

# Palliative Care Journal Watch

A partnership between Pallium Canada and several Divisions of Palliative Care and Medicine across Canada and Internationally:

University of Calgary, University of Alberta, Queens University, Hadassah-Hebrew University Medical Center

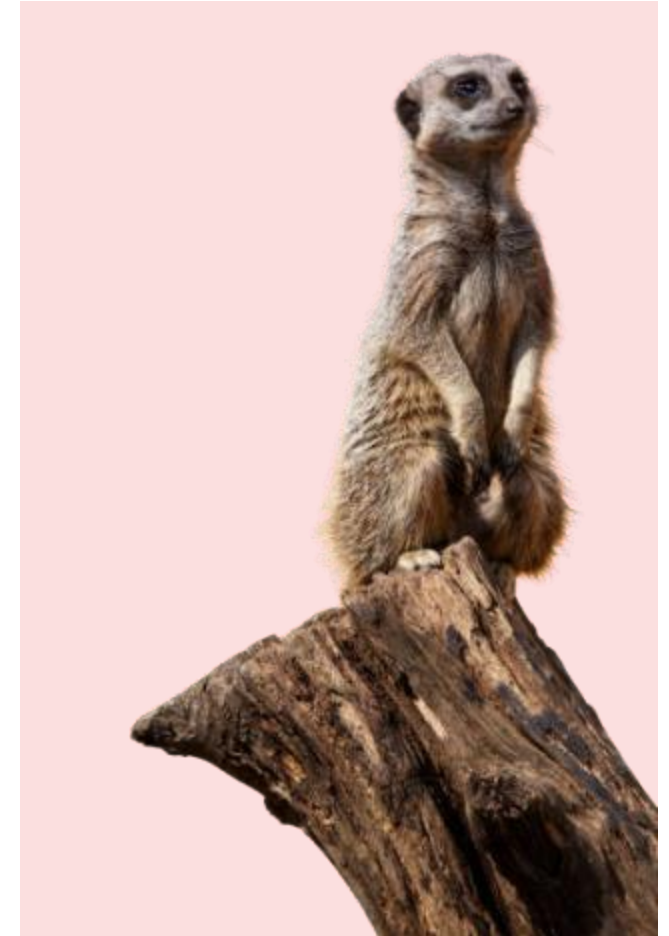


**Hosts & Panelists:** Dr. Jose Pereira, Dr. Leonie Herx, Dr. Sharon Watanabe, Dr. Aynharan Sinnarajah, Dr. Yoko Tarumi

**Date:** September 15th, 2025

# Welcome to the Palliative Care Journal Watch!

- Keeps you up to date on the latest peer-reviewed palliative care literature.
- Led by palliative care experts from several divisions of palliative care/medicine across Canada and internationally.
  - University of Calgary
  - University of Alberta
  - Queen's University
  - Hadassah-Hebrew University Medical Center, Israel
  - University of Navarra, Spain
- With the assistance of the Pallium Canada team
- We regularly monitor over 30 journals and highlight articles that challenge us to think differently about a topic or confirm our current practices.



# The Palliative Care ECHO Project

The Palliative Care ECHO Project is a 5-year national initiative to cultivate communities of practice and establish continuous professional development among health care providers across Canada who care for patients with life-limiting illness.

The Palliative Care ECHO Project is supported by a financial contribution from Health Canada. The views expressed herein do not necessarily represent the views of Health Canada.



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# What to expect from today's session

- We will present and discuss our featured selections and provide a list of honourable mentions.
- Please submit questions through the Q&A function.
- This session is being recorded and will be shared with registrants within the next week.

# Introductions

**Dr. José Pereira, MBChB, CCFP(PC), MSc, FCFP, PhD**

Professor, Faculty of Medicine, and Institute for Culture and Society, University of Navarra, Spain.

