

“Palliative Care for the Internist: 15 Ways to Improve Care for Your Patients with a Life-limiting Illness”

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Disclosure: There are no relevant financial relationships to disclose regarding this presentation

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My Background



- Internal Medicine-
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- Hospice & Palliative Care
Fellowship University of
Pittsburgh Medical Center
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Translational Science,
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- Chief Medical Officer, BJC
Hospice

Presentation Outline

- Background
- Communication Pearls
- Polypharmacy Pearls
- Symptom Management Pearls
 - Constipation
 - Nausea
 - Depression
 - Pain
 - Agitation
 - Secretions

Palliative Care Versus Hospice Care

Palliative Care

- Focus on improving quality of life and controlling symptoms
- At any point in a serious illness
- Patients often continuing curative therapies including chemotherapy and hospitalizations
- Home support varies by program
- Medications and equipment often have copays

Hospice Care

- Focus on improving quality of life and controlling symptoms
- Prognosis less than 6 months
- Focus on comfort focused therapies with patients often desiring to be at their homes without intensive therapies
- Home support includes home nurses, social workers, chaplains, and NPs/physicians
- Medications and equipment are typically without copays

The Problem



Original Investigation

Family Perspectives on Aggressive Cancer Care Near the End of Life

Alexi A. Wright, MD, MPH; Nancy L. Keating, MD, MPH; John Z. Ayanian, MD, MPP; Elizabeth A. Chrischilles, PhD; Katherine L. Kahn, MD; Christine S. Ritchie, MD, MSPH; Jane C. Weeks, MD, MSc¹; Craig C. Earle, MD, MSc; Mary B. Landrum, PhD

IMPORTANCE Patients with advanced-stage cancer are receiving increasingly aggressive medical care near death, despite growing concerns that this reflects poor-quality care.

OBJECTIVE To assess the association of aggressive end-of-life care with bereaved family members' perceptions of the quality of end-of-life care and patients' goal attainment.

DESIGN, SETTING, AND PARTICIPANTS Interviews with 1146 family members of Medicare patients with advanced-stage lung or colorectal cancer in the Cancer Care Outcomes Research and Surveillance study (a multiregional, prospective, observational study) who died by the end of 2011 (median, 144.5 days after death; interquartile range, 85.0-551.0 days).

EXPOSURES Claims-based quality measures of aggressive end-of-life care (ie, intensive care unit [ICU] admission or repeated hospitalizations or emergency department visits during the last month of life, chemotherapy \leq 2 weeks of death; no hospice or \leq 3 days of hospice services; and deaths occurring in the hospital).

MAIN OUTCOMES AND MEASURES Family member-reported quality rating of "excellent" for end-of-life care. Secondary outcomes included patients' goal attainment (ie, end-of-life care congruent with patients' wishes and location of death occurred in preferred place).

RESULTS Of 1146 patients with cancer (median age, 76.0 years [interquartile range, 65.0-87.0 years]; 55.8% male), bereaved family members reported excellent end-of-life care for 51.3%. Family members reported excellent end-of-life care more often for patients who received hospice care for longer than 3 days (58.8% [352/599]) than those who did not receive hospice care or received 3 or fewer days (43.1% [236/547]) (adjusted difference, 16.5 percentage points [95% CI, 10.7 to 22.4 percentage points]). In contrast, family members of patients admitted to an ICU within 30 days of death reported excellent end-of-life care less often (45.0% [68/151]) than those who were not admitted to an ICU within 30 days of death (52.3% [520/995]) (adjusted difference, -9.4 percentage points [95% CI, -18.2 to -0.6 percentage points]). Similarly, family members of patients who died in the hospital reported excellent end-of-life care less often (42.2% [194/460]) than those who did not die in the hospital (57.4% [394/686]) (adjusted difference, -17.0 percentage points [95% CI, -22.9 to -11.1 percentage points]). Family members of patients who did not receive hospice care or received 3 or fewer days were less likely to report that patients died in their preferred location (40.0% [152/380]) than those who received hospice care for longer than 3 days (72.8% [287/394]) (adjusted difference, -34.4 percentage points [95% CI, -41.7 to -27.0 percentage points]).

