AAHPM Special Article

Five Things Physicians and Patients Should Question in Hospice and Palliative Medicine

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Abstract

Overuse or misuse of tests and treatments exposes patients to potential harm. The American Board of Internal Medicine Foundation’s Choosing Wisely® campaign is a multiyear effort to encourage physician leadership in reducing harmful or inappropriate resource utilization. Via the campaign, medical societies are asked to identify five tests or procedures commonly used in their field, the routine use of which in specific clinical scenarios should be questioned by both physicians and patients based on the evidence that the test or procedure is ineffective or even harmful. The American Academy of Hospice and Palliative Medicine (AAHPM) was invited, and it agreed to participate in the campaign. The AAHPM Choosing Wisely Task Force, with input from the AAHPM membership, developed the following five recommendations: 1) Don’t recommend percutaneous feeding tubes in patients with advanced dementia; instead, offer oral-assisted feeding; 2) Don’t delay palliative care for a patient with serious illness who has physical, psychological, social, or spiritual distress because they are pursuing disease-directed treatment; 3) Don’t leave an implantable cardioverter-defibrillator activated when it is inconsistent with the patient/family goals of care; 4) Don’t recommend more than a single fraction of palliative radiation for an uncomplicated painful bone metastasis; and 5) Don’t use topical lorazepam (Ativan®), diphenhydramine (Benadryl®), and haloperidol (Haldol®) (ABH) gel for nausea. These recommendations and their supporting rationale should be considered by physicians, patients, and their caregivers as they collaborate in choosing those treatments.

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Key Words
Choosing Wisely®, palliative care, quality of life, dementia, artificial nutrition and hydration, percutaneous endoscopic gastrostomy, PEG, heart failure, implantable cardioverter-defibrillator, ICD, bone metastasis, bone pain, single-fraction radiation, nausea, lorazepam-haloperidol-diphenhydramine gel, ABH gel

Introduction
Advances in biomedical science and the development of novel therapies over the last 50 years have been unprecedented. Yet despite these advances, Americans experience inferior quality of care, efficiency, access, and health outcomes compared with the citizens of most other developed nations, all while health care costs rise at an unsustainable rate.² In the U.S., health care expenditures now consume more than 17% of gross domestic product.³ Although the causes underlying the paradox of spending more while achieving less are complex, overuse and inappropriate use of tests, procedures, and therapies have been cited as major contributors, accounting for perhaps 30% of all health care expenses.³ In 2008, the Congressional Budget Office⁴ estimated that $700 billion annually goes to health care spending that has not been shown to improve health outcomes. Of greatest concern, ineffective and nonbeneficial treatments may expose patients to harm from adverse effects, overtreatment, and delayed delivery of effective and beneficial treatments. At a time of dramatically increased spending, an aging population, and an increasing illness burden, it is absolutely necessary for physicians and patients to choose every treatment wisely.

In light of these challenges and with the goal of maximizing quality of care while minimizing the costs, Brody challenged medical societies to each create a “Top Five” list of tests or treatments that are commonly ordered, expensive, and have been shown not to provide any meaningful benefit to at least a major category of patients for whom they are commonly ordered. Brody⁵ summarized the concept of the Top Five list as “a prescription for how, within that specialty, the most money could be saved most quickly without depriving any patient of meaningful medical benefit.”

In response to Brody’s Top Five challenge, the American Board of Internal Medicine Foundation developed a multiyear effort called Choosing Wisely®. In 2012, nine medical societies developed and, in conjunction with Consumer Reports, publicized an initial series of Top Five lists. The American Academy of Hospice and Palliative Medicine (AAHPPM) was invited to participate, along with 15 additional medical societies, in the next wave of the campaign. Here, we report the five practices the AAHPPM Choosing Wisely Task Force recommends patients and physicians question in the practice of hospice and palliative medicine (HPM) (Table 1).

This list is not meant to serve as a rigid tool and should instead be used as a support for individualized decision-making born of conversations between physicians and patients. It also should be understood that these recommendations are not universally applicable to the situations and settings they address. There may be times when they are inappropriate in light of specific additional circumstances facing a patient.

These recommendations are provided for informational purposes only and do not constitute medical advice. They do not supersede the independent judgment of a medical professional, and the authors believe that an individual with specific medical questions should obtain medical advice from their health care provider.