Scientific Advisor and Co-Founder, Pallium Canada

**Dr. Leonie Herx, MD, PhD, CCFP(PC), FCFP**

Section Chief, Pediatric Palliative Medicine, Alberta

Health Services, Calgary Zone, Alberta

Director, Rotary Flames House, Children's Hospice & Palliative Care Services, Calgary, Alberta

Clinical Professor, Cumming School of Medicine, University of Calgary, Alberta

Senior Scientific Director, Palliative Institute, Alberta

**Guest panelist**

- **Dr. Yoko Tarumi:** Division of Palliative Care Medicine
- Department of Oncology, Faculty of Medicine and Dentistry, University of Alberta

**Dr. Sharon Watanabe, MD, FRCPC**

Director, Department of Symptom Control and Palliative Care, Cross Cancer Institute, Edmonton Zone, Alberta Health Services

Professor, Division of Palliative Care Medicine

Department of Oncology, Faculty of Medicine and Dentistry, University of Alberta

**Dr. Aynharan Sinnarajah, MD CCFP(PC) MPH**

Chair, Dr. Gillian Gilchrist Palliative Care Research Division of Palliative Care, Queen's University and Lakeridge Health, ON, Canada

# Disclosures

## Pallium Canada

- Foundation, Registered Charity
- Funded by:
  - Health Canada (through contribution agreements 2001-2007, 2013-2018), Patrick Gillin Family Trust (2013-2016), Li Ka Shing Foundation (2019 to 2022), CMA (2019 to 2022), Boehringer Ingelheim (dissemination of LEAP Lung courses 2019 to current).
  - Partnerships with some provincial ministries.
  - Revenues from LEAP course registration fees and licenses
  - Sales of Pallium Palliative Pocketbook.

**This ECHO program has received financial support from Health Canada (2022 to 2025)**

## Disclosures of Hosts/Guest Panelists:

- No conflicts of interest to disclose
  - Dr. José Pereira
  - Dr. Leonie Herx
  - Dr. Sharon Watanabe
  - Dr. Aynharan Sinnarajah
  - Dr. Yoko Tarumi

## Mitigating Potential Biases:

- The scientific planning committee had complete independent control over the development of course content.

# Featured articles

1. Soliman N, Moisset X, Ferraro MC, et al. **Pharmacotherapy and non-invasive neuromodulation for neuropathic pain: a systematic review and meta-analysis.** The Lancet Neurology. 2025;24(5):413-428. doi:10.1016/S1474-4422(25)00068-7
2. Kilpatrick K, Allard É, Jabbour M, Tchouaket E. **Factors that support home deaths for patients receiving at-home palliative and end-of-life care: a sequential mixed-methods explanatory study.** BMC Palliat Care. 2025;24(1):197. doi:10.1186/s12904-025-01840-0
3. Min JWS, Wang Y, Bollens-Lund E, et al. **Prevalence of Preoperative Palliative Care Needs and Association with Healthcare Use and Cost Among Older Adults Undergoing Major Elective Surgery.** Journal of the American College of Surgeons. Published online July 16, 2025. doi:10.1097/XCS.0000000000001491
4. Hui D, De La Rosa A, Tsai JS, et al. **Proportional Sedation for Persistent Agitated Delirium in Palliative Care: A Randomized Clinical Trial.** JAMA Oncol. Published online July 31, 2025. doi:10.1001/jamaoncol.2025.2212

# Featured Articles



# Pharmacotherapy and non-invasive neuromodulation for neuropathic pain: a systematic review and meta-analysis.

## Article Reference:

Soliman N, Moisset X, Ferraro MC, et al. Pharmacotherapy and non-invasive neuromodulation for neuropathic pain: a systematic review and meta-analysis. The Lancet Neurology. 2025;24(5):413-428. doi:10.1016/S1474-4422(25)00068-7

## Selected and Presented by:

Dr. Yoko Tarumi

## Background:

- Neuropathic pain, caused by a lesion or disease of the somatosensory nervous system, substantially affects patients' quality of life and imposes a substantial economic burden on individuals and society.
- Regardless of the aetiology of nerve damage, the treatment of neuropathic pain is challenging, requiring accurate diagnosis and biopsychosocial assessment and the application of evidence-based recommendations that consider efficacy and safety of available treatments.
- The Special Interest Group on Neuropathic Pain (NeuPSIG) of the International Association for the Study of Pain (IASP) published its first guidelines in 2007, with an update in 2015, incorporating the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) and unpublished trials.
- Since then, new pharmacological trials and neuromodulation techniques have been developed and evaluated, along with updated safety data and advances in evidence appraisal methods.

