

REVIEW

Rachel D. Havyer, MD, FAAHPM

Associate Professor of Medicine, Division of Community Internal Medicine, Geriatrics and Palliative Care, Mayo Clinic, Rochester, MN

Nauzley Abedini, MD, MSc

Cambia Palliative Care Center of Excellence at University of Washington Medicine, Seattle, WA; Assistant Professor of Medicine, Division of Gerontology and Geriatric Medicine, University of Washington, Seattle, WA

Robert L. Jayes, MD

Associate Professor of Medicine, Division of Geriatrics and Palliative Medicine, Georgetown University Medical Faculty Associates, Washington, DC

Brenda Matti-Orozco, MD

Division of General Internal Medicine and Palliative Medicine, Morristown Medical Center, Atlantic Health System, Morristown, NJ

Daniel H. Pomerantz, MD, MPH

Associate Professor of Medicine, Albert Einstein College of Medicine, New York, NY; Department of Medicine, Montefiore New Rochelle Hospital, New Rochelle, NY

Aziz A. Ansari, DO, SFHM, FAAHPM, FACP

Professor of Medicine, Division of Hospital Medicine, Loyola University Medical Center, Maywood, IL

Palliative care: An update for internists

ABSTRACT

All clinicians should maintain basic skills in general palliative care to help address the needs of patients and families. Because keeping up with the information provided by the growing palliative care literature can be challenging, we conducted a detailed search via Medline for palliative care articles published in 2020 in top peer-reviewed medical journals. Using a consensus-driven process of selection, we reviewed and summarized 11 articles to enhance knowledge of the practice-changing palliative care literature for general internists.

KEY POINTS

Transitions in health status provide important opportunities for internists to engage in advance-care planning with patients and complete physician orders for life-sustaining treatment (POLST) forms to improve delivery of goal-concordant care.

Internists can look for opportunities to improve patients' healthcare experience near end of life and reduce healthcare utilization by considering palliative care involvement for patients with non-cancer diagnoses.

Internists should be aware of the implications of COVID-19 on older adults' experience of loneliness and social isolation and its associated health consequences.

Patients with advanced cancer may benefit from as-needed olanzapine for chronic nausea or methylphenidate for fatigue.

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PALLIATIVE CARE (PC) USES AN interdisciplinary approach to optimize quality of life and goal-concordant care for patients and families facing serious illnesses. With increasing age and therapies for cancer and other chronic diseases, the need for PC at a population level is significant.¹ Internists are frequently called upon to address PC needs of patients, including advance-care planning, symptom control, and providing goal-concordant care.² Yet keeping up with the growing PC literature is challenging.

This article reviews important PC research articles published between January 1 and December 31, 2020, using a case-based format. After performing a Medline keyword search of PC terms (palliative, pain, end-of-life, symptom management, communication, hospice, terminal illness, advanced directives) of 15 leading peer-reviewed PC journals, all identified articles were reviewed, and 11 articles³⁻¹³ were selected for inclusion by ranking and consensus discussion based on the following factors: PC content, scientific rigor, impact on practice, and relevance to general medicine.

■ PALLIATIVE CARE FOR NON-CANCER ILLNESSES

Background

While most PC interventions involve patients with cancer, many patients with chronic non-cancer diagnoses also need significant coordinated and appropriate healthcare, especially at end of life.¹⁴

A meta-analysis and systemic review by Quinn et al³ measured the association between

healthcare use, quality of life, and symptom burden in PC interventions for adults with non-cancer illnesses.

Findings

The analysis included 28 PC intervention trials for heart failure, chronic obstructive pulmonary disease, and dementia.³ PC, compared with usual care, involved less emergency department use (20% vs 24%; odds ratio [OR] 0.82, 95% confidence interval [CI] 0.68–1.00) and fewer hospitalizations (38% vs 42%; OR 0.80, 95% CI 0.65–0.99). PC was not associated with improved quality of life (pooled standardized mean difference [SMD], 0.18, 95% CI, –0.24 to 0.61) and was associated with lower symptom burden, especially with interdisciplinary team involvement (pooled SMD –0.12, 95% CI, –0.20 to –0.03). PC was also associated with more advance-care planning compared with usual care (38% vs. 42%, OR 2.95, 95% CI 1.52–5.73).³

Implications

Although it is unclear what aspects of PC influenced outcomes, PC interventions can help reduce emergency department use, hospitalizations, symptom burden, and increase advance-care planning for non-cancer diagnoses.

