects and are susceptible to adverse effects from medications. Pain is often undertreated in patients with dementia, which can lead to functional disturbance and decreased quality of life. [46,47]

Patients with advanced dementia may not manifest typical pain behaviors, such as guarding or moaning, but instead may appear fearful, combative, agitated, or withdrawn. [48] Careful assessment of the patient’s behavior and facial expressions is essential in assessing pain. A study comparing patients with and without dementia receiving dressing changes for decubitus ulcers concluded that clinician observation of facial expressions and vocalizations are accurate in assessing the presence but not the intensity of pain in patients with dementia. [48] Common pain behaviors in cognitively impaired older patients include changes in sleep patterns or gait, decreased social interactions or withdrawal, rapid blinking or distorted expression, or increased crying. [49]

A number of structured tools for pain assessment in nonverbal patients are available, including the Pain Assessment in Advanced Dementia; these tools can be helpful but should be used as only one element of a complete history and physical examination. [49] The Assessment of Discomfort in Dementia (ADD) protocol, a structured protocol for nursing assessment of discomfort and treatment with nonpharmacologic interventions with escalation to nonopioid and then opioid analgesics, has been shown to decrease discomfort and behavioral disturbances without an increase in the use of antipsychotic medications. Nonpharmacologic interventions suggested in the ADD protocol include distraction with pleasant activities or interaction; cold and heat applied to painful areas; supervised ambulation or other physical activity, including use of a glide rocker; sensory stimulation, such as pet or music therapy; and conversation, storytelling, or life review for patients who are still verbal. [50] A similar protocol for empiric
treatment of pain with acetaminophen, morphine, or other agents in nursing home resi-
dents with moderate to severe dementia showed reduced agitation in the intervention
group compared with the control group. Empiric treatment for pain should always be
considered in patients with dementia and new behavioral disturbance.

Guidelines for pain management in the frail elderly population are applicable to pa-
tients with dementia; acetaminophen is first line and nonsteroidal anti-inflammatory
drugs should be avoided in this group because of significant toxicities. Opioids
should be considered in all patients with pain or behavioral disturbance not responsive
to acetaminophen. Patients with dementia should be monitored closely on initiation of
opioids because of side effects, including nausea, constipation, and sedation; opioids
can cause impaired sleep architecture but can improve sleep if they reduce pain.

Role of Specific Pharmacologic Agents for Dementia

There are 4 medications approved by the Food and Drug Administration (FDA) for the
treatment of symptoms of dementia; 3 acetylcholinesterase inhibitors (AChEIs: done-
pezil, rivastigmine, galantamine) and 1 N-methyl-D-aspartate receptor antagonist
(memantine). Although no treatment has been found to be disease-modifying, modest
improvements in cognitive function, activities of daily living (ADLs), and behavior have
been observed in some patients treated with AChEIs, memantine, or both in combina-
tion. The decision to prescribe these medications is based on identification of
appropriate target symptoms in individual patients, keeping in mind possible side ef-
fects (primarily gastrointestinal, sleep-related, and bradycardia in the case of AChEIs).

Although beneficial effects of these medications appear to be independent of demen-
tia severity, experts have questioned their use in the later stages of neurodegenerative
diseases, a time when polypharmacy is both common and associated with greater mor-
tality. Despite this, approximately 20% of persons with dementia are taking
either an AChEI or memantine at the time of transition to hospice care. Stopping these
medications may precipitate swifter decline in some patients or increase behavioral
problems. The decision to stop AChEIs or memantine, like the decision to start
them, should be done thoughtfully with involvement of family and care staff monitoring
for alterations in levels of alertness, confusion, and changes in behavior.

Management of Terminal Delirium in Patients with Advanced Dementia

Delirium at the end of life (terminal delirium) is common, affecting up to 88% of patients
during their final week of life, and is challenging to treat. There are several essential
questions in determining the approach to terminal delirium in patients with advanced
dementia. First, is the patient actively dying? Although delirium in the last months of life
may be reversible with treatment of underlying causes, such as infection, reversal is
unlikely within days to weeks of death. Brain function inevitably unravels as part of
the dying process, and attempts to reverse this may not be fruitful. Second, what is
the family caregiver’s perception of the patient’s quality of life before the delirium,
and does the caregiver think the delirium is causing the patient to suffer? In patients
who seemed comfortable and content before an acute episode of presumed terminal
delirium, a judicious, spare medical workup may sometimes be appropriate. This
might include a thorough physical examination, basic screening laboratory tests,
and perhaps a urinalysis or chest radiograph as directed by the physical examination.
Third, if family members, caregivers, or nursing staff express distress regarding a pa-
tient’s terminal delirium, does this reflect the patient’s suffering or the observers’ antici-
patory grief? Dying patients’ delirium can cause their loved ones to suffer. In several
studies, hallucinations and motor agitation were the features most associated with
caregiver and family distress. Family caregivers may sometimes ask for
aggressive interventions at the end of life as a part of their grieving process, and supportive listening and grief counseling are as important as attention to the patient’s symptoms.

