

**2019**

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# LITERATURE REVIEW

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## STATE-OF-THE-ART: THE YEAR'S LITERATURE IN REVIEW

PRESENTED BY:

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## LINKS TO ARTICLES

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Aromatherapy Versus Oral Ondansetron for Antiemetic Therapy Among Adult Emergency Department Patients: A Randomized Controlled Trial  
<https://doi.org/10.1016/j.annemergmed.2018.01.016>

Cannabis and Cannabinoids for the Treatment of People with Chronic Noncancer Pain Conditions: A Systematic Review and Meta-analysis of Controlled and Observational Studies  
[https://journals.lww.com/pain/Abstract/2018/10000/Cannabis\\_and\\_cannabinoids\\_for\\_the\\_treatment\\_of.6.aspx](https://journals.lww.com/pain/Abstract/2018/10000/Cannabis_and_cannabinoids_for_the_treatment_of.6.aspx)

Methadone as a First-Line Opioid in Cancer Pain Management: A Systematic Review  
<https://doi.org/10.1016/j.jpainsymman.2017.10.017>

Hyoscine Butylbromide for the Management of Death Rattle: Sooner Rather Than Later  
<https://doi.org/10.1016/j.jpainsymman.2018.08.018>

Haloperidol and Ziprasidone for Treatment of Delirium in Critical Illness  
<https://www.nejm.org/doi/full/10.1056/NEJMoa1808217>

Safe and Appropriate Use of Methadone in Hospice and Palliative Care: Expert Consensus White Paper  
<https://doi.org/10.1016/j.jpainsymman.2018.12.001>

Palliative Care Clinician Overestimation of Survival in Advanced Cancer: Disparities and Association with End-of-Life Care  
<https://doi.org/10.1016/j.jpainsymman.2018.10.510>

Fan Therapy Is Effective in Relieving Dyspnea in Patients with Terminally Ill Cancer: A Parallel-Arm, Randomized Controlled Trial  
<https://doi.org/10.1016/j.jpainsymman.2018.07.001>

Prevalence, Symptom Burden, and Natural History of Deep Vein Thrombosis in People with Advanced Cancer in Specialist Palliative Care Units (HIDDEN): A Prospective Longitudinal Observational Study  
<https://read.qxmd.com/read/30709436/prevalence-symptom-burden-and-natural-history-of-deep-vein-thrombosis-in-people-with-advanced-cancer-in-specialist-palliative-care-units-hidden-a-prospective-longitudinal-observational-study>

Predictors of Hospice Enrollment for Patients with Advanced Heart Failure and Effects on Health Care Use  
<http://heartfailure.onlinejacc.org/content/6/9/780>

Complementary and Alternative Medicine in Hospice and Palliative Care: A Systematic Review  
<https://doi.org/10.1016/j.jpainsymman.2018.07.016>

Rehabbed to Death  
<https://www.nejm.org/doi/full/10.1056/NEJMp1809354>



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2019 LITERATURE REVIEW

**Aromatherapy Versus Oral Ondansetron  
for Antiemetic Therapy Among  
Adult Emergency Department Patients:  
A Randomized Controlled Trial**

Annals of Emergency Medicine | Volume 72, Issue 2, 184 - 193

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*D. April, Michael & J. Oliver, Joshua & T. Davis, William &  
Ong, David & M. Simon, Erica & C. Ng, Patrick & J. Hunter, Curtis.*

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AVAILABLE ONLINE AT:

<https://doi.org/10.1016/j.annemergmed.2018.01.016>

## ABSTRACT

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Annals of Emergency Medicine | Volume 72, Issue 2, 184 - 193

### **Aromatherapy Versus Oral Ondansetron for Antiemetic Therapy Among Adult Emergency Department Patients: A Randomized Controlled Trial**

D. April, Michael & J. Oliver, Joshua & T. Davis, William & Ong, David & M. Simon, Erica & C. Ng, Patrick & J. Hunter, Curtis

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#### **STUDY OBJECTIVE**

We compare aromatherapy with inhaled isopropyl alcohol versus oral ondansetron for treating nausea among emergency department (ED) patients not requiring immediate intravenous access.

#### **METHODS**

In a randomized, blinded, placebo-controlled trial, we enrolled a convenience sample of adults presenting to an urban tertiary care ED with chief complaints including nausea or vomiting. We randomized subjects to 1 of 3 arms: inhaled isopropyl alcohol and 4 mg oral ondansetron, inhaled isopropyl alcohol and oral placebo, and inhaled saline solution placebo and 4 mg oral ondansetron. The primary outcome was mean nausea reduction measured by a 0- to 100-mm visual analog scale from enrollment to 30 minutes postintervention. Secondary outcomes included receipt of rescue antiemetic medications and adverse events.