■ PALLIATIVE CARE CONSULTATIONS REDUCE BURDENSOME INTERVENTIONS

Background

Patients near end of life have higher intensity of care that does not necessarily lead to better outcomes.¹⁴ Unpredictable disease trajectories associated with non-cancer diagnoses pose challenges in determining when to pursue a comfort-based approach.¹⁵

In this population-matched Canadian cohort study, Quinn et al¹⁴ measured the association between newly initiated PC in the last 6 months of life and healthcare use and location of death in adults dying from non-cancer vs cancer illnesses. Secondary outcomes included the rates of potentially burdensome interventions such as positive pressure ventilation, cardiopulmonary resuscitation, and initiation of dialysis.

Findings

PC involvement in patients dying from non-cancer illness related to chronic organ failure was associated with 12% reduction in both emergency department visits (adjusted rate ratio [ARR] 0.88, 95% CI 0.85–0.91) and hospital admissions (ARR 0.88, 95% CI 0.86–0.91); 41% reduction in intensive care unit (ICU) admissions (ARR 0.59, 95% CI 0.56–0.62); and increased odds of dying at home or nursing home vs dying in hospital (OR 1.67, 95% CI 1.60–1.74).⁴ Rates of potentially burdensome interventions were lower for those receiving PC (OR 0.66, 95% CI 0.64–0.69). Similar results were found for cancer patients. Unexpectedly, PC increased rates of emergency department visits (ARR 1.06, 95% CI 1.01–1.12) and hospital admissions (ARR 1.33, 95% CI 1.27–1.39) in patients dying from dementia. However, differences in these outcomes depended on patients' primary residence (nursing home vs. community). No association was found between healthcare use and PC for dementia patients living in the community compared with those in nursing homes. Community-dwelling dementia patients also had increased odds of dying at home (OR 1.35, 95% CI 1.23–1.49). The study only measured physician-led PC interventions; non-physician PC interventions could not be extrapolated.⁴

Implications

Like cancer, non-cancer diagnoses can benefit from specialty PC interventions at end of life and have the potential to reduce healthcare use and burdensome interventions.

■ TREATMENT-LIMITING PHYSICIAN ORDERS FOR LIFE-SUSTAINING TREATMENT

Background

While treatment-limiting physician orders for life-sustaining treatment (POLSTs) have been shown to ensure patient treatment preferences and thereby reduce some burdensome interventions at end of life,¹⁶ association with ICU care is less understood.

Lee et al⁵ conducted a retrospective cohort study of decedents with preexisting POLSTs who were hospitalized within 6 months of death to evaluate the association of POLSTs for medical interventions and ICU admission.

Palliative care interventions can reduce emergency department use, hospitalizations, and symptom burden for patients with non-cancer diagnoses

Findings

Of the 1818 decedents, ICU admissions occurred in 31% (95% CI, 26%–35%) with comfort-only orders, 46% (95% CI 42%–49%) with limited-intervention orders, and 62% (95% CI 58%–66%) with full-treatment orders.⁵ Patients with comfort-only or limited-intervention POLSTs were less likely to receive ICU admission (comfort only, ARR 0.53 [95% CI 0.45–0.62]; limited interventions, ARR 0.79 [95% CI 0.71–0.87]). However, 38% (95% CI 35%–40%) of patients with treatment-limiting POLSTs received POLST-discordant care. Factors associated with lower likelihood of POLST-discordant care were dementia with comfort-only orders, cancer, and older age. Traumatic injury was associated with a higher likelihood of POLST-discordant care. The incidence of POLST-discordant intensive care did not decrease significantly over the 8 years of study (comfort only, ARR 1.01 per year [95% CI 0.94–1.09; $P = .70$]; limited interventions, ARR 1.00 per year [95% CI 0.96–1.04; $P = .90$]).⁵

Implications

Treatment-limiting POLSTs were associated with lower rates of ICU admission compared with full-treatment POLSTs. As 38% of patients received POLST-discordant care, further work is necessary to help provide patients with goal-concordant care at end of life. Further, as the study excluded patients not hospitalized prior to death, this may over-estimate the overall prevalence of goal-discordant care.