CONCLUSIONS AND RELEVANCE Among family members of older patients with fee-for-service Medicare who died of lung or colorectal cancer, earlier hospice enrollment, avoidance of ICU admissions within 30 days of death, and death occurring outside the hospital were associated with perceptions of better end-of-life care. These findings are consistent with previous research.

Supplemental content at jama.com

CME Quiz at jamanetworkcme.com and CME Questions page 300

Author Affiliations: Author affiliations are listed at the end of this article.

JAMA. 2016 Jan 19;315(3):284-92

ORIGINAL ARTICLE

Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer

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Among patients with metastatic non–small-cell lung cancer, early palliative care led to significant improvements in both quality of life and mood. As compared with patients receiving standard care, patients receiving early palliative care had less aggressive care at the end of life but longer survival.

11.6 months vs. 8.9 months, $P=0.02$

Key Communication Skills

- Disclosing bad news
- Communicating prognostic information
- Addressing patients' and families' emotions
- Discussing end-of-life options including hospice



1) Disclosing Bad News (SPIKES)

- Setting Quiet location/tissues/pagers off
- Perception Ask what they have been told/believe
- Invitation Permission to discuss prognosis
- Knowledge Provide information without jargon
- Empathy Acknowledge emotions
- Summary Discuss next steps

2) NURSE Statements

- Naming emotion “I can’t imagine how frustrating this must be.”
- Understanding “If a doctor told me that I would be frustrated and have trouble trusting.”
- Respecting “All of us are so impressed with what a great job you have done taking care of Jack.”
- Supporting “We will be with there to support you through the rest of Jack’s illness.”
- Exploring “Could you share more about what “X” means to you?”

3) Tips for Talking about Hospice

- Talk first about what hospice is and the *support* it can provide long before you use the word “hospice”
- Learn how to address the hope for miracle or that God will intervene to help their loved one
- Know the power of “I wish” statements
- “What would your loved one say if they were doing the talking”



Other Tips

- It is okay to cry in front of your patients/families and they are almost always touched by it
- Expect to get some bizarre reactions when sharing really bad news
- Think of a really anxious situation you encountered before entering a challenging goals of care discussion. It will help ground you before entering these often emotional draining conversations

4) Preparing Families for End-of-Life

- Symptoms to make patients/families aware of:
- 1) Delirium/agitation
- 2) Secretions
- 3) Respiratory changes
- 4) Mottling/Cyanosis



Patient Experience in the Last Week of Life

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DOI: 10.1089/jpm.2013.0371

End-of-Life Dreams and Visions: A Longitudinal Study of Hospice Patients' Experiences

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Anne Banas, MD,¹ Pei C. Grant, PhD,¹ and Debra L. Luczkiewicz, MD¹

Abstract

Background: End-of-life dreams and visions (ELDVs) have been well documented throughout history and across cultures. The impact of pre-death experiences on dying individuals and their loved ones can be profoundly meaningful.

Objective: Our aim was to quantify the frequency of dreams/visions experienced by patients nearing the end of life, examine the content and subjective significance of the dreams/visions, and explore the relationship of these factors to time/proximity to death.

Methods: This mixed-methods study surveyed patients in a hospice inpatient unit using a semi-structured interview. Sixty-six patients admitted to a hospice inpatient unit between January 2011 and July 2012 provided informed consent and participated in the study. The semi-structured interviews contained closed and open-ended questions regarding the content, frequency, and comfort/distress of dreams/visions.

Results: Fifty-nine participants comprised the final sample. Most participants reported experiencing at least one dream/vision. Almost half of the dreams/visions occurred while asleep, and nearly all patients indicated that they felt real. The most common dreams/visions included deceased friends/relatives and living friends/relatives. Dreams/visions featuring the deceased (friends, relatives, and animals/pets) were significantly more comforting than those of the living, living and deceased combined, and other people and experiences. As participants approached death, comforting dreams/visions of the deceased became more prevalent.