#### **RESULTS**

We enrolled 122 subjects, of whom 120 (98.3%) completed the study. Of randomized subjects, 40 received inhaled isopropyl alcohol and oral ondansetron, 41 received inhaled isopropyl alcohol and oral placebo, and 41 received inhaled saline solution placebo and oral ondansetron. The mean decrease in nausea visual analog scale score in each arm was 30 mm (95% confidence interval [CI] 22 to 37 mm), 32 mm (95% CI 25 to 39 mm), and 9 mm (95% CI 5 to 14 mm), respectively. The proportions of subjects who received rescue antiemetic therapy in each arm were 27.5% (95% CI 14.6% to 43.9%), 25.0% (95% CI 12.7% to 41.2%), and 45.0% (95% CI 29.3% to 61.5%), respectively. There were no adverse events.

#### **CONCLUSION**

Among ED patients with acute nausea and not requiring immediate intravenous access, aromatherapy with or without oral ondansetron provides greater nausea relief than oral ondansetron alone.



2019 LITERATURE REVIEW

**Cannabis and Cannabinoids for  
the Treatment of People with  
Chronic Noncancer Pain Conditions:  
A Systematic Review and  
Meta-analysis of Controlled  
and Observational Studies**

PAIN | October 2018, Volume 159, Issue 10, p 1932–1954

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*Stockings, Emily; Campbell, Gabrielle; Hall, Wayne D.; Nielsen,  
Suzanne; Zagic, Dino; Rahman, Rakin; Murnion, Bridin; Farrell,  
Michael; Weier, Megan; Degenhardt, Louisa*

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AVAILABLE ONLINE AT:

[https://journals.lww.com/pain/Abstract/2018/10000/Cannabis\\_and\\_cannabinoids\\_for\\_the\\_treatment\\_of.6.aspx](https://journals.lww.com/pain/Abstract/2018/10000/Cannabis_and_cannabinoids_for_the_treatment_of.6.aspx)

## ABSTRACT

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PAIN | October 2018, Volume 159, Issue 10, p 1932–1954

### **Cannabis and Cannabinoids for the Treatment of People with Chronic Noncancer Pain Conditions: A Systematic Review and Meta-analysis of Controlled and Observational Studies**

Stockings, Emily; Campbell, Gabrielle; Hall, Wayne D.; Nielsen, Suzanne; Zagic, Dino; Rahman, Rakin; Murnion, Bridin; Farrell, Michael; Weier, Megan; Degenhardt, Louisa

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This review examines evidence for the effectiveness of cannabinoids in chronic noncancer pain (CNCP) and addresses gaps in the literature by: considering differences in outcomes based on cannabinoid type and specific CNCP condition; including all study designs; and following IMMPACT guidelines. MEDLINE, Embase, PsycINFO, CENTRAL, and clinicaltrials.gov were searched in July 2017. Analyses were conducted using Revman 5.3 and Stata 15.0. A total of 91 publications containing 104 studies were eligible ( $n = 9958$  participants), including 47 randomized controlled trials (RCTs) and 57 observational studies. Forty-eight studies examined neuropathic pain, 7 studies examined fibromyalgia, 1 rheumatoid arthritis, and 48 other CNCP (13 multiple sclerosis-related pain, 6 visceral pain, and 29 samples with mixed or undefined CNCP). Across RCTs, pooled event rates (PERs) for 30% reduction in pain were 29.0% (cannabinoids) vs 25.9% (placebo); significant effect for cannabinoids was found; number needed to treat to benefit was 24 (95% confidence interval [CI] 15-61); for 50% reduction in pain, PERs were 18.2% vs 14.4%; no significant difference was observed. Pooled change in pain intensity (standardized mean difference:  $-0.14$ , 95% CI  $-0.20$  to  $-0.08$ ) was equivalent to a 3 mm reduction on a 100 mm visual analogue scale greater than placebo groups. In RCTs, PERs for all-cause adverse events were 81.2% vs 66.2%; number needed to treat to harm: 6 (95% CI 5-8). There were no significant impacts on physical or emotional functioning, and low-quality evidence of improved sleep and patient global impression of change. Evidence for effectiveness of cannabinoids in CNCP is limited. Effects suggest that number needed to treat to benefit is high, and number needed to treat to harm is low, with limited impact on other domains. It seems unlikely that cannabinoids are highly effective medicines for CNCP.