Methods
The president of AAHPPM appointed a special task force to coordinate the development of the Academy’s list of “Five Things Physicians and Patients Should Question in Hospice and Palliative Medicine.” Chaired by a member of the Board of Directors who previously oversaw AAHPPM’s Education and Training Strategic Coordinating Committee, the task force included representatives of the Academy’s Quality and Practice...
Finally, the list was reviewed and approved by recommendations and refining their verbiage. Narrowing the list to five members’ feedback informed the task force’s final deliberation, which included narrowing the list to five recommendations and refining their verbiage. Finally, the list was reviewed and approved by the AAHPM Executive Committee and submitted to the American Board of Internal Medicine Foundation.

Table 1

<table>
<thead>
<tr>
<th>Five Things Physicians and Patients Should Question in Hospice and Palliative Medicine</th>
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<tbody>
<tr>
<td>1. Don’t recommend percutaneous feeding tubes in patients with advanced dementia; instead, offer oral-assisted feeding. In advanced dementia, studies have found that feeding tubes do not result in improved survival, prevention of aspiration pneumonia, or improved healing of pressure ulcers. Feeding tube use in such patients has actually been associated with pressure ulcer development, use of physical and pharmacologic restraints, and patient distress about the tube itself. Assistance with oral feeding is an evidence-based approach to provide nutrition for patients with advanced dementia and feeding problems; in the final phase of this disease, assisted feeding may focus on comfort and human interaction more than the nutritional goals.</td>
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<td>2. Don’t delay palliative care for a patient with serious illness who has physical, psychological, social, or spiritual distress because they are pursuing disease-directed treatment. Numerous studies—including randomized trials—provide evidence that palliative care improves pain and symptom control, improves family satisfaction with care, and reduces costs. Palliative care does not accelerate death and may prolong life in selected populations.</td>
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<td>3. Don’t leave an ICD activated when it is inconsistent with the patient/family goals of care. In about a quarter of patients with ICDs, the defibrillator fires within weeks preceding death. For patients with advanced irreversible diseases, defibrillator shocks rarely prevent death, may be painful to patients, and are distressing to caregivers/family members. Currently, there are no formal practice protocols to address deactivation; less than 10% of hospices have official policies. Advance care planning discussions should include the option of deactivating the ICD when it no longer supports the patient’s goals.</td>
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<td>4. Don’t recommend more than a single fraction of palliative radiation for an uncomplicated painful bone metastasis. As stated in the American Society for Radiation Oncology 2011 guideline, single-fraction radiation to a previously unirradiated peripheral bone or vertebral metastasis provides comparable pain relief and morbidity compared with multiple-fraction regimens while optimizing patient and caregiver convenience. Although it results in a higher incidence of later need for retreatment (20% vs. 8% for multiple-fraction regimens), the decreased patient burden usually outweighs any considerations of long-term effectiveness for those with a limited life expectancy.</td>
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<td>5. Don’t use topical lorazepam (Ativan), diphenhydramine (Benadryl), and haloperidol (Haldol) (ABH) gel for nausea. Topical drugs can be safe and effective, such as topical nonsteroidal anti-inflammatory drugs for local arthritis symptoms. Although topical gels are commonly prescribed in hospice practice, antinausea gels have not been proven effective in any large, well-designed, or placebo-controlled trials. The active ingredients in ABH are not absorbed to systemic levels that could be effective. Only diphenhydramine (Benadryl) is absorbed via the skin and then only after several hours and erratically at subtherapeutic levels. It is, therefore, not appropriate for “as needed” use. The use of agents given via inappropriate routes may delay or prevent the use of more effective interventions.</td>
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ICD = implantable cardioverter-defibrillator.

Results

The five recommendations are the following:

1. Don’t recommend percutaneous feeding tubes in patients with advanced dementia; instead, offer oral-assisted feeding.

Dementia is the fifth leading cause of death among Americans aged 65 years and older, and recent research suggests that this is an underestimate. Dementias are progressive diseases of cognitive and physical decline. In advanced dementia, 86% of patients develop an eating problem that increases risk for malnutrition and recurrent infections. Because they may view it as a choice between feeding and not feeding, families are often faced with what they perceive as a difficult decision on whether to insert a feeding tube. However, framing the decision in these stark terms ignores the relative risks and
benefits of tube feeding compared with continued oral feeding in advanced dementia.