In most cases of true terminal delirium in advanced dementia, an aggressive search for an underlying cause is not appropriate. Before embarking on any search for a cause, it is important to readress goals of care with the family decision maker and assess whether the decision maker perceives the patient’s quality of life to be acceptable based on his or her prior discussions and knowledge. Families often need permission to abandon the usual medical approach to new problems and to focus solely on symptom management.

Although most dying patients will experience delirium, there are few studies examining treatment strategies. A 2012 Cochrane Collaboration review of pharmacologic treatment of terminal delirium found only one trial that met their inclusion criteria. This study, by Breitbart and colleagues in 1996, randomized 30 hospitalized patients with AIDS and delirium to receive an antipsychotic (chlorpromazine or haloperidol) or the benzodiazepine lorazepam. Both antipsychotics were equally effective at improving symptoms of delirium, but all patients who received lorazepam developed either oversedation and/or increased confusion. Nonpharmacological strategies, resolution of underlying medical problems, and avoidance of deliriogenic medications are the foundations of management for all types of delirium. If medications are necessary, low-dose haloperidol is the treatment of choice, followed by atypical antipsychotics (quetiapine, risperidone, olanzapine) as second-line agents. Many clinicians will be more liberal with the dose and frequency of antipsychotics in terminal delirium than in other forms of delirium, giving low doses as often as every one or two hours. Opioids are also a mainstay of treatment of patients with dementia at the very end of life, as with patients dying of any disease, and should generally be added empirically, as pain can always be a contributor to delirium. Although opioids can contribute to delirium, a patient with true terminal delirium should generally have a trial of opioids in the hopes of improving comfort.

Management of Mood and Behavior

The neuropsychiatric complications of AD have been well-characterized in several studies, and affect up to 60% of community-dwelling and 80% of institutionalized patients with dementia. Patients with advanced dementia may experience apathy, fearfulness, agitation, and psychotic symptoms that can be difficult to diagnose and manage. Caregivers and medical providers should be vigilant for signs of an acute medical problem as the cause for any new behavioral or mental status change, as it is often difficult to distinguish between delirium and depression, for example, in patients with advanced dementia; see Table 1 for more details.

Diagnosing depression in persons with advanced dementia is frequently complicated by the presence of vegetative symptoms (poor sleep, low energy, anorexia) due to comorbid medical disorders or medication effects. Therefore, some experts advocate for a focus on emotional symptoms of depression, such as sadness and hopelessness, but this is challenging to assess in patients with limited communication. Persons with advanced dementia may express their depression behaviorally, by refusing to eat or engage with caregivers, or by becoming agitated and irritable.

There is insufficient evidence to recommend the routine use of antidepressants for depression in patients with advanced dementia. A small placebo-controlled study of sertraline in patients with dementia with a minimum Mini-Mental State Examination (MMSE) score of 10 and a mean MMSE of approximately 17 suggested improvement in scores on a standardized scale for depression in dementia, behavioral disturbance,
ADLs, and caregiver distress, but a Cochrane meta-analysis of trials in patients with a mean MMSE score of 19 (mild to moderate stage) concluded that there is only weak evidence for the efficacy of antidepressants in dementia. Small studies suggest that psychostimulants may be effective in treating symptoms of depression in the terminally ill, with a response seen quickly, but these have not been studied extensively in advanced dementia and we do not use these routinely in practice. The management of depression in advanced dementia requires both a high index of suspicion and a creative care plan that involves caregiver support; there is no evidence to support the initiation of antidepressants in patients with severe dementia (eg, MMSE <10) but a trial may be warranted in select patients with severe symptoms, such as anxiety, fearfulness, or dysphoria.