2019 LITERATURE REVIEW

# Methadone as a First-Line Opioid in Cancer Pain Management: A Systematic Review

Journal of Pain and Symptom Management | Volume 55, Issue 3, 998 - 1003

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*Sebastiano Mercadante, MD, and Eduardo Bruera, MD*

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AVAILABLE ONLINE AT:

<https://doi.org/10.1016/j.jpainsymman.2017.10.017>

## ABSTRACT

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Journal of Pain and Symptom Management | Volume 55, Issue 3, 998 - 1003

### **Methadone as a First-Line Opioid in Cancer Pain Management: A Systematic Review**

Sebastiano Mercadante, MD, and Eduardo Bruera, MD

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#### **AIM**

The objective of this review was to assess the existent evidence for the use of methadone as a first-line therapy in cancer pain management.

#### **METHODS**

A systematic literature search on MEDLINE and Embase databases was carried out from each database, setting up the date to August 30, 2017. Studies were included if methadone was a first-line drug as a Step 3 of World Health Organization analgesic ladder, or at low doses (Step 2), if they were conducted in adult patients with cancer pain, and if they contained outcomes on pain- and opioid-related adverse effects.

#### **RESULTS**

The initial search yielded 219 records. Ten articles were considered after the initial screening according to inclusion and exclusion criteria. They included three longitudinal open-label studies. In two studies methadone was initiated at low doses ( $\leq 10$  mg/day). These studies suggested that methadone was effective in providing analgesia and well tolerated as first opioid at different starting doses and in different conditions and settings. Five additional studies were randomized controlled studies with morphine in patients who had received opioids for moderate pain. Methadone, compared with oral morphine, or transdermal fentanyl, either at low (Step 2 level) or relatively higher doses (Step 3 level), provided similar analgesia with similar adverse effects profile with limited dose escalation in time.

#### **CONCLUSION**

Available data are not sufficient to draw net conclusion. However, open-label and controlled studies have shown that methadone may be effective as first-line drug in the management of cancer pain, providing analgesia and adverse effect profiles similar to those produced by other opioids. The finding that methadone doses tend to remain stable suggests that metabolic characteristics and extraopioid analgesic effects, as its well antihyperalgesic properties may be interesting potential advantages. Further studies should provide information regarding the long-term use of methadone or the need to switch from methadone to other opioids when a loss of analgesic response occurs.

2019 LITERATURE REVIEW

**Hyoscine Butylbromide for the  
Management of Death Rattle:  
Sooner Rather Than Later**

Journal of Pain and Symptom Management | Volume 56, Issue 6, 902 – 907

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*Mercadante S; Marinangeli F; Masedu F; Valenti M; Russo D; Ursini L;  
Massici A; Aielli F*

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AVAILABLE ONLINE AT:

<https://doi.org/10.1016/j.jpainsymman.2018.08.018>

## ABSTRACT

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Journal of Pain and Symptom Management | Volume 56, Issue 6, 902 – 907

### **Hyoscine Butylbromide for the Management of Death Rattle: Sooner Rather Than Later**

Mercadante S; Marinangeli F; Masedu F; Valenti M; Russo D; Ursini L; Massici A; Aielli F

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#### **CONTEXT**

Death rattle (DR) is a dramatic sign in the dying patient. Existing studies with anticholinergic agents are controversial, as this class of drugs has been commonly administered without considering the rationale of the mechanism of action. A meaningful use of these drugs may provide a better outcome.

#### **OBJECTIVES**

The aim of this study was to assess the efficacy of hyoscine butylbromide (HB), given prophylactically in comparison with HB administered once DR occurs.

#### **METHODS**

Dying patients having a score of  $\geq 3$  in the Richmond Agitation-Sedation Scale—palliative version were included in the study. HB (60 mg/day) was given when DR occurred (Group 1) or as pre-emptive treatment (Group 2). The onset of DR (death rattle free time) and intensity of DR were recorded at intervals until death.

#### **RESULTS**

Eighty-one and 51 patients were randomized to Group 1 and 2, respectively. Patients in Group 2 survived longer than those in Group 1 ( $P < 0.05$ ). DR occurred in 49 (60.5%) and three patients (5.9%) in Group 1 and 2, respectively ( $P = 0.001$ ). A significant difference in the number of patients reporting DR was found at intervals examined (30 minutes, one hour, and then every six hours until death [ $P = 0.001$ ]). In Group 1 and 2, DR free time was 20.4 (20.5) and 27.3 hours (25.2), respectively ( $P = 0.001$ ). In Group 1, the treatment was considered effective in 10 patients (20.4%) only, after a mean of 14.4 hours (SD 8.57).

#### **CONCLUSION**

The prophylactic use of HB is an efficient method to prevent DR, whereas the late administration produces a limited response, confirming data from traditional studies performed with anticholinergics. This could be considered a new paradigm to manage a difficult and dramatic sign, such as DR.