A substantial body of research provides evidence of the risks and benefits of percutaneous endoscopic gastrostomy (PEG) feeding tube insertions in people with advanced dementia. Observational studies have found that feeding tubes do not result in improved survival, prevention of aspiration pneumonia, or improved healing of pressure ulcers. Teno et al. conducted an analysis of national Medicare claims and the Minimum Data Set, using techniques that accounted for selection bias, and found no survival benefit of feeding tube insertions in people with advanced cognitive impairment. For nursing home residents with advanced dementia, the one-year survival rate after a feeding tube insertion is only 33.9%, with a median survival of 56 days.

It also should be noted that PEG feeding tubes are not without risk. Although the mortality rate with the insertion of a PEG feeding tube is small, people with advanced dementia who had a PEG tube insertion during an acute care hospitalization had more than two times the risk of developing a Stage II or higher pressure ulcer. A small study based on bereaved family member interviews reported that 25.9% of decedents with feeding tubes were physically restrained and 29.2% were pharmacologically restrained. Furthermore, they reported that nearly 40% of patients dying with dementia were bothered by the feeding tube.

Oral-assisted feeding represents a viable evidence-based option to maintain weight and caloric intake for patients with dementia. High-calorie supplements can support weight stabilization or weight gain for people with dementia; assisted feeding programs, modified foods, and appetite stimulants have a potential benefit but limited evidence. Feeding for comfort is an appropriate option in the final phase of illness in dementia. Families prefer and accept the option of oral-assisted feeding, rather than tube feeding, when they receive effective information and education.

2. Don’t delay palliative care for a patient with serious illness who has physical, psychological, social, or spiritual distress because they are pursuing disease-directed treatment.

Studies have shown that individuals dealing with a serious illness are at significant risk for untreated pain and other symptoms, high caregiver burden, poor communication with their health care providers, infrequent discussions about and documentation of medical goals and preferences, and high rates of hospitalization and burdensome treatments at the end of life. Despite these risks, the decision to focus on reducing the suffering of those dealing with a serious illness is often delayed until after potentially curative or life-prolonging treatment options have been exhausted, with studies showing that palliative care consultations occur very late in the disease trajectory. There is now convincing evidence that the delivery of palliative care concurrent with the disease-directed treatment can improve the quality of life, symptom control, and family satisfaction with care, all while reducing costs associated with aggressive end-of-life care. Palliative care does not shorten life expectancy and can improve survival in select populations.

The evidence that palliative care improves symptom control and leads to greater family satisfaction with care has been shown in both observational and randomized control trials. Ringdal et al. conducted a randomized trial of comprehensive palliative care services for patients with incurable cancer and life expectancy of two to nine months. One month after the patients’ deaths, families of the patients who received palliative care were more satisfied with most aspects of the care received. The most positive effects were in pain control, speed of symptom treatment, communication, quality of family conferences, and availability and thoroughness of physicians. Engelhardt et al. randomized 275 patients with chronic obstructive pulmonary disease, heart failure, or cancer and with recurrent hospital admissions to usual care or concurrent palliative care case management. Palliative care patients had increased satisfaction with care and communication and increased use of advance directives (69% vs. 48%, $P = 0.006$). Additionally, in a retrospective study, more time between the initial palliative care consultation and the patient’s death was associated with better family perceptions of care, most notably for communication and emotional support. Focusing on the relief of suffering and promoting shared decision-making through concurrent palliative care has been shown to lower costs and reduce rates of intensive care use and hospitalizations. Gade conducted a multicenter
randomized trial of interdisciplinary hospital-based palliative care, enrolling 517 patients with life-limiting illnesses. Individuals randomized to palliative care reported higher quality of care and better quality of communication. They also experienced fewer intensive care unit admissions and a net cost savings of $4855 per patient, with no difference in mortality. In an eight-hospital study of 4908 palliative care patients and more than 20,000 propensity score-matched controls, palliative care consultations were associated with $1696 direct cost savings per patient for patients discharged alive and $4908 direct cost savings per patient for patients who died in the hospital. In a controlled study of palliative care for New York Medicaid patients, palliative care access resulted in similar or greater cost savings.

Finally, there is some evidence that concurrent palliative care may prolong life in select populations. In a landmark study, Temel et al. randomized 151 outpatients with metastatic non-small cell lung cancer to either standard care or concurrent palliative care. Patients who received concurrent palliative care showed significant improvements in quality of life and mood. Despite lower use of aggressive end-of-life care, individuals randomized to concurrent palliative care showed a significant increase in survival compared with standard care (median survival 11.6 vs. 8.9 months; \( P = 0.02 \)).