Difficult behaviors that may manifest in advanced dementia include agitation, aggression, combativeness, and resistance to care, sometimes driven by hallucinations and delusions. Potentially effective strategies to manage difficult behaviors include skills training and education for caregivers, pleasant activity planning, environmental redesign, music therapy, and exercise. Involving caregivers is critical. Because some of these behaviors seem driven by psychotic symptoms, antipsychotics are frequently prescribed, despite no FDA approval for this indication. A meta-analysis of 16 randomized controlled trials concluded that risperidone and olanzapine are associated with both a significant improvement in aggression and psychosis and a significantly higher incidence of serious adverse cerebrovascular events and extrapyramidal side effects; most subjects included in the meta-analysis had severe dementia with a mean MMSE between 5 and 8. The evidence for negative outcomes led the FDA to add a warning to atypical antipsychotics about the risk of cerebrovascular events and death in patients with dementia. There are some limitations to these studies (designed and powered to study efficacy of antipsychotic, not causal relationship between drug and cerebrovascular accident or death; cerebrovascular events not validated in all studies; limited information on causes of death, comorbidity, concurrent medications), however, and although mechanisms for the adverse outcomes have been suggested, none have been proven. Although caution is warranted with antipsychotics in patients with mild to moderate dementia and behavioral disturbances that do not significantly impair the patient’s quality of life, clinicians and families may opt to use them more liberally in patients with more advanced dementia and significant behavioral disturbance if the benefits to the patient’s quality of life outweigh potential risks. A careful risk-benefit discussion should be had with the family,
weighing the risk of adverse events against the potential to improve the patient's quality of life if behavioral symptoms are causing severe distress.

The only other class of psychotropics that has some proven efficacy in management of behavioral disturbances in persons with dementia is the acetylcholinesterase inhibitors, although like antidepressants these have not been studied for this indication in patients with severe dementia. A Cochrane review showed modest but significant benefit in neuropsychiatric symptom scores in patients with an MMSE between 10 and 26. There is no evidence for efficacy of antidepressants, mood stabilizers, benzodiazepines, or trazodone. See Box 5 for a basic approach to the treatment of problematic behaviors in patients with advanced dementia.

**Role of Hospice and Barriers to Eligibility**

Hospice care is likely beneficial to patients with dementia and their families. Two studies identified that bereaved families of people dying with advanced dementia reported fewer unmet needs, a higher rating of the quality of care, and a better quality of dying if the person with dementia received hospice before death. People with advanced dementia who receive hospice services are less likely to die in the hospital than others with dementia who do not receive hospice. One small study found lower rates of depression and anxiety in bereaved spouses of people with AD when the person with dementia received hospice before death. However, studies have not found a clear improvement in pain assessment and management in patients enrolled in hospice, although one study showed that nursing home residents with advanced dementia enrolled in hospice were more likely to receive scheduled opioids for pain and treatment for dyspnea than those not receiving hospice services.

Although the use of hospice by people with advanced dementia has been increasing, this may change in the future. One reason is that "debility," a hospice diagnosis used until 2013 to qualify people with less advanced dementia plus other chronic

<table>
<thead>
<tr>
<th>Box 5</th>
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<tbody>
<tr>
<td><strong>Approach to the treatment of behavioral disturbances in patients with advanced dementia</strong></td>
</tr>
<tr>
<td>• Evaluate for occult medical problems and pain; treat if present.</td>
</tr>
<tr>
<td>• Simplify the patient's medication list if possible, reducing or stopping medications that may be deliriogenic.</td>
</tr>
<tr>
<td>• Look for environmental triggers and teach caregivers ways to manage behavior. Consider medications if these fail.</td>
</tr>
<tr>
<td>• Consider a trial of antidepressants if the patient shows signs of dysphoria or anxiety.</td>
</tr>
<tr>
<td>• Consider a trial of antipsychotics if the patient seems to be experiencing considerable distress from delusions and agitation.</td>
</tr>
<tr>
<td>o Although a very cautious approach is warranted in moderate dementia with behavioral disturbance, a more liberal approach may be warranted in patients with advanced dementia.</td>
</tr>
<tr>
<td>o Have a risk-benefit discussion with the patient's surrogate discussing the possible increased risk of stroke or death before starting antipsychotics.</td>
</tr>
<tr>
<td>▪ Consider checking a baseline electrocardiogram for prolonged QT interval depending on the risk-benefit discussion with the surrogate and their tolerance for risk.</td>
</tr>
<tr>
<td>▪ Reevaluate periodically for efficacy and side effects.</td>
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</table>