**2019 LITERATURE REVIEW**

# Haloperidol and Ziprasidone for Treatment of Delirium in Critical Illness

New England Journal of Medicine | December 27, 2018 379(26):2506

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*T.D. Girard, M.C. Exline, S.S. Carson, C.L. Hough, P. Rock, M.N. Gong, I.S. Douglas, A. Malhotra, R.L. Owens, D.J. Feinstein, B. Khan, M.A. Pisani, R.C. Hyzy, G.A. Schmidt, W.D. Schweickert, R.D. Hite, D.L. Bowton, A.L. Masica, J.L. Thompson, R. Chandrasekhar, B.T. Pun, C. Strength, L.M. Boehm, J.C. Jackson, P.P. Pandharipande, N.E. Brummel, C.G. Hughes, M.B. Patel, J.L. Stollings, G.R. Bernard, R.S. Dittus, and E.W. Ely, for the MIND-USA Investigators*

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**AVAILABLE ONLINE AT:**

<https://www.nejm.org/doi/full/10.1056/NEJMoa1808217>

## ABSTRACT

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New England Journal of Medicine | December 27, 2018 379(26):2506

### Haloperidol and Ziprasidone for Treatment of Delirium in Critical Illness

T.D. Girard, M.C. Exline, S.S. Carson, C.L. Hough, P. Rock, M.N. Gong, I.S. Douglas, A. Malhotra, R.L. Owens, D.J. Feinstein, B. Khan, M.A. Pisani, R.C. Hyzy, G.A. Schmidt, W.D. Schweickert, R.D. Hite, D.L. Bowton, A.L. Masica, J.L. Thompson, R. Chandrasekhar, B.T. Pun, C. Strength, L.M. Boehm, J.C. Jackson, P.P. Pandharipande, N.E. Brummel, C.G. Hughes, M.B. Patel, J.L. Stollings, G.R. Bernard, R.S. Dittus, and E.W. Ely, for the MIND-USA Investigators

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#### BACKGROUND

There are conflicting data on the effects of antipsychotic medications on delirium in patients in the intensive care unit (ICU).

#### METHODS

In a randomized, double-blind, placebo-controlled trial, we assigned patients with acute respiratory failure or shock and hypoactive or hyperactive delirium to receive intravenous boluses of haloperidol (maximum dose, 20 mg daily), ziprasidone (maximum dose, 40 mg daily), or placebo. The volume and dose of a trial drug or placebo was halved or doubled at 12-hour intervals on the basis of the presence or absence of delirium, as detected with the use of the Confusion Assessment Method for the ICU, and of side effects of the intervention. The primary end point was the number of days alive without delirium or coma during the 14-day intervention period. Secondary end points included 30-day and 90-day survival, time to freedom from mechanical ventilation, and time to ICU and hospital discharge. Safety end points included extrapyramidal symptoms and excessive sedation.

#### RESULTS

Written informed consent was obtained from 1183 patients or their authorized representatives. Delirium developed in 566 patients (48%), of whom 89% had hypoactive delirium and 11% had hyperactive delirium. Of the 566 patients, 184 were randomly assigned to receive placebo, 192 to receive haloperidol, and 190 to receive ziprasidone. The median duration of exposure to a trial drug or placebo was 4 days (interquartile range, 3 to 7). The median number of days alive without delirium or coma was 8.5 (95% confidence interval [CI], 5.6 to 9.9) in the placebo group, 7.9 (95% CI, 4.4 to 9.6) in the haloperidol group, and 8.7 (95% CI, 5.9 to 10.0) in the ziprasidone group ( $P=0.26$  for overall effect across trial groups). The use of haloperidol or ziprasidone, as compared with placebo, had no significant effect on the primary end point (odds ratios, 0.88 [95% CI, 0.64 to 1.21] and 1.04 [95% CI, 0.73 to 1.48], respectively). There were no significant between-group differences with respect to the secondary end points or the frequency of extrapyramidal symptoms.



## ABSTRACT

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### CONCLUSIONS

The use of haloperidol or ziprasidone, as compared with placebo, in patients with acute respiratory failure or shock and hypoactive or hyperactive delirium in the ICU did not significantly alter the duration of delirium. (Funded by the National Institutes of Health and the VA Geriatric Research Education and Clinical Center; MIND-USA ClinicalTrials.gov number, NCT01211522.)