An artificial boundary between disease-directed treatment and palliative care is unwarranted based on the aforementioned findings. When patients experience burdensome symptoms, difficult treatment choices, or emotional distress related to serious illness, palliative care should be offered in combination with disease-modifying therapies. The resulting treatment approach can promote physical and emotional support, improve shared decision-making, support family members, and coordinate care across settings.

3. Don’t leave an implantable cardioverter-defibrillator (ICD) activated when it is inconsistent with the patient/family goals of care.

As patients approach the end of life, the benefits and burdens of ICDs need to be readdressed in alignment with the patient and family goals of care. About a quarter of patients with ICDs experience a shock from their device within weeks of death. For patients with advanced irreversible diseases, defibrillator shocks rarely prevent death, may be painful, and are typically distressing to caregivers and family members. In addition, patients who are at the end of life often experience electrolyte disturbances, hypoxemia, acidosis, and organ failure, making these devices less effective. Barriers to timely deactivation have been shown to include both patient and physician factors. Patients may be unwilling to discuss deactivation, yet remain fearful about potential shocks. Often, they believe that physicians should make the decision regarding deactivation, and research shows that patients may not even realize that deactivation is an option.

Although most physicians believe that deactivation should be discussed with patients, this rarely occurs. Furthermore, physicians’ lack of comfort in discussions with patients has been shown to be a major barrier to deactivation. When discussions do occur, it is often in the last days of a patient’s life. Given these shortcomings, advance care planning discussions should include the option of deactivating the ICD when it no longer supports a patient’s goals, and Do Not Attempt Resuscitation orders should be consistent with deactivation of these devices.

Still, fewer than 10% of U.S. hospices have ICD deactivation policies. In a national survey of hospice organizations, only 42% of hospice patients with ICDs had their devices deactivated, and only 25% of hospices surveyed had a magnet available for emergency deactivation; of those that did, only 64% provided training in its use. Hospices that have a policy on ICDs are more likely to have patients with deactivated devices compared with those without a policy (73% vs. 38%, \( P < 0.001 \)). In spite of their relatively sparse use, such policies could be brought to scale in U.S. hospices, and a sample policy is available to aid organizations in creating ICD policies and procedures. Finally, it is recommended that hospices develop relationships with local electrophysiologists or device manufacturers to assure that reprogramming of a device can occur to reduce barriers to deactivation for home-bound patients.

The ethical principles around ICD deactivation are well established. Informed patients with decisional capacity, or their legally authorized decision-makers, can choose to refuse any and all treatments, including life-sustaining ones. Furthermore, there is no ethical distinction between withdrawing treatment (e.g.,
deactivating an ICD) and withholding treatment (e.g., not placing an ICD in the first place). In the face of a progressive disease, a patient may feel that the benefit of having an ICD prevent a fatal arrhythmia is outweighed by the burden of treatment. Not allowing deactivation forces a patient to suffer potential unwanted continued intervention and violates the ethical principles of autonomy, beneficence, and nonmaleficence. The outcome of deactivation allows for a patient’s natural death from disease progression. If for some reason a physician has a conscientious objection to deactivating a device, the physician has the obligation to transfer the patient to a physician who does not.

4. Don’t recommend more than a single fraction (SF) of palliative radiation for an uncomplicated painful bone metastasis.

Bone is the most common site of cancer metastasis, and although bone metastasis is most prevalent in breast and prostate cancers (found in ~70% at autopsy), it also is common in multiple myeloma and cancers of thyroid, kidney, and bronchial origin. Because bone metastasis is the leading cause of cancer-related pain, HPM specialists are frequently consulted to treat symptoms and address suffering associated with bone metastases.

This recommendation is based on the evidence-based practice guideline published by the American Society for Radiation Oncology (ASTRO) for palliation of bone metastases. The ASTRO guideline reports the findings of a systematic review of the literature concerning the comparative effectiveness of SF vs. multiple-fraction (MF) regimens of external beam radiotherapy (EBRT) for palliation of uncomplicated painful bone metastases (those not associated with spinal cord compression or an unstable pathological fracture).

Compared with an MF regimen, SF palliative EBRT provides equivalent short-term symptom relief, fewer side effects, and less inconvenience for patients. There is a higher incidence of symptom recurrence for SF compared with MF regimens (20% vs. 8%), but recurrences usually can be irradiated a second time. These findings are the same for both peripheral bone and vertebral metastases.