## Methods:

- Systematic review and meta-analysis
- Databases: PubMed, EMBASE, Clinical Trials.gov, International Clinical Trials Registry Platform
- Search date: 2013 to Feb 2024..
- Trial inclusion
  - Participants of any age
  - Neuropathic pain, including postherpetic neuralgia, diabetic and non-diabetic painful polyneuropathy, post-traumatic or postsurgical neuropathic pain, painful radiculopathy, central post-stroke pain, spinal cord injury pain, trigeminal neuralgia, erythromelalgia, multiple sclerosis-associated neuropathic pain, multi-aetiology neuropathic pains.
  - Excluded mixed aetiologies (e.g., neuropathic and non-neuropathic pain) and conditions such as complex regional pain syndrome, low back pain without radicular pain, fibromyalgia, and idiopathic orofacial pain.
  - At least 10 participants per group at the end of the treatment
  - Any pharmacological or neuromodulation intervention if administered for at least 3 weeks or single administration with at least 3 weeks of follow-up.
- Primary efficacy outcome: Proportion of responders (at least 50% reduction in baseline pain intensity, alternatively 30% or at least moderate pain relief).
- Risk difference and standardised mean difference (SMD) calculated. Random-effects model used for pairwise meta-analyses. Calculation of number needed to treat (NNT), based upon intention to treat (i.e., number of participants randomised) and number needed to harm (NNH), based on those who received intervention.
- Recommendations developed through a series of expert consensus meetings and anonymous online voting.

# Pharmacotherapy and non-invasive neuromodulation for neuropathic pain: a systematic review and meta-analysis.

## Article Reference:

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## Selected and Presented by:

Dr. Yoko Tarumi

## Key Results:

- 313 trials (284 pharmacological, 29 neuromodulation) included.
- 48 789 adult participants randomly assigned (20 611 female and 25 078 male participants, where sex was reported).
- Sample size 10 to 1269 participants, median 96 participants.
- Trial duration (treatment plus follow up) from 3 to 24 weeks, median 8 weeks.
- Assessed 89 pharmacological interventions and nine neuromodulation interventions.
- Estimates for primary efficacy and safety outcomes:
  - Tricyclic antidepressants (TCAs) NNT=4.6 (95% CI 3.2–7.7), NNH=17.1 (11.4–33.6; moderate certainty of evidence)
  - $\alpha 2\delta$ -ligands NNT=8.9 (7.4–11.10), NNH=26.2 (20.4–36.5; moderate certainty of evidence)
  - Serotonin and norepinephrine reuptake inhibitors (SNRIs) NNT=7.4 (5.6–10.9), NNH=13.9 (10.9–19.0; moderate certainty of evidence)
  - Botulinum toxin (BTX-A) NNT=2.7 (1.8–9.61), NNH=216.3 (23.5– $\infty$ ; moderate certainty of evidence)
  - Capsaicin 8% patches NNT=13.2 (7.6–50.8), NNH=1129.3 (135.7– $\infty$ ; moderate certainty of evidence)
  - Opioids NNT=5.9 (4.1–10.7), NNH=15.4 (10.8–24.0; low certainty of evidence)
  - Repetitive transcranial magnetic stimulation (rTMS) NNT=4.2 (2.3–28.3), NNH=651.6 (34.7– $\infty$ ; low certainty of evidence)
  - Capsaicin cream NNT=6.1 (3.1– $\infty$ ), NNH=18.6 (10.6–77.1; very low certainty of evidence),
  - Lidocaine 5% plasters NNT=14.5 (7.8–108.2), NNH=178.0 (23.9– $\infty$ ; very low certainty of evidence).