Conclusions: ELDVs are commonly experienced phenomena during the dying process, characterized by a consistent sense of realism and marked emotional significance. These dreams/visions may be a profound source of potential meaning and comfort for the dying, and therefore warrant clinical attention and further research.

- 87% of EOL patients experience dreams and visions
- The vast majority of dreams/visions are comforting
- Common topics
 - Reunions with deceased loved ones
 - Going on a trip
 - Meaningful experience

Kerr CW, Donnelly JP, Wright ST, Kuszczak SM, Banas A, Grant PC, Luczkiewicz DL. End-of-life dreams and visions: a longitudinal study of hospice patients' experiences. J Palliat Med. 2014 Mar;17(3):296-303.

5) Transportable Physician Orders for Patient Preferences (TPOPP) (Missouri POLST equivalent)

Kansas – Missouri Transportable Physician Orders for Patient Preferences (TPOPP) <small>The Physician Order set is based on the patient's current medical condition and preferences. Any section not completed indicates full treatment for that section. The original form should not be present at the time of emergency. A copied, faxed or electronic version of this form is valid.</small>			
Last Name:		First Name:	Middle Initial:
Date of Birth:		Last 4 SSN:	Gender: <input type="checkbox"/> M <input type="checkbox"/> F
A. CHECK ONE	CARDIOPULMONARY RESUSCITATION (CPR): Person has no pulse and is not breathing. If patient is not in cardiopulmonary arrest, follow orders in B and C. <input type="checkbox"/> Attempt Resuscitation/CPR (Selecting CPR in Section A requires selecting Full Treatment in Section B) <input type="checkbox"/> Do Not Attempt Resuscitation (DNAR/no CPR/Alive, Not/Not Dead)		
B. CHECK ONE	MEDICAL INTERVENTIONS: Person has pulse and/or is breathing. <input type="checkbox"/> Comfort Measures Only. Treat with dignity and respect. Keep clean, warm, and dry. Use medication by any route, positioning, wound care and other measures to relieve pain and suffering. Use oxygen, suction and manual treatment of airway obstruction as needed for comfort. Transfer to hospital only if comfort needs cannot be met in current location. TREATMENT GOAL: ATTEMPT TO MAXIMIZE COMFORT THROUGH SYMPTOM MANAGEMENT ONLY. <input type="checkbox"/> Limited Additional Interventions. In addition to care described in Comfort Measures Only, use medical treatment, antibiotics, and IV fluids as indicated. Do not intubate. May use non-invasive positive airway pressure. Generally avoid intensive care. Transfer to hospital only if treatment needs cannot be met in current location. TREATMENT GOAL: ATTEMPT TO RESTORE FUNCTION WITH TREATMENTS FOR REVERSIBLE CONDITIONS. <input type="checkbox"/> Full Treatment. In addition to care described in Comfort Measures Only and Limited Additional Interventions, use intubation, advanced airway interventions, mechanical ventilation, and defibrillation/cardioversion as indicated. Transfer to hospital if indicated. Include intensive care. TREATMENT GOAL: ATTEMPT TO PROLONG LIFE BY ALL MEDICALLY EFFECTIVE MEANS. Additional Orders: _____		
C. CHECK ONE	MEDICALLY ADMINISTERED NUTRITION: Offer food by mouth if feasible and desired. <input type="checkbox"/> No medically administered nutrition, including feeding tubes. <input type="checkbox"/> Medically administered nutrition, including feeding tubes, for trial period: _____ <input type="checkbox"/> Long term medically administered nutrition, including feeding tubes Additional Orders: _____		
D. CHECK ALL THAT APPLY	INFORMATION AND SIGNATURES Discussed with: <input type="checkbox"/> Patient/Resident <input type="checkbox"/> Agent/DPOA, healthcare <input type="checkbox"/> Parent of minor <input type="checkbox"/> Legal guardian <input type="checkbox"/> Health care surrogate <input type="checkbox"/> Other (specify): _____ Signature of patient or recognized decision maker <small>By signing this form, the recognized decision maker acknowledges that this request regarding above treatment measures is consistent with the known desires, and with the best interest, of the individual who is the subject of the form.</small> Print name: _____ Signature (required): _____ Relationship (note "not" if partner): _____ Address: _____ Phone: _____ Signature of physician <small>My signature below indicates to the best of my knowledge that these orders are consistent with the person's medical condition and preferences.</small> Print physician name: _____ Physician phone: _____ Physician signature (required): _____ Date: _____		
<small>© Center for Practical Bioethics, 1111 Main, Suite 200 (Marshall Building), Kansas City, MO 64103 816-251-1100</small>			<small>September 2012</small>