As previously noted, bone metastases are a common source of pain and morbidity in patients with advanced cancer, and HPM specialists are frequently consulted to manage their palliation. Cancer patients referred to HPM specialists often have limited performance status, coexisting visceral metastases, and shortened life expectancy. Such patients are likely to be burdened by short-term side effects, repeated trips to the radiation center, and transfers on and off the radiation treatment table. Because limited prognosis mitigates concern for a late recurrence of pain requiring retreatment, the primary goal of palliation is to restore quality of life as quickly as possible with the least burden to the patient and family. Therefore, for most patients considering palliative radiation for painful uncomplicated bone metastasis, SF (8 Gy) EBRT is the best recommendation.

The survival of patients with bone metastasis is associated with the origin of the primary cancer and presence of visceral metastases or skeletal-related events (SRE). Breast and prostate cancer patients with metastasis only to bone have median life expectancies measured in years. However, the median survival for patients with lung cancer metastatic to bone is only 9.7 months. The development of SRE (pathological fracture, cord compression, hypercalcemia, or any condition requiring bone surgery or radiation) increases mortality. A study of breast cancer patients in the Danish Cancer Registry reported a five-year survival rate of 75.8% for patients without bone metastasis, 8.3% for those with bone metastasis, and only 2.5% for those with SRE. Any patient who receives radiation for painful bone metastasis (by definition an SRE) has a shortened life expectancy, perhaps best expressed as months to a year or two.

EBRT provides relief of associated pain in 50%—85% of patients with bone metastasis, depending on what methods of pain assessment and definition of relief are applied. Up to a third of patients experience complete relief of pain at the treated site. SF treatment of 8 Gy to a previously unirradiated bone metastasis provides equivalent pain relief to various schedules of MF treatment (30 Gy in 10 fractions, 24 Gy in six fractions, or 20 Gy in five fractions). There is no significant difference between SF and MF regimens in the risk of developing subsequent cord compression or pathological fracture. The only therapeutic difference between SF and MF treatments is the incidence of recurrent pain requiring.
retreatment at the site (20% for SF compared with 8% for MF). Radiation oncologists may be more willing to retreat a site of recurrent pain if the previous treatment was SF rather than MF.\textsuperscript{57,58}

Acute radiation reactions are generally worse and more prolonged with MF than with SF treatment. The incidence of a temporary postirradiation flare in pain may be higher with SF but can be managed with anti-inflammatory drugs.\textsuperscript{59,60}

MF is more expensive than SF treatment. Given the equivalent short-term efficacy, SF is a more cost-effective option for most patients. Several authors have noted significant international variation in the use of SF treatment to palliate bone metastasis.\textsuperscript{56,61} Specifically, physicians in the U.S. use MF for painful bone metastasis more often than their counterparts in other countries, despite the evidence of therapeutic equivalence. The creators of the ASTRO guideline expressed a hope that it would drive a change in the patterns of care. Even if the costs of SF and MF regimens were equal, the decreased patient burden alone would be sufficient reason to recommend SF treatment for most patients seen in the HPM setting.

Physicians should tailor their recommendations to the individual patient’s condition, prognosis, and goals of care. MF treatment may be a reasonable option for a patient likely to live more than a few months who would have difficulty accessing retreatment if pain were to recur. Some patients with favorable tumor type, excellent performance status, and aggressive care goals may prefer MF treatment. Patients with complications such as cord compression or instability in weight-bearing bones require a multidisciplinary approach including orthopedic surgery, neurosurgery, radiation oncology, and palliative medicine working in concert. In addition to EBRT, practitioners should consider other treatment modalities for painful bone metastasis, including anti-inflammatory drugs, other analgesic drugs, bisphosphonates, radiopharmaceuticals, and surgery.

5. Don’t use topical lorazepam (Ativan\textsuperscript{®}), diphenhydramine (Benadryl\textsuperscript{®}), and haloperidol (Haldol\textsuperscript{®}) (ABH) gel for nausea.