■ EARLY PALLIATIVE CONSULTS CLARIFY PATIENT ICU GOALS-OF-CARE

Background

Although PC appears to improve quality of life for patients,¹⁷ studies of PC impact in the ICU are mixed with varying study designs and measured outcomes.

Ma et al⁶ employed a single-center cluster, randomized crossover trial with 6-week wash-out period to determine if early triggered multidisciplinary PC consults in the ICU would improve end-of-life outcomes. They used predetermined criteria to select patients at high risk of mortality who were randomized to PC consultation by an interprofessional team within 48 hours of ICU admission vs standard care.

Findings

Of the 233 enrolled patients, 199 (97 intervention, 102 control) were eligible to be analyzed, and the primary outcome of transition to do-not-resuscitate/do-not-intubate was significantly more frequent (50.5% vs 23.4%, $P < .0001$) and occurred earlier ($P < .0001$) with PC intervention in both unadjusted and adjusted models.⁶ For secondary outcomes, transfer to hospice occurred significantly more frequently (18.6% vs 4.9%, $P = .0026$), and mechanical ventilation was of shorter median duration (4 vs 6 days, $P = .0415$) with PC intervention. There was no significant change in hospital, ICU, and 30-day mortality or hospital or ICU length of stay.⁶

Implications

Early targeted interprofessional PC consultations in the ICU increased transitions to do-not-resuscitate/do-not-intubate by hospital discharge, increased hospice referrals, and reduced days on mechanical ventilation. Further study is warranted to fully understand the cost implications of routine PC consultations in the ICU.

■ BRIEF COACHING SESSIONS CAN IMPROVE RESIDENT COMMUNICATIONS OF GOALS OF CARE

Background

In teaching hospitals, resident physicians frequently initiate goals-of-care discussions and facilitate end-of-life care but may feel uncomfortable with these discussions.¹⁸

Rodenbach et al⁷ aimed to improve internal medicine resident PC skills through 2 didactics and thrice-weekly coaching sessions (averaging 16 minutes per session) during inpatient rotation. Residents completed pre- and post-rotation surveys of their preparedness in discussing PC topics.

Findings

Residents rated coaching sessions as useful and reported improved preparedness in goals-of-care conversations.⁷ Residents asked questions centered on the following PC topics: communication (68.3%), pain (9.7%), non-pain symptoms (9.2%) and ethics (4.9%). During the 14-month intervention period, 42 residents cared for 232 at-risk patients (those

Treatment-limiting physician orders for life-sustaining treatment were associated with lower ICU admissions

> 65 years with ≥ 2 hospitalizations in past 6 months or any patient > 90 years). Among at-risk patients, documented goals-of-care discussions rose from 5.2% to 12.9% before hospitalization, and from 25.0% to 57.3% before discharge. Rates of POLST completion did not differ between pre-intervention and intervention groups.⁷

Implications

Brief coaching sessions can integrate PC education into a busy clinical service, improve resident preparedness, and increase likelihood that residents will facilitate and document goals-of-care discussions with hospitalized patients.

■ 3 WISHES PROJECT (3WP): ENHANCE PATIENT DIGNITY, REFLECT PATIENT IDENTITY, AND HONOR END-OF-LIFE PREFERENCES

Background

The 3 Wishes Project (3WP) elicits and implements wishes from dying ICU patients, family members, and clinicians to celebrate the legacy and life of patients through acts of compassion.¹⁹

Vanstone et al⁸ completed a mixed-methods study with 730 patients from 4 North American, tertiary care ICUs, eliciting 3,407 (from 11 wish categories) and implementing 3,325 wishes. Qualitative data were gathered from 75 family members, 72 clinicians, and 20 managers or hospital administrators.

Findings

The value of 3WP included family honoring the lives and legacies of loved ones while inspiring compassionate clinical care.⁸ Examples of performed wishes included dressing the patient in their own clothing, having a celebration in the patient's room, and providing transportation to enable others to visit the patient in the hospital. Family members reported an enhanced care experience with redirection of attention from the illness to the person's identity. Transferability factors included family appreciation and a collaborative ICU culture committed to dignity-conserving end-of-life care. 3WP was affordable (mean cost \$5.19 per wish) after minimal investment for reusable materials.

