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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):1–5.

Rave Reviews

Summaries with Commentaries

Sleep Deprivation Affects Tau Phosphorylation in Human Cerebrospinal Fluid

Background. Amyloid-β deposition in the brain (as plaques) and hyperphosphorylated tau intracellular aggregation (as tangles) are hallmarks of Alzheimer’s
disease.1 How does sleep affect phosphorylated tau (P-tau)?

Design and Participants. This study measured tau and P-tau residues in cerebrospinal fluid (CSF) collected in a previous study to understand how sleep affects P-tau. Cognitively normal, amyloid-β-negative participants were randomized 1:1:1 to 36 hours of sleep deprivation, increased sleep with sodium oxybate (increased slow wave sleep [when neuronal activity, and therefore amyloid-β and tau release, were hypothesized to be lowest]), or normal sleep. Mass spectrometry measured tau and P-tau residue concentrations (threonine-181, serine-202, and threonine-217) in CSF serial samples. General linear mixed models were used.

Results. Controls (n=7) were age mean=48 years (SD=9.2), 71% female, and 57% Black. Sleep-deprived (n=7) were 48 (10), 57%, and 57%. Drug (n=6) were 51 (9.8), 50%, and 67%. Unphosphorylated threonine-181, serine-202, and threonine-217 mean overnight concentrations increased 30%–50% above baseline in sleep-deprived vs. control and drug but showed no differences between control and drug. Mean overnight P-threonine-181 changes were similar to threonine-181, with P-threonine-181 increased 40%–50% above baseline in sleep-deprived vs. control and drug. However, P-serine-202 showed no differences between sleep-deprived and control or drug and control. P-threonine-217 increased 60%–80% in sleep-deprived vs. control, with no change for drug. Each P-tau species responded to deprivation in opposite directions. The mean overnight P-threonine-217/threonine-217 ratio increased 15%–20% above baseline for sleep-deprived. However, the between-group P-threonine-181/threonine-181 ratio was unchanged, and the mean overnight P-serine-202/threonine-217 ratio decreased from baseline more for sleep-deprived vs. controls (all P<0.01).

Commentary. Sleep disturbance is a common problem in AD and a recent meta-analysis suggests it may be an important risk factor in 15% of AD patients.2 This small study found sleep deprivation alters the release of truncated tau protein into the CSF. Interestingly, the level of tau phosphorylation was also altered but only at select residues. With only eight normal subjects in this study, we do not know if or how the findings differ in AD patients. The results do suggest a tau regulatory system that, if understood, could provide needed insights into the role of tau aggregation in AD. An important question is whether treating sleep disorders can prevent or delay the onset of AD. A similar clinical analogy is the need to control chronic pain to prevent anxiety and depression,3 which highlights the importance of palliating symptoms.

Bottom Line. Sleep deprivation alters tau processing and may increase the risk of AD.

Reviewers. Kenneth Cornetta, MD, Indiana University School of Medicine, Indianapolis, IN

Source. Barthélemy NR, Liu H, Lu W, Kotzbauer PT, Bateman RJ, Lucey BP. Sleep deprivation affects tau phosphorylation in human cerebrospinal fluid. Ann Neurol. 2020;87(5):700–709.

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Pandemic as Teacher—Forcing Clinicians to Inhabit the Experience of Serious Illness

Background. Healthcare workers on the front lines of the coronavirus response face reports every day regarding how many of their colleagues have been diagnosed with COVID-19.1,2 How does this pandemic present a growth opportunity for clinicians?

Design and Participants. This article discussed how the pandemic has disrupted clean distinctions in professional roles and is forcing clinicians to gain new insights into the experience of seriously ill patients. One way this merging is happening is all too literal: clinicians themselves are getting sick and dying. More immediately, many find themselves caring for other clinicians. The likelihood of falling ill has led many clinicians to tackle advance care planning with their families. Clinicians are inhabiting the reality of serious illness in other ways, too, even if they are not infected or working with infected patients. They are not permitted to go outside without masks, to shake hands, or to hug friends/family—restrictions all too familiar to patients with immunodeficiencies. And the unsettling uncertainty about the pandemic’s duration/extent is familiar to any patient with cancer. In addition, the pandemic has brought losses/threats to clinicians’ identities that echo those resulting from illness. Many have lost graduations, weddings, favorite restaurants, childcare, income, jobs, and the freedom to go to their offices. Inhabiting some of the harsh realities of serious illness, including uncertainty, loss of control, and challenges to identity, may help clinicians gain a deeper understanding of patients’ experiences with illness.