## Key Discussion Points:

- The findings provided the basis for a strong recommendation for use of TCAs,  $\alpha 2\delta$ -ligands, and SNRIs as **first-line treatments**; a weak recommendation for capsaicin 8% patches, capsaicin cream, and lidocaine 5% plasters as **second-line recommendation**; a weak recommendation for BTX-A, rTMS, and opioids as **third-line treatments** for neuropathic pain.
- The evidence in the review is not sufficient to confidently make recommendations for specific patient populations.
- The distinction between weak and strong opioids is increasingly questioned, as the risks associated with this therapeutic class depend mainly on dose. With opioid crisis in mind, all opioids were recommended to be restricted to third-line in patients with worsening pain who have not responded to other reasonable treatments, with the shortest possible duration of use, and early and ongoing review, considering the risk.
- Although the effect size of M1-rTMS was greater than that of many drug treatments, this was proposed as the third-line owing to the low certainty of evidence, low availability, and high cost.
- Cannabinoids received a so-called weak against recommendation.
- No conclusions for drug combinations. A 2023 systematic review and meta-analysis of combinations (opioids with antidepressants or  $\alpha 2\delta$ -ligands, and  $\alpha 2\delta$ -ligands with antidepressants) showed no greater efficacy and found similar safety compared with each drug alone.

# Pharmacotherapy and non-invasive neuromodulation for neuropathic pain: a systematic review and meta-analysis.

## Article Reference:

Soliman N, Moisset X, Ferraro MC, et al. Pharmacotherapy and non-invasive neuromodulation for neuropathic pain: a systematic review and meta-analysis. The Lancet Neurology. 2025;24(5):413-428. doi:10.1016/S1474-4422(25)00068-7

## Selected and Presented by:

Dr. Yoko Tarumi

## Strengths:

- The recommendations are based on the quality of available evidence and expert consensus, with representation from 13 countries and every continent. This updated guideline included sensitivity analyses to evaluate the effect of potential biases, and qualitatively assessed each treatment's adverse effects, cost, and accessibility. Additionally, lived experience partners were engaged from inception.
- Acknowledged the increased risk of TCA adverse effects in older adults, as well as an increased risk of drug-related death in people taking both  $\alpha 2\delta$ -ligands and opioids particularly regarding pregabalin.
- Acknowledged that interpretation of these results and subsequent recommendations must account for possible limitations.

## Limitations:

- Shortage of data prevented the authors from analysing dose–response relationships and some trials used lower than maximum recommended doses. For example, some studies used pregabalin 300 mg/day as an active control group, which is half the maximum recommended dose
- A notable lack of detail regarding how adverse events were measured and classified, influenced on information provided in this review.

# Pharmacotherapy and non-invasive neuromodulation for neuropathic pain: a systematic review and meta-analysis.

## Article Reference:

Soliman N, Moisset X, Ferraro MC, et al. Pharmacotherapy and non-invasive neuromodulation for neuropathic pain: a systematic review and meta-analysis. The Lancet Neurology. 2025;24(5):413-428. doi:10.1016/S1474-4422(25)00068-7

## Selected and Presented by:

Dr. Yoko Tarumi

## Additional Comments:

- This review did not include a study by Tesfaye S et al. re: combination pharmacotherapy: the efficacy of three of the most prescribed first-line drugs for DPNP and their combinations not only for the primary outcome of pain relief, but also for secondary outcomes including quality of life, mood, and sleep.