Each site sustained 3WP after study completion. Cultural sensitivity and adaptation may be needed for more vulnerable, diverse, or disadvantaged populations.⁸

Implications

When championed by compassionate local clinicians, 3WP is a valuable, transferrable, affordable, and sustainable program at end of life in the ICU.

■ COVID-RELATED LONELINESS AND END OF LIFE

Background

Loneliness is the subjective feeling of being left out, isolated, and lacking companionship, afflicting up to 32% of adults over age 55.^{20–23} It is associated with increased rates of depression, functional decline, cognitive decline, and premature death.^{21–23} Older adults with multimorbidity, recent life transitions, shrinking social networks, and poor socioeconomic status are frequently at risk for loneliness.^{20–24} The COVID-19 pandemic has been associated with increased risk of loneliness in older adults.²⁴

Abedini and colleagues⁹ explored the relationship of loneliness end-of-life experience in older adults by conducting a secondary data set analysis of the Health and Retirement Study, a nationally representative, longitudinal survey of lonely and non-lonely American decedents over age 50 who died between 2004 and 2014 (n = 8,700). Postmortem interviews were performed with next-of-kin after participant death.

Findings

Approximately one-third of the 2,896 decedents (34%) were lonely near end of life.⁹ Lonely older adults had statistically significant higher odds of suffering from pain, difficulty breathing, severe fatigue, and confusion in the last year of life, were more likely to have higher total symptom burden at end of life, more likely to die in a nursing home rather than at home (ARR 1.78; 95% CI, 1.30–2.42), and more likely to use life support in the last 2 years of life (ARR 1.36; 95% CI, 1.08–1.71). This study was limited by its cross-sectional design and inability to assess causality.⁹

The 3 Wishes Project includes honoring the lives and legacies of loved ones while inspiring compassionate clinical care

Implications

While this study was not conducted during the COVID-19 pandemic, loneliness is associated with higher symptom burden and poorer end-of-life outcomes. Given COVID-19 has exacerbated social isolation and loneliness,²⁴ clinicians should consider screening for and documenting loneliness routinely across care settings to identify high-risk older adults.

■ FAMILY VISITATION REDUCES POST-OPERATIVE DELIRIUM AFTER SURGERY

Background

Delirium affects up to 50% of older hospitalized adults, increasing hospital length of stay, functional decline, risk of subsequent dementia, and mortality, all leading to \$164 billion in annual healthcare costs in the United States.^{25,26} Multimodal, nonpharmacologic interventions like Hospital Elder Life Programs (HELP) have been shown to improve postoperative delirium outcomes, but typically rely on volunteers.^{25,26}

Wang and colleagues¹⁰ evaluated whether family rather than volunteer-based HELP programs could reduce postoperative delirium and associated complications. They conducted a single-blind, cluster randomized control trial in patients over age 70 on 6 surgical floors in a Chinese hospital assessing tailored-HELP intervention vs usual care. Families received education and nurse supervision as part of the intervention.

Findings

Of the 281 patients enrolled, postoperative delirium occurred in 2.6% of intervention patients vs 19.4% in usual care patients (RR 0.14, 95% CI 0.05–0.38).¹⁰ Intervention patients had significantly less functional decline and cognitive decline at discharge, and mean length of stay was 4.26 days shorter. Generalizability is limited as China has higher numbers of patients per nurse, longer length of stay owing to lack of post-acute care facilities, and surgeons less commonly perform surgery on frail patients. Hence, the patient population may have been younger and possibly more robust compared to the United States population.¹⁰

Implications

Use of family caregivers rather than volunteers as participants in HELP interventions can reduce postoperative delirium and improve outcomes in older hospitalized patients in China. While this study did not evaluate the implications of COVID-19 on family-based interventions, other studies have shown that visitor restriction during the COVID-19 pandemic is associated with increased incidence of delirium,²⁷ and hence involvement of family should be considered to help reduce postoperative delirium.

■ PHYSICIAN ENGAGEMENT WITH INTERPRETERS FOR END-OF-LIFE CONVERSATIONS

Background

Approximately 26 million people living in the United States have limited English-proficiency that can negatively impact their healthcare experience and outcomes.^{11,28,29} Use of medical interpreters in language-discordant patient encounters improves outcomes,^{28,29} but little is known about the views of medical interpreters around best practices for end-of-life conversations.