conditions and evidence of decline, is no longer an acceptable hospice diagnosis. In late 2014, providers will be required to designate the type of dementia when certifying a patient for hospice. Although Medicare has hospice eligibility criteria for AD, it does not have specific criteria for other dementias. If a patient with advanced non-AD has comfort-focused goals, to certify that individual for hospice care it will be important to make a clear case that the patient has declined, and has had complications of end-stage dementia, such as infections and/or weight loss. The hospice organization will work with the provider to determine if the patient is hospice eligible. If a patient is not deemed to be hospice eligible, providers should be aware of additional resources in their communities, such as home care and palliative care programs. In addition to regulatory barriers to hospice enrollment by people with advanced dementia, additional barriers include dementia not being recognized as a terminal illness, difficulty in estimating prognosis in advanced dementia, and challenges reimbursing for hospice services in nursing facilities. The current hospice eligibility criteria for dementia are noted in Box 6.

ADVANCE CARE PLANNING IN PATIENTS WITH DEMENTIA

Advance care planning is an essential part of care in persons with dementia and should start soon after diagnosis. Dementia management quality measures call for

<table>
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<tr>
<th>Box 6</th>
<th>Medicare hospice eligibility criteria for dementia</th>
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<tr>
<td></td>
<td>This section is specific for Alzheimer dementia and related disorders, and may not be appropriate for other types of dementia, such as vascular dementia.</td>
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<tr>
<td></td>
<td>Patients with dementia should show all the following characteristics:</td>
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<tr>
<td></td>
<td>1. Stage 7 or beyond according to the Functional Assessment Staging Tool (FAST)</td>
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<tr>
<td></td>
<td>2. Unable to ambulate without assistance</td>
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<tr>
<td></td>
<td>3. Unable to dress without assistance</td>
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<td></td>
<td>4. Unable to bathe without assistance</td>
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<td></td>
<td>5. Urinary and fecal incontinence, intermittent or constant</td>
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<td></td>
<td>6. No consistently meaningful verbal communication: stereotypical phrases only or the ability to speak is limited to 6 or fewer intelligible words</td>
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<td></td>
<td>Patients should have 1 of the following within the past 12 months:</td>
</tr>
<tr>
<td></td>
<td>1. Aspiration pneumonia</td>
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<td></td>
<td>2. Pyelonephritis or other upper urinary tract infection</td>
</tr>
<tr>
<td></td>
<td>3. Septicemia</td>
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<tr>
<td></td>
<td>4. Decubitus ulcers, multiple, stage 3 or 4</td>
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<tr>
<td></td>
<td>5. Fever, recurrent after antibiotics</td>
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<tr>
<td></td>
<td>6. Inability to maintain sufficient fluid and calorie intake with 10% weight loss during the previous 6 months or serum albumin less than 2.5 g/dL</td>
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<tr>
<td></td>
<td>Note that these criteria may exclude some patients with dementia who have a life expectancy of less than 6 months, and may include others who will live longer than 6 months, and may be discharged from hospice. When patients have significant comorbidities, these should be considered when making a hospice referral.</td>
</tr>
<tr>
<td></td>
<td>Adapted from Centers for Medicare and Medicaid Services. Local Coverage Determination (LCD): Hospice Determining Terminal Status (L32015).</td>
</tr>
</tbody>
</table>
comprehensive counseling regarding end-of-life decision making, the assignment of a surrogate decision maker, and plans for symptom management at the end of life within 2 years of diagnosis. In the United States, aggressive life-sustaining care, including cardiopulmonary resuscitation (CPR), is the default, despite its futility in patients with a terminal illness, such as advanced dementia. Studies suggest that most elderly patients would not want CPR or other life-prolonging measures if they were to develop dementia; however, many patients with dementia continue to receive CPR and other life-sustaining treatments. Advance directives are imperfect, and some have suggested a paradigm shift in which aggressive care would not be the default for patients with dementia; barring such a dramatic change in policy, advance directives and continued thoughtful conversations about goals of care are necessary. Early discussions with the patient and family should focus on detailed information about prognosis and the natural course of dementia. This allows the patient and family to come to terms with the diagnosis and understand what they may face in the future. Early completion of a power of attorney for health care, finances, and other legal decisions is also important, to ensure that the patient’s affairs will be managed appropriately when they lose the ability to do so.