Tesfaye S, Sloan G, Petrie J, White D, Bradburn M, Julious S, Rajbhandari S, Sharma S, Rayman G, Gouni R, Alam U, Cooper C, Loban A, Sutherland K, Glover R, Waterhouse S, Turton E, Horspool M, Gandhi R, Maguire D, Jude EB, Ahmed SH, Vas P, Hariman C, McDougall C, Devers M, Tsalidis V, Johnson M, Rice ASC, Bouhassira D, Bennett DL, Selvarajah D; OPTION-DM trial group. Comparison of amitriptyline supplemented with pregabalin, pregabalin supplemented with amitriptyline, and duloxetine supplemented with pregabalin for the treatment of diabetic peripheral neuropathic pain (OPTION-DM): a multicentre, double-blind, randomised crossover trial. Lancet. 2022 Aug 27;400(10353):680-690. doi: 10.1016/S0140-6736(22)01472-6. Epub 2022 Aug 22. Erratum in: Lancet. 2022 Sep 10;400(10355):810. doi: 10.1016/S0140-6736(22)01661-0. PMID: 36007534; PMCID: PMC9418415.

## Practice Impact:

- When taking recommendation on cancer-related neuropathic pain, one should consider that “pure” neuropathic pain is less prominent than mixed mechanism.
- How accurately palliative care practitioners are making diagnosis of neuropathic pain using NeupSIG criteria and selecting treatment options is not known.
- Availability of treatment modalities such as capsaicin 8% patches, capsaicin cream, and lidocaine 5% plasters, BTX-A, and rTMS in Canadian clinical settings also impacts on treatment decisions.

# Discussion

Factors that support home deaths for patients receiving at-home palliative and end-of-life care: a sequential mixed-methods explanatory study.

**Article Reference:**

Kilpatrick K, Allard É, Jabbour M, Tchouaket E. Factors that support home deaths for patients receiving at-home palliative and end-of-life care: a sequential mixed-methods explanatory study. BMC Palliat Care. 2025;24(1):197. doi:10.1186/s12904-025-01840-0

**Presented by:**

Dr. Jose Pereira

## Background

- Many patients, across age groups and diseases, receive or wish to receive palliative and end-of-life care (PEoLC) in their homes.
- Access to respite care represents an unmet need

### Study goals:

1. Identify the factors associated with remaining at home and home death or definitive transfer for patients receiving PEoLC;
2. Explore the importance of these factors from the perspective of different groups (patients, caregivers, service providers, etc).

## Methods

- A mixed-methods, sequential explanatory design (QUANT-QUAL)
- Anonymized administrative data (QUANT):
  - Administrative data from a non-government not-for-profit at-home palliative care organization in Québec, Canada from 2015 to 2024 ( $n = 5931$ )
- Semi-structured interviews (QUAL)
  - 73 semi-structured interviews:
    - 44 (60%) were with patients & caregivers
    - 29 (40%) healthcare providers (e.g. RNs, MDs, SW, etc)

Factors that support home deaths for patients receiving at-home palliative and end-of-life care: a sequential mixed-methods explanatory study.

**Article Reference:**

Kilpatrick K, Allard É, Jabbour M, Tchouaket E. Factors that support home deaths for patients receiving at-home palliative and end-of-life care: a sequential mixed-methods explanatory study. BMC Palliat Care. 2025;24(1):197. doi:10.1186/s12904-025-01840-0

**Presented by:**

Dr. Jose Pereira

## Key Results

### Quant phase

- 26% of patients lived alone & 94% had cancer.
- Mean home care service contacts 31.4 (25% ≤ 3)
- Home death occurred in almost 30% of cases.
  - Time from admission to home death: mean 89 days, median 32
- Factors associated with home deaths:
  - Access to respite care (2.7x higher)
  - Living alone (almost 50% lower)
  - Receiving psychological care (20% lower)
  - Having been hospitalized (70% lower)
- Factors associated with definitive transfers:
  - Number of services/visits (lower risk as number of visits increase)
  - Sex (1.14 times higher if female)
  - Psychological care (1.44 times higher risk)
  - Volunteer and transportation support (2.23 times higher)
  - Covid infection (1.87 times)
- Factors associated with time to definitive transfers:
  - Slower time for those receiving respite care; faster if living alone



Factors that support home deaths for patients receiving at-home palliative and end-of-life care: a sequential mixed-methods explanatory study.