Nausea and vomiting account for 18% of palliative care consultations at some cancer centers,\textsuperscript{62} and many patients cannot swallow drugs. Topical drugs can be safe and effective, such as topical nonsteroidal anti-inflammatory drugs for local arthritis symptoms.\textsuperscript{63} Topical antinausea gels commonly are prescribed in hospice practice, with one large hospice pharmacy reporting two-thirds of patients getting a prescription for an antinausea gel.\textsuperscript{60} However, antinausea gels have not been proven effective in any well-designed or placebo-controlled trials, and the available evidence is from small patient series.\textsuperscript{64}

The active ingredients in one commonly prescribed antinausea gel, ABH, are not absorbed to systemic levels that could be effective by any known mechanism. Smith et al.\textsuperscript{29} had 10 healthy volunteers apply the standard 1.0 mL dose (2 mg of lorazepam, 25 mg of diphenhydramine, and 2 mg of haloperidol in a pluronic lecithin organogel), rubbed on the volar surface of the wrists as is done in practice. Blood samples were obtained at 0, 30, 60, 90, 120, 180, and 240 minutes. No lorazepam (A) or haloperidol (H) was detected in any sample from any of the 10 patients, down to a level of 0.05 ng/mL. Most volunteers had undetectable levels of diphenhydramine at most time points, with a maximum concentration observed in a single volunteer of 0.30 ng/mL at 240 minutes. The therapeutic level of diphenhydramine has been estimated at 25–112 ng/mL.\textsuperscript{65} Therefore, none of the lorazepam (A), haloperidol (H), or diphenhydramine (B) in ABH gel is absorbed in sufficient quantities to be effective in the treatment of nausea and vomiting.

This is an important issue for quality of care, safety, and cost. The advantage of ABH and other gels is the easy patient-controlled application and the low cost. But the use of agents given via ineffective routes may delay or prevent the use of more effective interventions, causing suffering and even more expense by precipitating hospital admission. Therefore, the use of ABH and similar gels is not recommended until there is evidence of their effectiveness.

**Discussion**

Over the past 10 years, the field of palliative care has grown and evolved with a remarkable, unprecedented rapidity. Palliative care now can claim recognized medical and nursing
subspecialties with defined domains of knowledge and skills and an expanding evidence base. Perhaps equally important, palliative care is gaining widespread recognition as a specialty that helps patients, families, and providers to achieve an improved quality of life.

Much of this growth is attributable to the way that palliative care promotes open and honest communication with patients and their families about treatment goals. Indeed, a chief contribution of palliative care to the national dialogue about end-of-life care has been the recognition that such communication can help patients to avoid treatment that they do not want. More generally, this focus on communication, decision-making, and patient-centered outcomes has raised questions about the risks and potential benefits of interventions that are used routinely.

This article highlights two such interventions—feeding tubes for those with advanced dementia and ICDs near the end of life—the benefits of which are highly questionable. The discussion above argues convincingly that their use should be the focus of much more careful decision-making by patients and health care providers. More broadly, this article suggests opportunities for palliative care providers to find ways to shape practices that are more consistent with the existing evidence.

But palliative medicine is not immune to questions about its own practice. For instance, the use of MF radiation therapy and ABH gel in palliative care settings offers a valuable cautionary lesson. Just as providers in other fields may reach for unproven treatments in the hope of prolonging life, palliative care providers also may rely on unproven interventions out of a desire to enhance the quality of life.

This lesson highlights the fact that as the field of palliative care continues to develop, there is an urgent need to ensure its evidence base keeps pace with those of other fields. In particular, palliative care will need to carefully examine its own treatments, making a substantial investment in comparative effectiveness research. More generally, palliative care needs to aspire to an evidence base in which all palliative interventions—from opioids to family meetings—can demonstrate effectiveness.

Of course, there are challenges to conducting high-quality comparative effectiveness research in HPM settings. For instance, the ethical concerns that come with seriously ill patient populations create challenges that can be substantial. Also, unlike many fields, there is not yet a clear consensus about all the outcomes that should define “effectiveness” in palliative care. However, none of these challenges is insurmountable. In fact, there is a growing body of evidence that evaluates palliative care interventions using both prospective randomized controlled trials and retrospective propensity score-adjusted cohorts.

More such studies are needed in two areas. First, a productive line of research would rigorously evaluate novel treatments. The ability to generate new treatments and advance the science of comfort is perhaps the most visible evidence of palliative care’s success as a field. However, a second parallel effort also is needed. Just as it is essential to develop and test novel interventions, it will be equally important to critically examine the risks and potential benefits of the existing palliative treatments that are widely used but unproven. Research along both these pathways will help to ensure that the palliative care evidence base continues to grow and that the actual practice of palliative care is consistent with the evidence that exists.

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