Commentary. Carl Jung reminds us that “[a] good half of every treatment that probes at all deeply consists in the doctor’s examining himself, for only what he can put right in himself can he hope to put right in the patient. This, and nothing else, is the meaning of the Greek myth of the wounded physician.”5 Like...
Chiron—the mythical centaur and teacher of Asclepius—with his nonhealing wound, COVID-19 can offer us an opportunity to look at how we inhabit the realm of serious illness. According to Dr. deLima Thomas, this reflection may allow for a more authentic understanding, improved clinical practices, and enhanced systems of care for our patients.

**Bottom Line.** Reflecting on the way COVID-19 has affected us individually and collectively, especially those working in healthcare, allows us to better appreciate the experience of seriously ill patients with the hope that this may transform ourselves and our care for others in the process.

**Reviewers.** Craig D. Blinderman, MD MA FAAHPCM, NewYork-Presbyterian Hospital/Columbia University Irving Medical Center and Columbia University, New York, NY

**Source.** deLima Thomas J. Pandemic as teacher—forcing clinicians to inhabit the experience of serious illness [published online ahead of print May 20, 2020]. *N Engl J Med.* https://doi.org/10.1056/NEJMp2015024.

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**Intergroup Anxiety in Pain Care: Impact on Treatment Recommendations Made by White Providers for Black Patients**

**Background.** Race disparities in pain care have been well documented, with Black patients at high risk for receiving suboptimal care. How does intergroup anxiety impact pain treatment decisions?

**Design and Participants.** This study tested whether providers’ trait-level intergroup anxiety impacts their state-level (ie, in-the-moment) comfort and, ultimately, their pain treatment decisions while treating patients. A planned secondary analysis was conducted of a perspective-taking intervention (randomized controlled trial) to reduce pain treatment disparities. Using the validated Intergroup Anxiety Scale, providers indicated (from 1–10) how awkward, self-conscious, accepted, confident, defensive, careful, apprehensive, uncertain, anxious, comfortable, impatient, and trusting they feel when treating patients who are culturally different from themselves. Then, providers watched videos and read vignettes for 12 virtual human patients (varied by race and socioeconomic status) with chronic back pain. Using visual analogue scales, providers responded to the question “Rate your level of comfort in providing care for this patient” and rated their likelihood of using an opioid analgesic, referral to a pain specialist, physical therapy, and a nonopioid analgesic. Descriptive statistics and mediation models were used.

**Results.** Providers (n=436) were 68% white. White providers were mean age=30 years (SD=3.2) and 59% male. Specialties included anesthesiology (19%), primary/internal/family medicine (18%), and pediatrics (14%). White providers with higher trait-level intergroup anxiety reported lower state-level comfort treating Black patients and were thereby likelier to recommend opioid (indirect effect=0.76, 95% CI=0.21–1.51) and pain specialty (0.91, 0.26–1.78) treatments and less likely to recommend nonopioid analgesics (−0.45, −0.94−−0.12) (P<0.001). Neither trait-level intergroup anxiety nor state-level comfort influenced decisions for physical therapy.

**Commentary.** This study provides important information to better understand intrapersonal and interpersonal contributions to racial disparities in pain care when there is patient-provider racial discordance. Should the current findings be replicated in future studies, they would support interventions to help providers become more aware of their trait-level intergroup anxiety and manage their state-level reactions to patients who are racially/ethnically different from themselves. Though this study looked particularly at White physicians treating Black patients for pain, further study of disparities in other groups also is needed. Given that previous research typically has found that Black patients receive fewer and weaker opioids than white patients, which differs from the findings from this study, ongoing research is required to clarify these discrepancies.

**Bottom Line.** Greater focus and further investigation are required to elucidate and address mechanisms of racial disparities in pain care and to optimize pain care delivery in racially diverse patients.

**Reviewers.** Mona Patel Kathuria, DO FAAHPCM, Veteran Affairs New Jersey Care System, East Orange and Lyons, NJ

**Source.** Grant AD, Miller MM, Hollingshead NA, Anastas TM, Hirsh AT. Intergroup anxiety in pain
care: impact on treatment recommendations made by white providers for black patients. Pain. 2020;161(6):1264–1269.