**2019 LITERATURE REVIEW****Safe and Appropriate Use  
of Methadone in Hospice  
and Palliative Care:  
Expert Consensus White Paper**

Journal of Pain and Symptom Management | Volume 57, Issue 3, 635 - 645.e4

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*Mary Lynn McPherson, PharmD, MA, MDE, BCPS, CPE, Kathryn A. Walker, PharmD, BCPS, CPE, Mellar P. Davis, MD, FCCP, FAAHPM, Eduardo Bruera, MD, Akhila Reddy, MD, Judith Paice, PhD, RN, Kasey Malotte, PharmD, BCPS, Dawn Keshelle Lockman, PharmD, MA, Charles Wellman, MD, Shelley Salpeter, MD, Nina M. Bembien, PharmD, BCPS, James B. Ray, PharmD, CPE, Bernard J. Lapointe, MD, and Roger Chou, MD*

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**AVAILABLE ONLINE AT:**

<https://doi.org/10.1016/j.jpainsymman.2018.12.001>

## ABSTRACT

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Journal of Pain and Symptom Management | Volume 57, Issue 3, 635 - 645.e4

### **Safe and Appropriate Use of Methadone in Hospice and Palliative Care: Expert Consensus White Paper**

Mary Lynn McPherson, PharmD, MA, MDE, BCPS, CPE, Kathryn A. Walker, PharmD, BCPS, CPE, Mellar P. Davis, MD, FCCP, FAAHPM, Eduardo Bruera, MD, Akhila Reddy, MD, Judith Paice, PhD, RN, Kasey Malotte, PharmD, BCPS, Dawn Keshelle Lockman, PharmD, MA, Charles Wellman, MD, Shelley Salpeter, MD, Nina M. Bembien, PharmD, BCPS, James B. Ray, PharmD, CPE, Bernard J. Lapointe, MD, and Roger Chou, MD

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Methadone has several unique characteristics that make it an attractive option for pain relief in serious illness, but the safety of methadone has been called into question after reports of a disproportionate increase in opioid-induced deaths in recent years. The American Pain Society, College on Problems of Drug Dependence, and the Heart Rhythm Society collaborated to issue guidelines on best practices to maximize methadone safety and efficacy, but guidelines for the end-of-life scenario have not yet been developed. A panel of 15 interprofessional hospice and palliative care experts from the U.S. and Canada convened in February 2015 to evaluate the American Pain Society methadone recommendations for applicability in the hospice and palliative care setting. The goal was to develop guidelines for safe and effective management of methadone therapy in hospice and palliative care. This article represents the consensus opinion of the hospice and palliative care experts for methadone use at end of life, including guidance on appropriate candidates for methadone, detail in dosing, titration, and monitoring of patients' response to methadone therapy.

2019 LITERATURE REVIEW

**Palliative Care Clinician  
Overestimation of Survival in  
Advanced Cancer:  
Disparities and Association  
with End-of-Life Care**

Journal of Pain and Symptom Management | Volume 57, Issue 2, 233 – 240

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*Robert Gramling, MD, DSc, Elizabeth Gajary-Coots, MA, RN, Jenica Cimino, BA, Kevin Fiscella, MD, MPH, Ronald Epstein, MD, Susan Ladwig, MPH, Wendy Anderson, MD, MS, Stewart C. Alexander, PhD, Paul K. Han, MD, MPH, David Gramling, PhD, and Sally A. Norton, PhD, RN*

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AVAILABLE ONLINE AT:

<https://doi.org/10.1016/j.jpainsymman.2018.10.510>

## ABSTRACT

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Journal of Pain and Symptom Management | Volume 57, Issue 2, 233 – 240

### **Palliative Care Clinician Overestimation of Survival in Advanced Cancer: Disparities and Association with End-of-Life Care**

Robert Gramling, MD, DSc, Elizabeth Gajary-Coots, MA, RN, Jenica Cimino, BA, Kevin Fiscella, MD, MPH, Ronald Epstein, MD, Susan Ladwig, MPH, Wendy Anderson, MD, MS, Stewart C. Alexander, PhD, Paul K. Han, MD, MPH, David Gramling, PhD, and Sally A. Norton, PhD, RN

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#### **CONTEXT**

Clinicians frequently overestimate survival time in serious illness.

#### **OBJECTIVE**

The objective of this study was to understand the frequency of overestimation in palliative care (PC) and the relation with end-of-life (EOL) treatment.

#### **METHODS**

This is a multisite cohort study of 230 hospitalized patients with advanced cancer who consulted with PC between 2013 and 2016. We asked the consulting PC clinician to make their “best guess” about the patients’ “most likely survival time, assuming that their illnesses are allowed to take their natural course” (<24 hours; 24 hours to less than two weeks; two weeks to less than three months; three months to less than six months; six months or longer). We followed patients for up to six months for mortality and EOL treatment utilization. Patients completed a brief interviewer-facilitated questionnaire at study enrollment.