**Article Reference:**

Kilpatrick K, Allard É, Jabbour M, Tchouaket E. Factors that support home deaths for patients receiving at-home palliative and end-of-life care: a sequential mixed-methods explanatory study. BMC Palliat Care. 2025;24(1):197. doi:10.1186/s12904-025-01840-0

**Presented by:**

Dr. Jose Pereira

## Key Results

### Qual phase

- Important to accept help (Including aids such as wheelchairs)
- Importance of timely access to home care and if crisis
- Inconsistency of services (types, frequency) across community centres
- Need to respect patients' wishes related to EOL care and home death.
- Contribution of palliative care physicians (good but varied)
- Rapid access to care team (nursing) when needed (safety)

### Strengths & Limitations

- Strength: Study design (views of various stakeholders)
- Limitations: One large urban area in one Canadian province, COVID-19 pandemic. What about patients who did not receive at-home care?

### Key Discussion points and Practice Impact

- Important factors that contribute to PEOLC at home
- respite care, nursing care to meet needs such as hygiene, pain and symptom management, psychological support and holistic care
- This model includes: stable home care teams, quality nursing care and hygiene, respite care, psychological care for patients receiving PEOLC and their caregivers, volunteer support.



# Discussion

# Prevalence of Preoperative Palliative Care Needs and Association with Healthcare Use and Cost Among Older Adults Undergoing Major Elective Surgery.

## Article Reference:

Min JWS, Wang Y, Bollens-Lund E, et al. Prevalence of Preoperative Palliative Care Needs and Association with Healthcare Use and Cost Among Older Adults Undergoing Major Elective Surgery. Journal of the American College of Surgeons. Published online July 16, 2025. doi:10.1097/XCS.0000000000001491

## Presented by:

Dr. Sharon Watanabe

## Background

- Up to 40% of older adults with serious illness (SI) undergo surgery.
- This population is at risk of greater pain and depressive symptoms, with higher functional and care partner needs.
- The American College of Surgeons recommends provision of palliative care (PC) to adults with SI undergoing major surgery.
- Little is known about prevalence of PC needs in this population and their association with healthcare utilization and costs.

## Methods

- Data sources: Health and Retirement Study (HRS) linked to fee-for-service Medicare claims 2007-2019
- Study population: Adults  $\geq 66$  years who underwent major elective surgery within 2 ys of last HRS interview
- Exposures
  - SI: advanced age, functional/cognitive disability, cancer, chronic pulmonary/cardiac/liver/renal disease, dementia, frailty, nursing home residence
  - Preoperative PC needs: pain, depressive symptoms, functional dependence, care partner needs
- Outcomes: Healthcare utilization and costs during 1 year period post surgical admission
- Covariates: Age, sex, ethnicity, marital status
- Analysis: Compare 1) without SI, 2) with SI without PC needs, 3) with SI and PC needs; Pearson's chi-square, t-test. Uni/multivariable regression analyses for associations.

# Prevalence of Preoperative Palliative Care Needs and Association with Healthcare Use and Cost Among Older Adults Undergoing Major Elective Surgery.

## Article Reference:

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## Presented by:

Dr. Sharon Watanabe

## Key Results

- 2499 eligible, 1580 (63.2%) with SI, of whom 1249 (78.8%) had PC needs preoperatively (moderate-severe pain 53.8%, major depressive symptoms 31.1%, functionally dependent 12.8%, unpaid care 25.4%)
- SI with PC needs vs. no SI: Higher rate of post-operative complications, longer LOS, higher rate of ICU admissions, more likely to be discharged to non-home location, higher 1 year. mortality
- SI independently associated with increased total hospital days, hospital readmission and ED visits over 1 year
- SI with PC needs had significantly higher rates of healthcare utilization (highest with depressive symptoms)
- SI incurred higher healthcare costs at 90 days and 1 year
- SI and PC needs (especially depressive symptoms) incurred the highest costs

## Key discussion points

- This study represents one of the first efforts to systematically characterize older adults with SI undergoing surgery and examine modifiable PC needs and their impact on the healthcare system.
- Highlights the importance of early identification of at-risk older adults so that appropriate PC interventions may be administered perioperatively to mitigate downstream repercussions.