Improving Access to Palliative Care



[Khandelwal N¹](#), [Kross EK](#), [Engelberg RA](#), [Coe NB](#), [Long AC](#), [Curtis JR](#). Estimating the effect of palliative care interventions and advance care planning on ICU utilization: a systematic review. 2015 May;43(5):1102-11.

Minimizing Polypharmacy



Advances in Oncology: Impact of Palliative Chemotherapy on Quality of Life

JAMA Oncol. 2015 Sep;1(6):778-84.

Chemotherapy Use, Performance Status, and Quality of Life at the End of Life

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 Invited Commentary page 785

IMPORTANCE Although many patients with end-stage cancer are offered chemotherapy to improve quality of life (QOL), the association between chemotherapy and QOL amid progressive metastatic disease has not been well-studied. American Society for Clinical Oncology guidelines recommend palliative chemotherapy only for solid tumor patients with good performance status.

OBJECTIVE To evaluate the association between chemotherapy use and QOL near death (QOD) as a function of patients' performance status.

DESIGN, SETTING, AND PARTICIPANTS A multi-institutional, longitudinal cohort study of patients with end-stage cancer recruited between September 2002 and February 2008. Chemotherapy use (n = 158 [50.6%]) and Eastern Cooperative Oncology Group (ECOG) performance status were assessed at baseline (median = 3.8 months before death) and patients with progressive metastatic cancer (N = 312) following at least 1 chemotherapy regimen were followed prospectively until death at 6 outpatient oncology clinics in the United States.

MAIN OUTCOMES AND MEASURES Patient QOD was determined using validated caregiver ratings of patients' physical and mental distress in their final week.

RESULTS Chemotherapy use was not associated with patient survival controlling for clinical setting and patients' performance status. Among patients with good (ECOG score = 1) baseline performance status, chemotherapy use compared with nonuse was associated with worse QOD (odds ratio [OR], 0.35; 95% CI, 0.17-0.75; P = .01). Baseline chemotherapy use was not associated with QOD among patients with moderate (ECOG score = 2) baseline performance status (OR, 1.06; 95% CI, 0.51-2.21; P = .87) or poor (ECOG score = 3) baseline performance status (OR, 1.34; 95% CI, 0.46-3.89; P = .59).

CONCLUSIONS AND RELEVANCE Although palliative chemotherapy is used to improve QOL for patients with end-stage cancer, its use did not improve QOD for patients with moderate or poor performance status and worsened QOD for patients with good performance status. The QOD in patients with end-stage cancer is not improved, and can be harmed, by chemotherapy use near death, even in patients with good performance status.

6) Risks and Benefits of Statins in Advanced Illness

JAMA Intern Med. 2015; 175(5): 691-700.

Original Investigation

Safety and Benefit of Discontinuing Statin Therapy in the Setting of Advanced, Life-Limiting Illness A Randomized Clinical Trial

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IMPORTANCE For patients with limited prognosis, some medication risks may outweigh the benefits, particularly when benefits take years to accrue, statins are one example. Data are lacking regarding the risks and benefits of discontinuing statin therapy for patients with limited life expectancy.

OBJECTIVE To evaluate the safety, clinical, and cost impact of discontinuing statin medications for patients in the palliative care setting.