#### **RESULTS**

Median survival was 37 days (interquartile range: 12 days, 97 days) and 186/230 (81%) died during the follow-up period. Forty-one percent of clinicians’ predictions were accurate. Among inaccurate prognoses, 85% were overestimates. Among those who died, overestimates were substantially associated with less hospice use (ORadj: 0.40; 95% CI: 0.16–0.99) and later hospice enrollment (within 72 hours of death ORadj: 0.33; 95% CI: 0.15–0.74). PC clinicians were substantially more likely to overestimate survival for patients who identified as Black or Latino compared to others (ORadj: 3.89; 95% CI: 1.64–9.22). EOL treatment preferences did not explain either of these findings.

#### **CONCLUSION**

Overestimation is common in PC, associated with lower hospice use and a potentially mutable source of racial/ethnic disparity in EOL care.

**2019 LITERATURE REVIEW****Fan Therapy Is Effective in  
Relieving Dyspnea in Patients  
with Terminally Ill Cancer:  
A Parallel-Arm, Randomized  
Controlled Trial**

Journal of Pain and Symptom Management | Volume 56, Issue 4, 493 - 500

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*Jun Kako, MHSc, RN, OCNS, Tatsuya Morita, MD, Takuhiro Yamaguchi, PhD,  
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Uchitomi, MD, PhD, Hironobu Inoguchi, MA, and Eisuke Matsushima, MD, PhD*

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**AVAILABLE ONLINE AT:**

<https://doi.org/10.1016/j.jpainsymman.2018.07.001>

## ABSTRACT

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Journal of Pain and Symptom Management | Volume 56, Issue 4, 493 - 500

### **Fan Therapy Is Effective in Relieving Dyspnea in Patients with Terminally Ill Cancer: A Parallel-Arm, Randomized Controlled Trial**

Jun Kako, MHSc, RN, OCNS, Tatsuya Morita, MD, Takuhiro Yamaguchi, PhD, Masamitsu Kobayashi, MSN, RN, OCNS, Asuko Sekimoto, MSN, RN, Hiroya Kinoshita, MD, Asao Ogawa, MD, PhD, Sadamoto Zenda, MD, PhD, Yosuke Uchitomi, MD, PhD, Hironobu Inoguchi, MA, and Eisuke Matsushima, MD, PhD

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#### **CONTEXT**

Dyspnea is a common distressing symptom among patients with advanced cancer.

#### **OBJECTIVE**

The objective of this study was to determine the effect of fan therapy on dyspnea in patients with terminally ill cancer.

#### **METHODS**

This parallel-arm, randomized controlled trial included 40 patients with advanced cancer from a palliative care unit at the National Cancer Center Hospital in Japan. All patients experienced dyspnea at rest with a score of at least three points on a subjective 0- to 10-point Numerical Rating Scale (NRS), showed peripheral oxygen saturation levels of  $\geq 90\%$ , had an Eastern Cooperative Oncology Group grade of 3 or 4, and were aged 20 years or more. In one group, a fan was directed to blow air on the patient's face for five minutes. This group was compared to a control group wherein air was blown to the patient's legs. Patients were randomly assigned to each group. The main outcome measure was the difference in dyspnea NRS scores between fan-to-face and fan-to-legs groups.

#### **RESULTS**

No significant differences were seen in baseline dyspnea NRS between groups (mean score, 5.3 vs. 5.1,  $P = 0.665$ ). Mean dyspnea changed by  $-1.35$  points (95% CI,  $-1.86$  to  $-0.84$ ) in patients assigned to receive fan-to-face and by  $-0.1$  points ( $-0.53$  to  $0.33$ ) in patients assigned to receive fan-to-legs ( $P < 0.001$ ). The proportion of patients with a one-point reduction in dyspnea NRS was significantly higher in the fan-to-face arm than in the fan-to-legs arm (80% [ $n = 16$ ] vs. 25% [ $n = 5$ ],  $P = 0.001$ ).

#### **CONCLUSION**

Fan-to-face is effective in alleviating dyspnea in patients with terminally ill cancer.