# Prevalence of Preoperative Palliative Care Needs and Association with Healthcare Use and Cost Among Older Adults Undergoing Major Elective Surgery.

## Article Reference:

Min JWS, Wang Y, Bollens-Lund E, et al. Prevalence of Preoperative Palliative Care Needs and Association with Healthcare Use and Cost Among Older Adults Undergoing Major Elective Surgery. Journal of the American College of Surgeons. Published online July 16, 2025. doi:10.1097/XCS.0000000000001491

## Presented by:

Dr. Sharon Watanabe

## Strengths

- HRS is designed to be nationally representative

## Limitations

- Selection bias – findings may not be generalizable
- Out-of-pocket costs not accounted for
- Unable to make causal inference re independent effects of PC needs on outcomes
- Data on PC needs limited to what was collected in HRS (no information on symptoms besides pain or depression; no quality-of-life measures)
- Lag time between HRS interview and surgery
- Authors do not discuss who should address PC needs (specialist PC implied)

## Practice Impact

- Elective surgery presents an opportunity to screen for PC needs in older adults with SI
- Integration of a palliative approach to care in the surgical setting (with specialist PC for more complex situations) is warranted

# Discussion

# Proportional Sedation for Persistent Agitated Delirium in Palliative Care: A Randomized Clinical Trial.

## Article Reference:

Hui D, De La Rosa A, Tsai JS, et al. Proportional Sedation for Persistent Agitated Delirium in Palliative Care: A Randomized Clinical Trial. JAMA Oncol. Published online July 31, 2025. doi:10.1001/jamaoncol.2025.2212

## Selected and presented by:

Dr. Leonie Herx

## Background

- Delirium common and highly distressing syndrome, affects >90% of patients in last days/weeks of life, with 50-70% develop restlessness/agitation; often irreversible in last days of life & non-pharmacologic measures often inadequate
- Neuroleptics & benzodiazepines often prescribed for patients with persistent agitation in the last days of life
- Risk-to-benefit ratio of these medications is ill-defined
- Proportional sedation often considered for persistent agitated delirium and may include: 1) neuroleptic dose escalation, 2) rotation to another class eg benzodiazepines, 3) combination of neuroleptic & benzodiazepine.
- No RCT has assessed these three strategies against placebo
- This study aimed to compare the effect of haloperidol dose escalation, rotation to lorazepam, combination therapy with haloperidol plus lorazepam, & placebo on restlessness/agitation intensity in patients with advanced cancer and delirium admitted to palliative care.

## Methods

- Multicentre, randomized, double blind, parallel group trial at 3 acute PCUs in Taiwan & US; July 2019-June 2023
- Inclusion criteria: 18 yrs+; advanced cancer; admitted to APCU; delirium with persistent restlessness and/or agitation RASS 1+ despite nonpharmacologic therapies and standard-dose haloperidol (4mg/d+ in past 24 hrs)
- Intervention: scheduled haloperidol, lorazepam, combination of haloperidol plus lorazepam, or placebo q4hrs, continued until discharge/death/ study withdrawal. 30-day f/up after medication administration
- Randomization: 1:1:1:1 ratio, stratified by site and RASS score
- Medications in all 4 groups had identical volume & appearance
- At enrollment, all patients started open label haloperidol 2mg IV q6hr & 2mg IV q1hr PRN and monitored for persistent agitation/restlessness until RASS 1+ then started blinded phase with IV medication q4hrs & rescue q1hr PRN RASS 1+.
- Outcomes: Primary - change in RASS scores during first 24 hours; Secondary - 1) use of rescue neuroleptics or benzodiazepines for breakthrough restlessness or agitation during first 24 hrs; 2) proportion of patients with target RASS (0 to -2) during first 24 hrs, 3) proportion of patients achieving “treatment response” (RASS reduction of 1.5+); 4) change in delirium severity (Memorial Delirium Assessment Scale score) at 0 & 24hrs; 5) proportion of patients perceived as comfortable (independently by RNs & caregivers); 6) adverse events. Overall survival also documented.