DESIGN, SETTING, AND PARTICIPANTS This was a multicenter, parallel-group, unblinded, pragmatic clinical trial. Eligibility included adults with an estimated life expectancy of between 1 month and 1 year, statin therapy for 3 months or more for primary or secondary prevention of cardiovascular disease, recent deterioration in functional status, and no recent active cardiovascular disease. Participants were randomized to either discontinue or continue statin therapy and were monitored monthly for up to 1 year. The study was conducted from June 3, 2011, to May 2, 2013. All analyses were performed using an intent-to-treat approach.

INTERVENTIONS Statin therapy was withdrawn from eligible patients who were randomized to the discontinuation group. Patients in the continuation group continued to receive statins.

MAIN OUTCOMES AND MEASURES Outcomes included death within 60 days (primary outcome), survival, cardiovascular events, performance status, quality of life (QOL), symptoms, number of nonstatin medications, and cost savings.

RESULTS A total of 381 patients were enrolled; 189 of these were randomized to discontinue statins, and 192 were randomized to continue therapy. Mean (SD) age was 74.1 (11.6) years, 22.0% of the participants were cognitively impaired, and 48.8% had cancer. The proportion of participants in the discontinuation vs continuation groups who died within 60 days was not significantly different (23.8% vs 20.3%; 90% CI, -3.5% to 10.5%; $P = .36$) and did not meet the noninferiority end point. Total QOL was better for the group discontinuing statin therapy (mean McGill QOL score, 711 vs 6.85; $P = .04$). Few participants experienced cardiovascular events (13 in the discontinuation group vs 11 in the continuation group). Mean cost savings were \$3.37 per day and \$716 per patient.

CONCLUSIONS AND RELEVANCE This pragmatic trial suggests that stopping statin medication therapy is safe and may be associated with benefits including improved QOL, use of fewer nonstatin medications, and a corresponding reduction in medication costs. Thoughtful patient-provider discussions regarding the uncertain benefit and potential decrement in QOL associated with statin continuation in this setting are warranted.

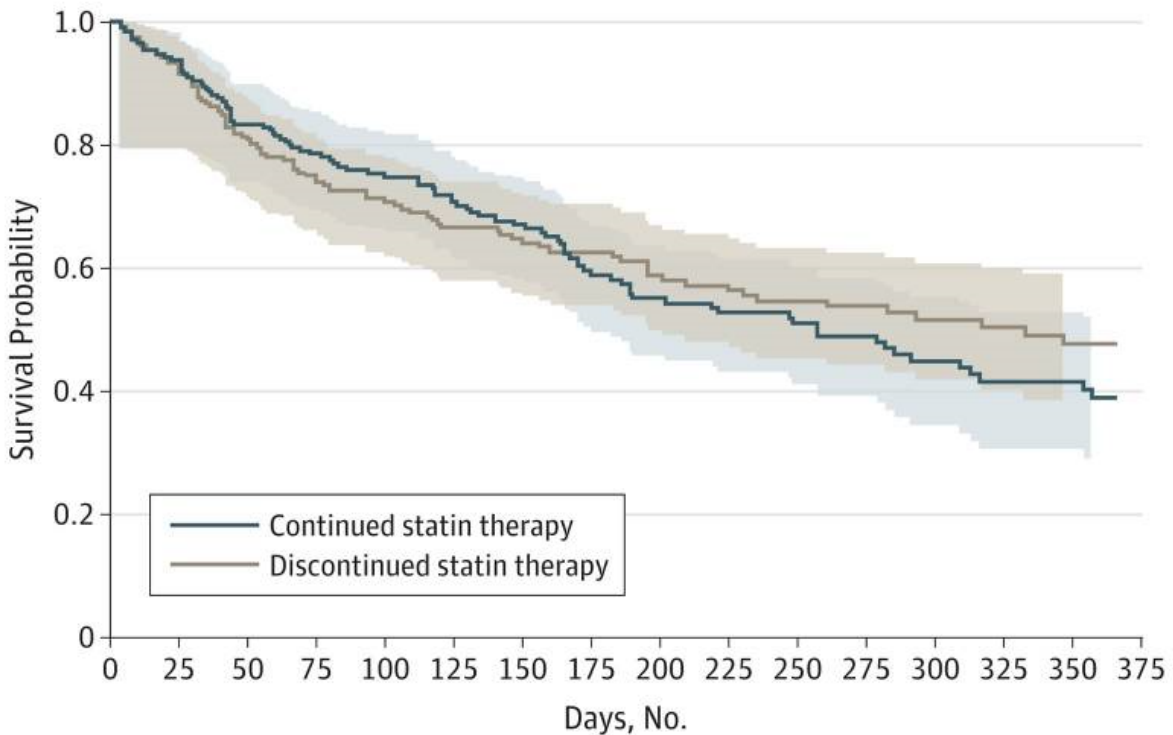
TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01415934