Silva and colleagues¹¹ conducted 12 semi-structured interviews with Spanish and Chinese interpreters at a New York City hospital.

Findings

Qualitative analysis demonstrated that interpreters felt conflict between the need to translate words directly vs portraying messages in a culturally appropriate manner.¹¹ They felt high emotional burden when unprepared, and expressed challenges with interpreting end-of-life terms that are not commonly used in their culture (ie, do-not-resuscitate, intubation, resuscitation, PC).¹¹

Implications

In-person interpretation should be used whenever possible for end-of-life conversations. Pre-meetings and debriefings can ensure that interpreters are prepared for challenging end-of-life conversations with reduced emotional burden. Interpreting within the normative cultural context rather than literal translation should be emphasized.

Use of family caregivers in Hospital Elder Life Programs reduced postoperative delirium and improved outcomes in older hospitalized patients

■ OLANZAPINE IMPROVES CHRONIC NAUSEA IN ADVANCED CANCER

Background

Chronic nausea is a distressing symptom in advanced cancer. While case reports and retrospective data suggest olanzapine may be helpful, there have been limited data from randomized control trials.³⁰

Navari et al¹² conducted a multicenter, double-blind, placebo-controlled pilot randomized control trials to study the use of olanzapine (5 mg/day orally) for chronic nausea in 30 patients (15 per arm) with advanced incurable cancer who continued to have chronic nausea \geq 7 days after completing chemotherapy or radiation therapy. Patients were permitted to use their prior anti-emetics as needed. Numerical scores for symptom intensity (appetite, nausea, fatigue, sedation, pain, well-being) and number of vomiting episodes were measured daily for 7 days.

Findings

Median nausea scores improved at day 1 in olanzapine arm to 2 (range, 2–3) compared with 9 (range, 8–10) in placebo arm.¹² The reduction in nausea scores in olanzapine arm was 8 points (95% CI, 7–8, $P < .001$) more than the placebo arm at 1 week. Additionally, olanzapine reduced vomiting, fatigue, pain and improved appetite and well-being (all $P < .05$). No adverse events were reported. After the protocol was broken, nearly all placebo patients transitioned to olanzapine with marked efficacy and minimal toxic effects. Patients only discontinued olanzapine when they were unable to take oral medications or died. While this pilot study had a small sample size, it did show substantial symptomatic improvement.¹²

Implications

Olanzapine 5 mg daily is effective and well-tolerated for chronic nausea and vomiting associated with advanced cancer.

■ METHYLPHENIDATE IMPROVES FATIGUE IN ADVANCED CANCER

Background

Fatigue is a common symptom that impacts quality of life in advanced cancer. Systematic reviews of methylphenidate for cancer-related fatigue have shown statistically significant re-

duction in fatigue, although less often clinically significant to patients.³¹

Pedersen and colleagues¹³ conducted a prospective, controlled, double-blind, paired design study to evaluate the efficacy of methylphenidate as needed for management of fatigue in advanced cancer. Inpatient PC patients at a single institution in Denmark received a box of randomly arranged tablets of 10-mg methylphenidate or placebo to take in predetermined order up to every 3 hours as needed for fatigue over the course of a week with subsequent measures of symptoms 2 and 5 hours after tablet administration.

Findings

Twenty-eight of 38 enrolled participants were evaluable.¹³ Mean change (decrease) in tiredness scores (on a 100-point visual analogue scale) at 2 and 5 hours was 20 and 17 after methylphenidate administration and 8 and 5 after placebo administration, respectively. Comparing mean differences, a significant decrease for methylphenidate compared with placebo was observed after 2 ($P = .004$) and 5 hours ($P = .001$), respectively. Methylphenidate was also significantly more effective compared with placebo regarding secondary measures of drowsiness and activity at 2 hours ($P < .001$ and $P = .008$, respectively). No serious adverse events were reported. Limitations of the study are short follow-up time, and the 3-hour interval of tablet administration may not have been long enough for washout of the prior tablet.¹³

Implications

10 mg of methylphenidate as needed provided statistically and clinically significant impact on fatigue scores in PC patients with advanced cancer. Studies of longer duration are needed.