Traditional health care advance directives are inadequate for patients with dementia and many other chronic debilitating illnesses because they often address the person’s wishes in the case of a persistent vegetative state or immediately terminal condition, but do not recognize the many end-of-life circumstances that can occur. The Five Wishes Advance Directive, which is a legal advance directive in most states, is more comprehensive and may be helpful for people with dementia and their families. It does not require legal assistance or a notary in many states, although there is a small charge for its use. Video decision support tools for advance directives are now used by some health systems and have been used to assist in decisions regarding future care if an individual were to develop dementia. Studies suggest that the use of these videos may result in patients with dementia being less likely to choose aggressive care at the end of life, having more stable preferences over time, and being more likely to concur with their surrogate about their end-of-life choices. Advance care planning conversations with patients with dementia and their surrogates should include discussions about sites of future care, preferences regarding nutrition and antibiotics, and reassurances that every effort to ensure comfort will be taken, regardless of their other care choices. A discussion of whether the patient should be hospitalized near the end of life is an important element of advance care planning with patients with dementia in nursing facilities. End-of-life hospitalizations can be burdensome to frail elders with dementia, but are common. “Do Not Hospitalize” orders are reasonable for many patients with advanced dementia, and can be enacted but are relatively rare nationally. Although advance care planning is helpful, it is not universal among patients with dementia and their families. Barriers include lack of knowledge or avoidance on the part of providers, failure to discuss the prognosis of dementia in detail, and the burdens of illness and caregiving. Important elements in advance care planning for people with dementia are listed in Box 7.

The POLST program, although not specific to patients with dementia, has been an important recent development, and is especially relevant to patients with advanced dementia living in nursing facilities. The National POLST Paradigm Program started in Oregon in 1991 as an effort to increase the ability to honor patient preferences for end-of-life care. The POLST system identifies patients’ wishes regarding medical treatment and creates portable medical orders, including wishes regarding resuscitation status, hospitalization, artificial nutrition, and antibiotics. Mature, endorsed, or developing POLST programs are available in 43 states. The POLST program has
be proven to increase the number of patients in nursing facilities who have documented treatment preferences that are honored by the facility and their providers. Clinicians caring for patients with advanced dementia must become comfortable with helping surrogates make decisions for their loved ones. A study of surrogate decision makers who had recently made decisions for elderly hospitalized patients identified communication needs of surrogates as frequent communication, information, and emotional support, and found that the surrogates formed strong relationships with medical teams rather than individuals in the inpatient setting. Although surrogates should be making decisions using the principle of substituted judgment, they need education to ensure that this occurs. One study of surrogate decision makers in Germany using experimental vignettes suggested that family surrogates of patients with dementia tend to refer to their own preferences and decide intuitively, as compared to professional guardians. The family decision makers were less likely to consent to aggressive measures including a feeding tube.

Physician-assisted suicide is legal in 4 states in the United States, but the related laws specify that those requesting physician-assisted suicide must have decisional capacity. Those with advanced dementia, however, are no longer able to make their own medical decisions; thus, they are currently not eligible for physician-assisted suicide. Advance directives for euthanasia are legally recognized in the Netherlands, but are rarely used. Two US ethicists recently speculated on whether advance directives for physician-assisted suicide could be implemented in the United States, but this seems unlikely to become legal in the current political climate.

THE CAREGIVER IN ADVANCED DEMENTIA

Being the primary caregiver for a person with dementia is an arduous and potentially dangerous occupation. Numerous studies have noted the serious negative effects on physical health, quality of life, and mortality for primary caregivers of people with dementia. The dementia caregiving experience often lasts for years, extending the
<table>
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<tr>
<th>Patient Characteristics</th>
<th>Caregiver Experiences</th>
<th>Possible Interventions</th>
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<tbody>
<tr>
<td><strong>Mild dementia (MMSE ~ 30–20)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mild forgetfulness and word-finding trouble</td>
<td>• Having to help more with planning, remembering, finances</td>
<td>• Diagnose and stage dementia in patient</td>
</tr>
<tr>
<td>• Difficulty remembering appointments</td>
<td>• Fearfulness about diagnosis and the future</td>
<td>• Diagnose and treat any mood problems in patient</td>
</tr>
<tr>
<td>• Trouble with complex planning or multistep instructions</td>
<td></td>
<td>• Counsel patient and family about legal issues, driving, advance care planning</td>
</tr>
<tr>
<td>• May have social withdrawal</td>
<td></td>
<td>• Refer to memory clinic for diagnostic dilemmas or complex behavioral problems</td>
</tr>
<tr>
<td>• May develop depression or anxiety related to cognitive decline</td>
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| **Moderate dementia (MMSE ~ 20–10)** | | |
| • More language impairment | • Increasing burden of care | • Refer to caregiver support groups |
| • Difficulty with short-term memory, sequences, chronologies | • Frustration at memory trouble, language | • Counsel regarding getting more help in the home |
| • More trouble with IADLs | • Having to decrease working/activities to provide care | • Refer patient for driving evaluation |
| • Some trouble with ADLs | • Increased vigilance, as may not be able to leave patient alone | • Monitor caregiver for emergence of depression, fatigue |
| • No longer able to drive or perform complex tasks | • Poor sleep | • Involve family and friends to provide material and emotional support |
| • Beginnings of paranoia or fearfulness | • Depression, anxiety, resentment, anger, grief | • Begin discussion about next steps in care: hiring help in the home, move to supported living situation |
| • May wander or get lost, leave stove on, succumb to scams | | |