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Overtreatment of Older Adults with Limited Life Expectancy

Background. Many older adults with limited life expectancy (LLE) are potentially overtreated for their illnesses. Among specific medications used in treating nursing home residents, what is the prevalence of discontinuation/reduction?

Deintensification of Diabetes Medications Among Veterans at the End of Life in VA Nursing Homes

Design and Participants. This retrospective cohort study used linked Veterans Affairs (VA) and Medicare clinical/administrative data and Minimum Data Set assessments (MDSAs) to examine diabetes medication deintensification in older veterans with diabetes and LLE and/or advanced dementia (LLE/AD). Discontinuation/reduction for a 7-day period was evaluated among veterans (admitted to VA community living centers [VA-CLC] 2009–2015 with hemoglobin [Hb]A1c measured ≤90 days post-admission) who were potentially overtreated (HbA1c ≤7.5% and receiving hypoglycemic medications).

Results. Of 6,960 participants, >40% were potentially overtreated. Cumulative incidence of deintensification at 90 days was 46%. Higher baseline HbA1c values were associated with lower likelihood of deintensification (eg, HbA1c 7.0–7.5% vs. <6.0%, aRR=.57, 95% CI=.50–.66). Compared to nonsulfonylurea oral agents (eg, metformin), other treatment regimens were likelier to be deintensified (aRR=1.31–1.88), except for basal insulin (aRR=.59, .52–.66). The only factor associated with increased likelihood of deintensification was documented end-of-life status (aRR=1.12, 1.01–1.25). Admission from home/assisted living (aRR=.85, .75–.96), obesity (aRR=.88, .78–.99), and peripheral vascular disease (aRR=.90, .81–.99) were associated with less deintensification.

Incidence and Predictors of Aspirin Discontinuation in Older Adult Veteran Nursing Home Residents at End of Life

Design and Participants. This retrospective cohort study determined incidence and predictors of aspirin discontinuation in veterans with LLE/AD (≥65 y) who were taking aspirin for secondary prevention at VA-CLC admission, stratified by whether their limited prognosis (LP) was explicitly documented at admission. Linked VA and Medicare clinical/administrative data and MDSAs were used. Veterans were admitted for ≥7 days (2009–2015), had a history of coronary artery disease and/or stroke/transient ischemic attack, and used aspirin ≤1 week of VA-CLC admission. The primary outcome was discontinuation ≤90 days post-admission, defined as 14 consecutive days of no receipt.

Results. Cumulative incidence of discontinuation was 27% (95% CI=26%–28%) in the full sample (n=13,844), 34% (33%–36%) in residents with explicit LP documentation, and 24% (23%–25%) in residents with no such documentation. Independent variables associated with aspirin discontinuation differed in residents with (FY2012 vs. FY2009 admission and residing in large metropolitan vs. rural areas) vs. without (Hispanic ethnicity/race vs. White and requiring an IV feeding tube) explicit LP documentation at admission.

Prevalent Statin Use in Long-Stay Nursing Home Residents with Life-Limiting Illness

Design and Participants. This cross-sectional study evaluated statin pharmacotherapy in Medicare- and Medicaid-certified long-stay nursing home residents (age ≥65 years) with life-limiting illness, using Medicare Part D claims. Life-limiting illness was operationally defined to capture those near end-of-life using evidence-based criteria to identify progressive terminal conditions or LPs (<6 months).

Results. Of 424,212 participants, 34% with life-limiting illness were prescribed statins (65–75 years=44% and >75 years=31%). Partitioning the life-limiting illness definition into its four components, use rates differed by the clinical basis of component definitions: For the diagnosis-based samples (serious illness or percutaneous coronary intervention conditions), use remained relatively consistent to overall rates by age. For the prognosis-based samples (<6 month documented prognosis or palliative care consult), use ranged 9%–23%. Of those with a prognosis <6 months, 23% of the 65–75 years and 12% of the >75 years groups were on statins. Factors positively associated with use included minority race/ethnicity, use of >5 concurrent medications, and atherosclerotic cardiovascular disease or risk factors.