**2019 LITERATURE REVIEW**

**Prevalence, Symptom Burden,  
and Natural History of Deep Vein  
Thrombosis in People with  
Advanced Cancer in Specialist  
Palliative Care Units (HIDDEN):  
A Prospective Longitudinal  
Observational Study**

Lancet Haematology | 2019, 6 (2): e79-e88

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*Clare White, Simon I R Noble, Max Watson, Flavia Swan, Victoria L Allgar, Eoin Napier, Annmarie Nelson, Jayne McAuley, Jennifer Doherty, Bernadette Lee, Miriam J Johnson*

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**AVAILABLE ONLINE AT:**

<https://read.qxmd.com/read/30709436/prevalence-symptom-burden-and-natural-history-of-deep-vein-thrombosis-in-people-with-advanced-cancer-in-specialist-palliative-care-units-hidden-a-prospective-longitudinal-observational-study>

## ABSTRACT

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Lancet Haematology | 2019, 6 (2): e79-e88

### **Prevalence, Symptom Burden, and Natural History of Deep Vein Thrombosis in People with Advanced Cancer in Specialist Palliative Care Units (HIDDEN): A Prospective Longitudinal Observational Study**

Clare White, Simon I R Noble, Max Watson, Flavia Swan, Victoria L Allgar, Eoin Napier, Annmarie Nelson, Jayne McAuley, Jennifer Doherty, Bernadette Lee, Miriam J Johnson

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#### **BACKGROUND**

The prevalence of deep venous thrombosis in patients with advanced cancer is unconfirmed and it is unknown whether current international thromboprophylaxis guidance is applicable to this population. We aimed to determine prevalence and predictors of femoral deep vein thrombosis in patients admitted to specialist palliative care units (SPCUs).

#### **METHODS**

We did this prospective longitudinal observational study in five SPCUs in England, Wales, and Northern Ireland (four hospices and one palliative care unit). Consecutive adults with cancer underwent bilateral femoral vein ultrasonography on admission and weekly until death or discharge for a maximum of 3 weeks. Data were collected on performance status, attributable symptoms, and variables known to be associated with venous thromboembolism. Patients with a short estimated prognosis (<5 days) were ineligible. The primary endpoint of the study was the prevalence of femoral deep vein thrombosis within 48 h of SPCU admission, analysed by intention to treat. This study is registered with the ISRCTN registry, number ISRCTN97567719.

#### **FINDINGS**

Between June 20, 2016, and Oct 16, 2017, 343 participants were enrolled (mean age 68.2 years [SD 12.8; range 25-102]; 179 [52%] male; mean Australian-modified Karnofsky performance status 49 [SD 16.6; range 20-90]). Of 273 patients with evaluable scans, 92 (34%, 95% CI 28-40) had femoral deep vein thrombosis. Four participants with a scan showing no deep vein thrombosis on admission developed a deep vein thrombosis on repeat scanning over 21 days. Previous venous thromboembolism ( $p=0.014$ ), being bedbound in the past 12 weeks for any reason ( $p=0.003$ ), and lower limb oedema ( $p=0.009$ ) independently predicted deep vein thrombosis. Serum albumin concentration ( $p=0.43$ ), thromboprophylaxis ( $p=0.17$ ), and survival ( $p=0.45$ ) were unrelated to deep vein thrombosis.

## ABSTRACT

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### INTERPRETATION

About a third of patients with advanced cancer admitted to SPCUs had a femoral deep vein thrombosis. Deep vein thrombosis was not associated with thromboprophylaxis, survival, or symptoms other than leg oedema. These findings are consistent with venous thromboembolism being a manifestation of advanced disease rather than a cause of premature death. Thromboprophylaxis for SPCU inpatients with poor performance status seems to be of little benefit.

### FUNDING

National Institute for Health Research (Research for Patient Benefit programme).



2019 LITERATURE REVIEW

# Predictors of Hospice Enrollment for Patients with Advanced Heart Failure and Effects on Health Care Use

JACC: Heart Failure | Sep 2018, 6 (9) 780-789

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*Laura P. Gelfman, Yolanda Barrón, Stanley Moore, Christopher M. Murtaugh, Anuradha Lala, Melissa D. Aldridge and Nathan E. Goldstein*

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AVAILABLE ONLINE AT:

<http://heartfailure.onlinejacc.org/content/6/9/780>

## ABSTRACT

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JACC: Heart Failure | Sep 2018, 6 (9) 780-789

### **Predictors of Hospice Enrollment for Patients with Advanced Heart Failure and Effects on Health Care Use**

Laura P. Gelfman, Yolanda Barrón, Stanley Moore, Christopher M. Murtaugh, Anuradha Lala, Melissa D. Aldridge and Nathan E. Goldstein

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#### **OBJECTIVES**

This study sought to: 1) identify the predictors of hospice enrollment for patients with heart failure (HF); and 2) determine the impact of hospice enrollment on health care use.

#### **BACKGROUND**

Patients with HF rarely enroll in hospice. Little is known about how hospice affects this group's health care use.

#### **METHODS**

Using a propensity score–matched sample of Medicare decedents with  $\geq 2$  HF discharges within 6 months, an Outcome and Assessment Information Set (OASIS) assessment, and subsequent death, we used Medicare administrative, claims, and patient assessment data to compare hospitalizations, intensive care unit stays, and emergency department visits for those beneficiaries who enrolled in hospice and those who did not.