■ CONCLUSION

Recent PC research provides important guidance to general medicine clinicians in symptom management, advance-care planning, and communication training in order to maximize compassionate care to patients and family members with serious illness. ■

■ DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

A small pilot study of olanzapine showed symptomatic improvement for chronic nausea and vomiting associated with advanced cancer

REFERENCES

1. Morin L, Aubry R, Frova L, et al. Estimating the need for palliative care at the population level: a cross-national study in 12 countries. *Palliat Med* 2017; 31(6):526–536. doi:10.1177/0269216316671280
2. Quill TE, Abernethy AP. Generalist plus specialist palliative care—creating a more sustainable model. *N Engl J Med* 2013; 368(13):1173–1175. doi:10.1056/NEJMp1215620
3. Quinn KL, Shurrab M, Gitau K, et al. Association of receipt of palliative care interventions with health care use, quality of life, and symptom burden among adults with chronic noncancer illness: a systematic review and meta-analysis. *JAMA* 2020; 324(14):1439–1450. doi:10.1001/jama.2020.14205
4. Quinn KL, Stukel T, Stall NM, et al. Association between palliative care and healthcare outcomes among adults with terminal non-cancer illness: population based matched cohort study. *BMJ* 2020; 370:m2257. doi:10.1136/bmj.m2257
5. Lee RY, Brumback LC, Sathitratanaheewin S, et al. Association of physician orders for life-sustaining treatment with ICU admission among patients hospitalized near the end of life. *JAMA* 2020; 323(10):950–960. doi:10.1001/jama.2019.22523
6. Ma J, Chi S, Buettner B, et al. Early palliative care consultation in the medical ICU: a cluster randomized crossover trial. *Crit Care Med* 2019; 47(12):1707–1715. doi:10.1097/CCM.0000000000004016
7. Rodenbach R, Kavalieratos D, Tamber A, et al. Coaching palliative care conversations: evaluating the impact on resident preparedness and goals-of-care conversations. *J Palliat Med* 2020; 23(2):220–225. doi:10.1089/jpm.2019.0165
8. Vanstone M, Neville TH, Clarke FJ, et al. Compassionate end-of-life care: mixed-methods multisite evaluation of the 3 wishes project. *Ann Intern Med* 2020; 172(1):1–11. doi:10.7326/M19-2438
9. Abedini NC, Choi H, Wei MY, Langa KM, Chopra V. The relationship of loneliness to end-of-life experience in older Americans: a cohort study. *J Am Geriatr Soc* 2020; 68(5):1064–1071. doi:10.1111/jgs.16354
10. Wang YY, Yue JR, Xie DM, et al. Effect of the tailored, family-involved hospital elder life program on postoperative delirium and function in older adults: a randomized clinical trial. *JAMA Intern Med* 2020; 180(1):17–25. doi:10.1001/jamainternmed.2019.4446
11. Silva MD, Tsai S, Sobota RM, Abel BT, Reid MC, Adelman RD. Missed opportunities when communicating with limited English-proficient patients during end-of-life conversations: insights from Spanish-speaking and Chinese-speaking medical interpreters. *J Pain Symptom Manage* 2020; 59(3):694–701. doi:10.1016/j.jpainsymman.2019.10.019
12. Navari RM, Pywell CM, Le-Rademacher JG, et al. Olanzapine for the treatment of advanced cancer-related chronic nausea and/or vomiting: a randomized pilot trial. *JAMA Oncol* 2020; 6(6):895–899. doi:10.1001/jamaoncol.2020.1052
13. Pedersen L, Lund L, Petersen MA, Sjogren P, Groenvold M. Methylphenidate as needed for fatigue in patients with advanced cancer. A prospective, double-blind, and placebo-controlled study. *J Pain Symptom Manage* 2020; 60(5):992–1002. doi:10.1016/j.jpainsymman.2020.05.023
14. Tanuseputro P, Wodchis WP, Fowler R, et al. The health care cost of dying: a population-based retrospective cohort study of the last year of life in Ontario, Canada. *PLoS One* 2015; 10(3):e0121759. doi:10.1371/journal.pone.0121759