Commentary. These three retrospective studies examined the use of aspirin, statins, and diabetes control in older adults with LLE residing in nursing home. Despite patients’ LLE, only about one third discontinued aspirin use, one third were still prescribed statins, and more than 40% of individuals with diabetes were
over-treated. There is ongoing debate regarding aspirin use for secondary prevention; one could argue that the risks outweigh the benefits in older adults with LLE. This study has shown that stopping statin therapy is safe and improved quality of life in patients with LLE. Both the American Geriatrics Society and the American Diabetes Association recommend less-stringent glycemic control for older adults with LLE. Despite current evidence and guidelines, these studies highlight the ongoing challenges to deprescribing and deintensifying treatment for individuals with LLE.

**Bottom Line.** Overtreatment still is common in older adults with LLE; patient-centered care involving the interdisciplinary team to initiate shared decision-making conversations is the key to preventing overtreatment in this vulnerable population.

**Reviewer.** Sik Kim Ang, MD, University of Massachusetts-Baystate Medical School, Springfield, MA

**Sources.** Niznik JD, Hunnicutt JN, Zhao X, et al. De-intensification of diabetes medications among veterans at the end of life in VA nursing homes. *J Am Geriatr Soc.* 2020;68(4):736–745.

Springer SP, Mor MK, Sileanu F, et al. Incidence and predictors of aspirin discontinuation in older adult veteran nursing home residents at end of life. *J Am Geriatr Soc.* 2020;68(4):725–735.

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**Association of Physician Orders for Life-Sustaining Treatment with ICU Admission Among Patients Hospitalised Near the End of Life**

**Background.** Approximately 20%–30% of Americans near the end of life receive care in the intensive care unit (ICU). For patients with Physician Orders for Life-Sustaining Treatment (POLST), how often is their end-of-life care consistent with POLST-ordered limitations?

**Design and Participants.** This retrospective cohort study (2010–2017) in a two-hospital academic healthcare system evaluated associations between POLST orders for medical interventions (comfort-only, limited-interventions, full-treatment) and ICU admission for patients hospitalized ≤6 months pre-death. Modified Poisson regression was used.

**Results.** Among 1,818 decedents (age mean=71 [SD=15] years; 41% women; 26% non-white/Hispanic, 22% had comfort-only, 42% limited-interventions, and 36% full-treatment. 31% (95% CI=26%–35%) of patients with comfort-only were admitted to the ICU, 46% (42%–49%) with limited-interventions, and 62% (58%–66%) with full-treatment. ≥1 life-sustaining treatment (mechanical ventilation, vasopressors, dialysis, or cardiopulmonary resuscitation) occurred in 14% (11%–17%) with comfort-only and 20% (17%–23%) with limited-interventions. Versus patients with full-treatment, those with comfort-only and limited-interventions were less likely to receive intensive care (comfort-only: 31% vs. 62%, aRR=0.53 [95% CI=0.45–0.62]; limited-interventions: 46% vs. 62%, aRR=0.79 [0.71–0.87]). Across patients with comfort-only and limited-interventions, 38% (35%–40%) received POLST-discordant care. Patients with (vs. without) cancer were less likely to receive POLST-discordant care (comfort-only: 23% vs. 36%, aRR=0.60 [0.43–0.85]; limited-interventions: 31% vs. 49%, aRR=0.63 [0.51–0.78]). Patients admitted for traumatic injury were likelier to receive POLST-discordant care (21% vs. 34%, aRR=0.44 [0.29–0.67]). Patients admitted for traumatic injury were likelier to receive POLST-discordant care (comfort-only: 45% vs. 27%, aRR=1.52 [1.08–2.14]; limited-interventions: 56% vs. 39%, aRR=1.36 [1.09–1.68]). In patients with limited-interventions, older age was associated with less POLST-discordant care (aRR=0.93 per 10 years [0.88–1.00]) (All P<0.05).

**Commentary.** The study’s main finding further demonstrates the varied efficacy of POLST in preserving end-of-life preferences in various circumstances. Secondary findings suggest opportunities. Though intended to provide guidance, instructive directives (eg, POLST, living will) can be voided by patients or surrogates in favor of aggressive care and vice versa. Unlike those with cancer and dementia, patients with less predictable prognostic trajectories, or their surrogates, may be inclined to supplant an existing POLST. Considering these, POLST provisions must be reviewed upon hospitalization because the context may be dissimilar from when the form was signed. Preferences must be clarified with both
patient and surrogate to ensure shared understanding. Palliative care consultation or advance care planning aids may be helpful during POLST completion or review.7,8

**Bottom Line.** Though ICU admission was less likely for patients with treatment-limiting POLSTs, some patients in the study, including nearly a third with comfort-only status, received intensive care in the last 6 months of life.