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- Supplemental content at jamanernalmedicine.com

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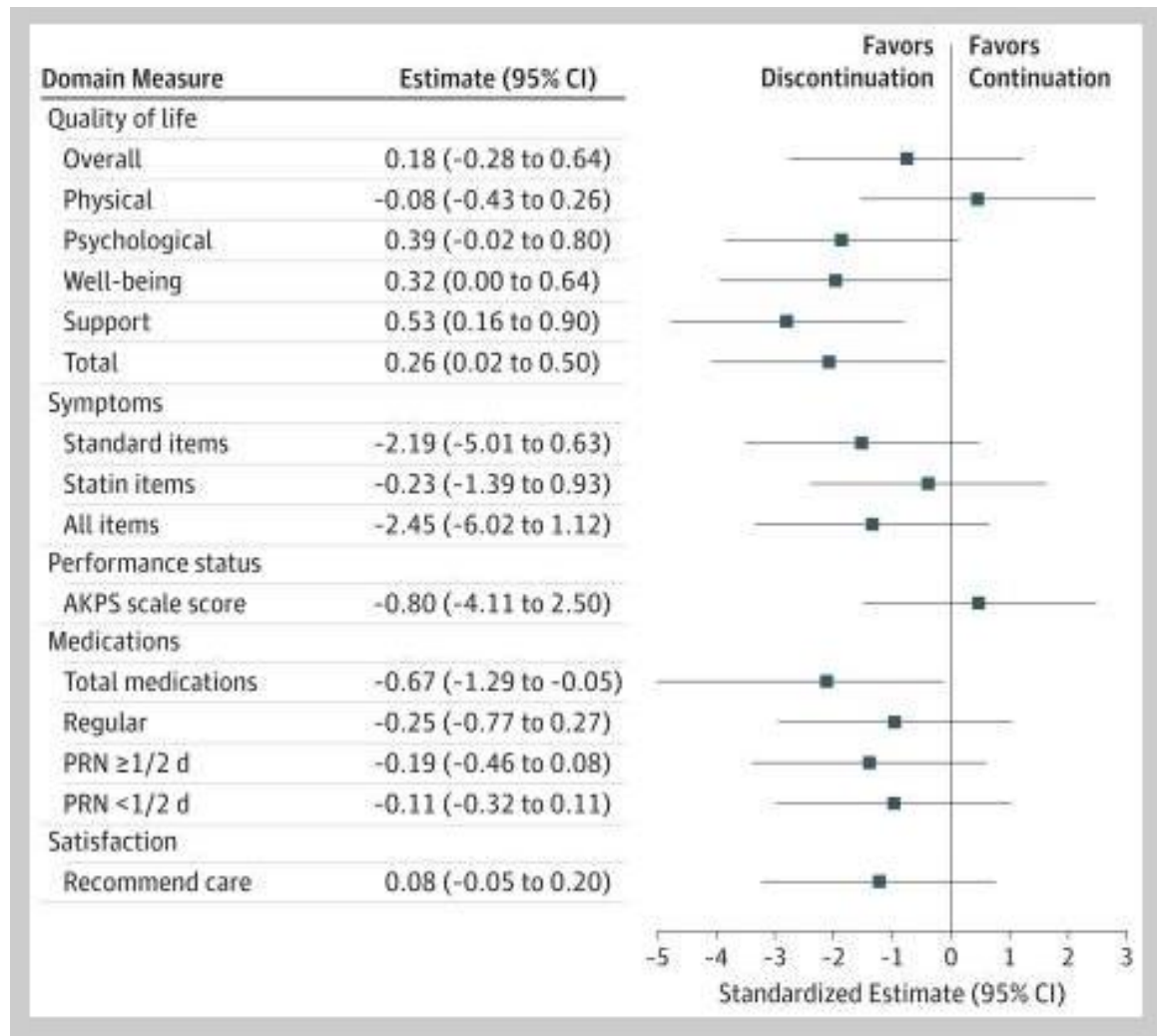
Statin in Advanced Illness (Survival Impact)