15. Lunney JR, Lynn J, Foley DJ, Lipson S, Guralnik JM. Patterns of functional decline at the end of life. *JAMA* 2003; 289(18):2387–2392. doi:10.1001/jama.289.18.2387
16. Hickman SE, Keevern E, Hammes BJ. Use of the physician orders for life-sustaining treatment program in the clinical setting: a systematic review of the literature. *J Am Geriatr Soc* 2015; 63(2):341–350. doi:10.1111/jgs.13248
17. Kavalieratos D, Corbelli J, Zhang D, et al. Association between palliative care and patient and caregiver outcomes: a systematic review and meta-analysis. *JAMA* 2016; 316(20):2104–2114. doi:10.1001/jama.2016.16840
18. Rhodes RL, Tindall K, Xuan L, Paulk ME, Halm EA. Communication about advance directives and end-of-life care options among internal medicine residents. *Am J Hosp Palliat Care* 2015; 32(3):262–268. doi:10.1177/1049909113517163
19. Cook D, Swinton M, Toledo F, et al. Personalizing death in the intensive care unit: the 3 Wishes Project: a mixed-methods study. *Ann Intern Med* 2015; 163(4):271–279. doi:10.7326/M15-0502
20. Masi CM, Chen HY, Hawkey LC, Cacioppo JT. A meta-analysis of interventions to reduce loneliness. *Pers Soc Psychol Rev* 2011; 15(3):219–266. doi:10.1177/1088868310377394
21. Rico-Urbe LA, Caballero FF, Martín-María N, Cabello M, Ayuso-Mateos JL, Miret M. Association of loneliness with all-cause mortality: a meta-analysis. *PLoS One* 2018; 13(1):e0190033. doi:10.1371/journal.pone.0190033
22. Perissinotto CM, Stijacic Cenzer I, Covinsky KE. Loneliness in older persons: a predictor of functional decline and death. *Arch Intern Med* 2012; 172(14):1078–1083. doi:10.1001/archinternmed.2012.1993
23. Perissinotto C, Holt-Lunstad J, Periyakoil VS, Covinsky K. A practical approach to assessing and mitigating loneliness and isolation in older adults. *J Am Geriatr Soc* 2019; 67(4):657–662. doi:10.1111/jgs.15746
24. Wong SYS, Zhang D, Sit RWS, et al. Impact of COVID-19 on loneliness, mental health, and health service utilization: a prospective cohort study of older adults with multimorbidity in primary care. *Br J Gen Pract* 2020; 70(700):e817–e824. doi:10.3399/bjgp20X713021
25. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet* 2014; 383(9920):911–922. doi:10.1016/S0140-6736(13)60688-1
26. Oh ES, Fong TG, Hshieh TT, Inouye SK. Delirium in older persons: advances in diagnosis and treatment. *JAMA* 2017; 318(12):1161–1174. doi:10.1001/jama.2017.12067
27. Kandori K, Okada Y, Ishii W, Narumiya H, Maebayahi Y, Izuka R. Association between visitation restriction during COVID-19 pandemic and delirium incidence among emergency admission patients: a single-center retrospective observational cohort study in Japan. *J Intensive Care* 2020. doi:10.21203/rs.3.rs-80164/v1
28. Fiscella K, Franks P, Doeschler MP, Saver BG. Disparities in health care by race, ethnicity, and language among the insured: findings from a national sample. *Med Care* 2002; 40(1):52–59. doi:10.1097/00005650-200201000-00007
29. Karliner LS, Jacobs EA, Chen AH, Mutha S. Do professional interpreters improve clinical care for patients with limited English proficiency? A systematic review of the literature. *Health Serv Res* 2007; 42(2):727–754. doi:10.1111/j.1475-6773.2006.00629.x
30. Licup N. Olanzapine for nausea and vomiting. *Am J Hosp Palliat Care* 2010; 27(6):432–434. doi:10.1177/1049909110369532
31. Tomlinson D, Robinson PD, Oberoi S, et al. Pharmacologic interventions for fatigue in cancer and transplantation: a meta-analysis. *Curr Oncol* 2018; 25(2):e152–e167. doi:10.3747/co.25.3883

Address: Rachel D. Havyer, MD, FAAHPM, Division of Community Internal Medicine, Geriatrics and Palliative Care, Mayo Clinic, 200 First St. SW, Rochester, MN 55905; havyer.rachel@mayo.edu