**Reviewer.** Renato V. Samala, MD MHPE HMDC FACP FAAHPM, Cleveland Clinic, Cleveland, OH

**Source.** Lee RY, Brumback LC, Sathitratanacheewin 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.

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**Bereaved Parents’ Views on End-of-Life Care for Children with Cancer: Quality Marker Implications**

**Background.** Despite increased numbers of pediatric palliative care programs and advances in pediatric palliative oncology, children with cancer are dying with pain, and bereaved families suffer distress, poor health, work impairment, and financial hardship.1–4 What are bereaved parents’ perspectives on end-of-life (EOL) care?

**Design and Participants.** This qualitative study explored parental preferences for EOL care intensity to begin to establish quality markers for pediatric oncology EOL care. A convenience sample of bereaved parents whose children (aged 0–21 years) had died of cancer ≥6 months before was enrolled. Semistructured interviews were recorded and transcribed, and study team consensus and content analyses identified themes. Related quotes were scored to reflect preferred level of medically aggressive care (5-point scale: 1 [supported comfort care] to 5 [supported medically aggressive care]). Analysis included descriptive statistics and Kruskal-Wallis and Wilcoxon rank-sum tests.

**Results.** Children (n=24) died 1998–2017, age mean=9.8 years (SD=5.2) (46% leukemia/lymphoma, 50% solid tumors). Sixty-three percent died in the hospital (38% at home), and 63% had home nursing/hospice support. Twenty-eight parents (64% female, 46% Spanish-speaking) were interviewed median=6 years post-death (range=1–23), yielding 30 hours. Themes included: 1) home death preference (unless home support was inadequate), nonaggressive care, and continued anticancer therapy; 2) programs/policies that could alleviate barriers limiting a family’s time with a dying child (visiting restrictions and financial strain); 3) the need to prepare the family for death (what would happen to the child’s body), and 4) perceived abandonment. Scores reflecting the preferred level of medically aggressive care varied by subtheme: median=1.6 for hospital death (IQR=1.4–2.6), 2.4 for medically invasive care (IQR=1.4–3.4), and 3.2 for end-of-life chemotherapy (IQR=2.8–4.4) (P=.002). This variation was present in English (not Spanish) interviews (P=.005).

**Commentary.** We’re not really sure what quality EOL care looks like for children. For example, only two of the National Quality Forum’s ~200 EOL quality metrics are pediatric specific. Although home death is an accepted metric in adult EOL care, pediatric studies
have yielded conflicting results.\textsuperscript{5,6} This small survey showed that a majority of parents, especially in Hispanic families, preferred home death. Despite this, Hispanic children were more likely to experience hospital deaths, often because of inadequate support at home in areas such as symptom management and support for siblings. Whereas the adult literature deems limited ICU care and avoidance of chemotherapy at the EOL as quality measures,\textsuperscript{7} this study suggests that parents often are willing to accept the latter, reflecting their continued hope for cure (or, at least, life prolongation).

**Bottom Line.** Quality pediatric EOL care may differ from that of adults, including the continued use of antineoplastic treatment and overcoming barriers to home death.

**Reviewers.** Sue S. Sreedhar MD, Pediatric Palliative Care Consultant, St. Petersburg, FL

**Source.** Johnston EE, Molina J, Martinez I, et al. Bereaved parents’ views on end-of-life care for children with cancer: quality marker implications. *Cancer*. 2020;126(14):3352–3359.

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**Olanzapine for the Treatment of Advanced Cancer–Related Chronic Nausea and/or Vomiting: A Randomized Pilot Trial**

**Background.** Nausea/vomiting, unrelated to chemotherapy, can be substantial symptoms in patients with advanced cancer.\textsuperscript{1–3} Does olanzapine decrease nausea/vomiting in patients with advanced cancer?