| **Severe dementia (MMSE<10)** | | |
| • Physical manifestations begin: weakness, gait impairment, falls, swallowing trouble | • Fatigue may be severe | • Refer to palliative medicine for goals of care discussion |
| • Difficulty recognizing familiar people | • Medical complications emerge (eg, hypertension) | • Encourage caregiver to have close follow-up with their own PCP |
| • Unable to perform any IADLs | • May feel guilt for placing patient in supervised care setting | • Encourage respite, scheduled time away, exercise, self-care |
| • Marked difficulty with ADLs | | • Encourage support group and/or personal therapy |
| • Apraxia | | |
| • May have paranoia, delusions, agitation, aggression | | |

| **End-stage** | | |
| • May be mute, bed-bound | • Significant burden of daily care | • Transition to hospice, either at home or in facility |
| • Requires complete care for ADLs | • Grief and/or relief at time of death | • Refer to bereavement support groups |

Abbreviations: ADLs, activities of daily living; IADLs, instrumental ADLs; PCP, primary care provider.
grief process. Dementia caregivers experience significant levels of depressive symptoms and more than half describe being “on duty” 24 hours a day at the end of their loved ones’ lives. Difficult behaviors are cited as the most stressful part of dementia caregiving, and tend to increase in the later stages of disease. Clinicians should be aware of the psychic toll of caregiving over years, addressing it gently but directly in the course of assisting these surrogate decision makers who are also under considerable stress. For example, a wife who is now a caregiver for her husband and who has cooked for and fed him for 20 years of marriage may be very conflicted over decisions related to artificial nutrition near the end of life. After eliciting her understanding of the situation and her understanding of her husband’s prior wishes, the clinician could gently explore the possibility that she is experiencing guilt and anticipatory grief relating her inability to continue to nurture him with food as she always has. Possible interventions to help caregivers are usually stage dependent, and the patient/caregiver dyad often needs additional help when the patient progresses to a new stage (e.g. from mild to moderate dementia). Caregivers continue to need support after the death of the person with dementia, as the grief process is often complicated and prolonged by depression and feelings of guilt. Primary care providers for bereaved family members who have lost a loved one with dementia or any illness should be aware of the natural course of grief, and in the case of dementia should be aware that caregiving is often a more prolonged and intense role. Please see Table 2 for a summary of important issues related to caregiving in dementia.

FUTURE DIRECTIONS

Although end-of-life care in general has improved over time with the growth of palliative care as a specialty and stronger evidence for improved outcomes for patients and families, many people with dementia still receive suboptimal end-of-life care. Barriers to excellent end-of-life care in people with dementia still exist and were discussed in detail in this article.

An ambitious “wish list” for addressing these barriers might include the following:

- More palliative care education at all levels of medical and nursing training, which would include education about end-of-life care in dementia, caregiver support, and grief counseling.
- Reforms in the payment structure, which would provide more resources for non-pharmacologic interventions and caregiver support.
- Targeted educational interventions for specialist and generalist physicians involved in the placement of percutaneous feeding tubes in patients with dementia emphasizing the lack of evidence for this practice.
- Changes in Medicare rules liberalizing access to palliative care and hospice services for patients with dementia who have comfort-oriented goals.

As the population ages, with more individuals being afflicted by dementia, we need to find ways to ensure that these vulnerable adults receive quality end-of-life care.

REFERENCES


90. Department of Health and Human Services. Medicare program; FY 2014 hospice wage index and payment rate update; Hospice quality reporting requirements; and Updates on payment reform. Federal Register 2013;78(152):1–49.