#### **RESULTS**

The propensity score–matched sample included 3,067 beneficiaries in each group with a mean age of 82 years; 53% were female, and 15% were Black, Asian, or Hispanic. For objective 1, there were no differences in the characteristics, symptom burden, or functional status between groups that were associated with hospice enrollment. For objective 2, in the 6 months after the second HF discharge, the hospice group had significantly fewer emergency department visits (2.64 vs. 2.82;  $p = 0.04$ ), hospital days (3.90 vs. 4.67;  $p < 0.001$ ), and intensive care unit stays (1.25 vs. 1.51;  $p < 0.001$ ); they were less likely to die in the hospital (3% vs. 56%;  $p < 0.001$ ), and they had longer median survival (80 days vs. 71 days; log-rank test  $p = 0.004$ ).

#### **CONCLUSIONS**

Beneficiaries' characteristics, including symptom burden and functional status, do not predict hospice enrollment. Those patients who enrolled in hospice used less health care, survived longer, and were less likely to die in the hospital. A tailored hospice model may be needed to increase enrollment and offer benefits to patients with HF.

2019 LITERATURE REVIEW

**Complementary and Alternative  
Medicine in Hospice and Palliative Care:  
A Systematic Review**

Journal of Pain and Symptom Management | Volume 56, Issue 5, 781 - 794.e4

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*Yvette S. Zeng, PharmD, Connie Wang, PharmD Candidate, Kristina E.  
Ward, PharmD, and Anne L. Hume, PharmD*

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AVAILABLE ONLINE AT:

<https://doi.org/10.1016/j.jpainsymman.2018.07.016>

## ABSTRACT

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### **Complementary and Alternative Medicine in Hospice and Palliative Care: A Systematic Review**

Yvette S. Zeng, PharmD, Connie Wang, PharmD Candidate, Kristina E. Ward, PharmD, and Anne L. Hume, PharmD

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#### **CONTEXT**

The aim of palliative care is to improve quality of life for patients with serious illnesses by treating their symptoms and adverse effects. Hospice care also aims for this for patients with a life expectancy of six months or less. When conventional therapies do not provide adequate symptom management or produce their own adverse effects, patients, families, and caregivers may prefer complementary or alternative approaches in their care.

#### **OBJECTIVES**

The objectives of this study were to evaluate the available evidence on the use of complementary or alternative medicine (CAM) in hospice and palliative care and to summarize their potential benefits.

#### **METHODS**

A defined search strategy was used in reviewing literature from major databases. Searches were conducted using base terms and the symptom in question. Symptoms included anxiety, pain, dyspnea, cough, fatigue, insomnia, nausea, and vomiting. Studies were selected for further evaluation based on relevancy and study type. References of systematic reviews were also assessed. After evaluation using quality assessment tools, findings were summarized and the review was structured based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

#### **RESULTS**

Out of 4682 studies, 17 were identified for further evaluation. Therapies included acupressure, acupuncture, aromatherapy massage, breathing, hypnotherapy, massage, meditation, music therapy, reflexology, and reiki. Many studies demonstrated a short-term benefit in symptom improvement from baseline with CAM, although a significant benefit was not found between groups.

#### **CONCLUSION**

CAM may provide a limited short-term benefit in patients with symptom burden. Additional studies are needed to clarify the potential value of CAM in the hospice or palliative setting.



2019 LITERATURE REVIEW

## Rehabbed to Death

New England Journal of Medicine | January 31, 2019 380(5):408

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*Lynn A. Flint, M.D., Daniel J. David, R.N., Ph.D., and Alexander K. Smith, M.D., M.P.H.*

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## ABSTRACT

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New England Journal of Medicine | January 31, 2019 380(5):408

### **Rehabbed to Death**

Lynn A. Flint, M.D., Daniel J. David, R.N., Ph.D., and Alexander K. Smith, M.D., M.P.H.

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For a substantial minority of older adults, a stay in a post-acute care facility is the gateway into a cycle between the hospital and the nursing home that spans the final months of life. Certain Medicare and Medicaid policies perpetuate this cycle.

In 2013, a total of 23% of hospitalized Medicare beneficiaries were discharged to a postacute care facility, 87% of them to a skilled nursing facility.

Of Medicare beneficiaries who died between 2006 and 2011, one in eight had cycled from hospital to skilled nursing facility to hospital during the last year of life.

Although the majority of older adults face functional disability in the last 2 years of life, the Medicare home health benefit does not provide continuous assistance with activities of daily living (e.g., bathing, dressing, and using the bathroom).