**Design and Participants.** This double-blind, placebo-controlled trial (2017–2019) evaluated olanzapine for treating chronic nausea/vomiting unrelated to chemotherapy in patients with advanced cancer. Outpatients, who had nausea/vomiting for ≥1 week (worst daily nausea numeric rating scores >3 on 0–10 scale) without having had chemotherapy/ radiotherapy in the prior 14 days, received oral olanzapine (5 mg) or placebo, daily for 7 days. Patient-reported change in nausea numeric rating scores were collected daily, from baseline to the last treatment day. The Wilcoxon rank-sum test was used.

**Results.** Thirty patients (15/arm, 53\% female, and age mean=63 years [range=39–79]) were enrolled from three universities. Baseline median nausea scores in all patients were 9 out of 10 (range=8–10). After 1 day and 1 week, the median nausea scores in the placebo arm were 9 out of 10 (range=8–10) on both days vs. the olanzapine arm scores of 2 out of 10 (range=2–3) after day 1 and 1 out of 10 (range=0–3) after 1 week. After 1 week, the reduction in nausea scores in the olanzapine arm was 8 points (95\% CI=7–8) higher than that of the placebo arm (P<.001). Correspondingly, olanzapine-receiving patients reported less emesis (P<.001), less use of other antiemetic drugs, better appetite (P<.001), less sedation (P=.08), less fatigue (P=.004), better well-being (P<.001), and less pain (P=.01). One placebo-receiving patient stopped treatment early because of lack of perceived benefit. No olanzapine-receiving patients reported any adverse events.

**Commentary.** Nausea and vomiting are symptoms that deeply affect the quality of life of many patients with cancer. A prior large, randomized phase III study previously demonstrated that 10 mg of olanzapine daily on days 1–4 is an effective anti-emetic when combined with an NK1-receptor antagonist, a 5-HT3–receptor antagonist, and dexamethasone in patients receiving highly emetogenic chemotherapy.\textsuperscript{4} This small, randomized, placebo-controlled study showed that patient reports of nausea unrelated to chemotherapy or radiotherapy improved starting at 1 day after initiation of a lower daily dose of olanzapine (5 mg). Other beneficial effects included fewer patient reports of emesis, antiemetic use, and sedation and improved appetite and sense of well-being.

**Bottom Line.** Five mg of olanzapine daily may be an effective anti-emetic option in patients with advanced...
cancer and chronic nausea unrelated to chemotherapy or radiotherapy.

Reviewer: Shelly S. Lo, MD, Loyola University Stritch School of Medicine, Maywood, IL

Source. 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):1–5.

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Rave Reviews
Davies N, Schiowitz B, Rait G, Vickerstaff V, Sampson EL. Decision aids to support decision-making in dementia care: a systematic review. Int Psychogeriatr. 2019;31(10):1403–1419.

This is a systematic review of peer-reviewed literature that investigated the use of decision-making aids in patients with dementia. The authors focused on three topics: eating/feeding preferences, place of care, and goals of care. They found that using these aids, which included written, audio, and video formats, improved communication between patients and caregivers and understanding of goals of care and reduced decisional conflict.

Yusufov M, Braun IM, Pirl WF. A systematic review of substance use and substance use disorders in patients with cancer. Gen Hosp Psychiatry. 2019;60:128–136.

This systematic review examined substance use disorders in patients with cancer at various stages of disease, including advanced cancer. Substances involved included alcohol and prescription opioids; cannabis and tobacco were excluded. The authors found that substance use disorders occurred in 2%–35% of patients, and that risk factors needed to be better clarified in this population. In addition, there are a dearth of studies that have investigated illicit substance use in cancer patients.

Inglet S, Winter B, Yost SE, et al. Clinical data for the use of cannabis-based treatments: a comprehensive review of the literature [published online ahead of print, 2020 Jun 2]. Ann Pharmacother. 2020;1060028020930189.

This review focused on cannabis use for symptom management in various diseases and examined the reported efficacy of cannabis on specific symptoms. It also, notably, included an extensive table that details cannabis formulations, THC:CBD ratios, and doses that were used for each relevant disease and symptom, as well as known data for cannabis for end-of-life symptoms.

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American Academy of Hospice and Palliative Medicine 8735 W. Higgins Road, Suite 300
Chicago, IL 60631, USA
Phone: 847-375-4712
Fax: 877-734-8671
E-mail: info@aahpm.org
Website: www.aahpm.org