# Proportional Sedation for Persistent Agitated Delirium in Palliative Care: A Randomized Clinical Trial.

## Article Reference:

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## Selected and presented by:

Dr. Leonie Herx

## Key Results

- 245 (8%) eligible of 2888 screened; 111 (45%) enrolled & randomized;
  - Of these, 75 (68%) developed breakthrough restlessness & proceeded to blinded treatments
- Primary outcome analysis included 72 patients: mean age 64 yrs, 58% male, median MDAS score 24. Baseline characteristics similar between groups.
- **Primary Outcome – RASS score change at 24 hours after blinded treatment:**
  - Lorazepam group -significantly lower RASS scores than haloperidol group (mean diff -2.1,  $p<0.001$ )
  - Combination group - significantly lower RASS scores than haloperidol group (mean diff -2.0,  $p<0.002$ )
  - No differences between haloperidol vs placebo, and between lorazepam vs combination
- **Secondary Outcomes**
  - Rescue doses: combination (32%), lorazepam (37%), and haloperidol (56%) groups overall had fewer patients who required rescue medication doses for breakthrough restlessness/agitation vs placebo (83%); statistically significant ( $p=0.006$ ).
  - MDAS scores: no significant differences in changes
  - Adverse Events: no significant differences between groups (hypotension, hypoxia most common)
  - Survival: no significant differences between groups
  - Perceived comfort: combination & lorazepam groups perceived to be more comfortable by nurses than haloperidol and placebo (100%, 92%, 60%, 68%, respectively); no differences between groups by caregiver-perceived comfort



# Proportional Sedation for Persistent Agitated Delirium in Palliative Care: A Randomized Clinical Trial.

## Article Reference:

Hui D, De La Rosa A, Tsai JS, et al. Proportional Sedation for Persistent Agitated Delirium in Palliative Care: A Randomized Clinical Trial. JAMA Oncol. Published online July 31, 2025. doi:10.1001/jamaoncol.2025.2212

## Selected and presented by:

Dr. Leonie Herx

## Key discussion points

- Lorazepam alone and in combination with haloperidol was superior to haloperidol alone in reducing persistent agitation/restlessness in patients with delirium at end of life (lower RASS scores, fewer breakthrough episodes of restlessness/agitation, fewer rescue doses, and greater perceived comfort)
- Patients who received scheduled medications, including haloperidol alone, received significantly fewer rescue medications for breakthrough restlessness & agitation vs placebo suggesting that scheduled medications represent a more proactive approach to preventing breakthrough restlessness and agitation in this setting.

## Strengths

- Multicentre, double blind, randomized, parallel group trial
- Measured restlessness and/or agitation as primary outcome (vs only delirium severity)

## Limitations

- Specific context of delirium at end of life on a specialist palliative care unit – not generalizable to other settings or delirium outside end of life.
- Did not examine other medications commonly used for delirium and agitation eg olanzapine, chlorpromazine etc
- Only examined intravenous route (subcutaneous route more common across settings, jurisdictions)

## Practice Impact

Proactive use of scheduled lorazepam may reduce persistent restlessness and/or agitation in patients with advanced cancer and delirium at the end of life.



# Discussion

# Honourable Mentions

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# Wrap-up

- Please fill out our feedback survey a link has been shared in the chat!
- A recording of this webinar and a copy of the slides will be e-mailed to registrants within the next week.
- To listen to this session and previous sessions, check out the **Palliative Care Journal Watch** podcast.



NOTE: recordings, slides and links to articles from all our sessions are available at [www.echopalliative.com/palliative-care-journal-watch/](http://www.echopalliative.com/palliative-care-journal-watch/).

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# Thank You



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