No. at risk

Continued statin therapy	192	149	105	64	47	32	21
Discontinued statin therapy	189	135	93	68	52	36	26

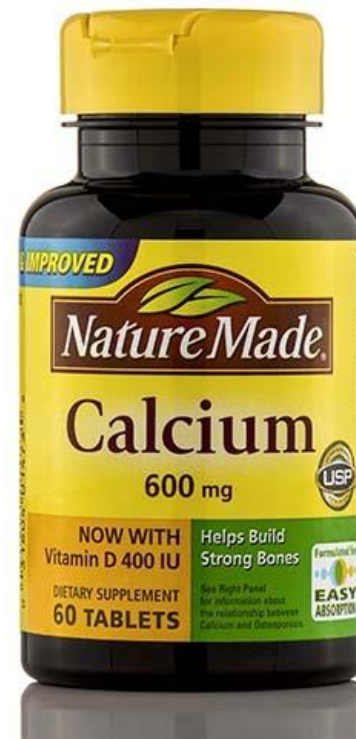
Statins in Advanced Illness: Impact on Quality of Life



7) Challenges of Calcium Supplementation in Patients with Advanced Disease

Symptoms of Hypercalcemia

- Constipation
- Fatigue
- Dyspepsia
- Depression
- Anxiety
- Cognitive decline
- Agitation
- Anorexia
- Nausea
- Polyuria



8) Success of Drug Discontinuation: Anti-hypertensives

Table 2. Success Rate of Drug Discontinuation (DD) According to Types of Drugs

Drug Group	Patients Using Drug, No.	DD Suggested, No. (% ^a)	DD Actually Performed, No. (%)	Specific Compliance, % ^b	Eventual DD Success Rate, % ^c
Antihypertensives	95 ^d	58 (61)	50 (53)	86	84
β-Blockers	26	15 (58)	11 (42)	73	67
Calcium channel blockers	22	13 (59)	11 (50)	85	85
Diuretics	11	11 (100)	10 (91)	91	91
ACE inhibitors	32	9 (28)	8 (25)	89	89
α-Blockers	8	6 (75)	2 (25)	33	33
Nitrates	5	5 (100)	5 (100)	100	100
Furosemide	18	14 (78)	13 (72)	92	79
Aspirin	24	2 (8)	2 (8)	100	100
Statins	26	18 (69)	14 (54)	78	72
Sulfonylurea	6	5 (83)	5 (83)	100	100
Metformin	11	5 (45)	3 (27)	60	60
H ₂ blockers	8	8 (100)	6 (75)	75	75
Omeprazole	18	10 (56)	9 (50)	90	90
Benzodiazepines	36 ^e	36 (100)	35 (97) ^e	97	97
SSRIs	33	13 (39)	11 (33)	85	77
Other antidepressants	12	10 (83)	9 (75)	90	90
Antipsychotics	8	3 (37)	3 (37)	100	100
Levodopa-carbidopa	10	7 (70)	5 (50)	71	71

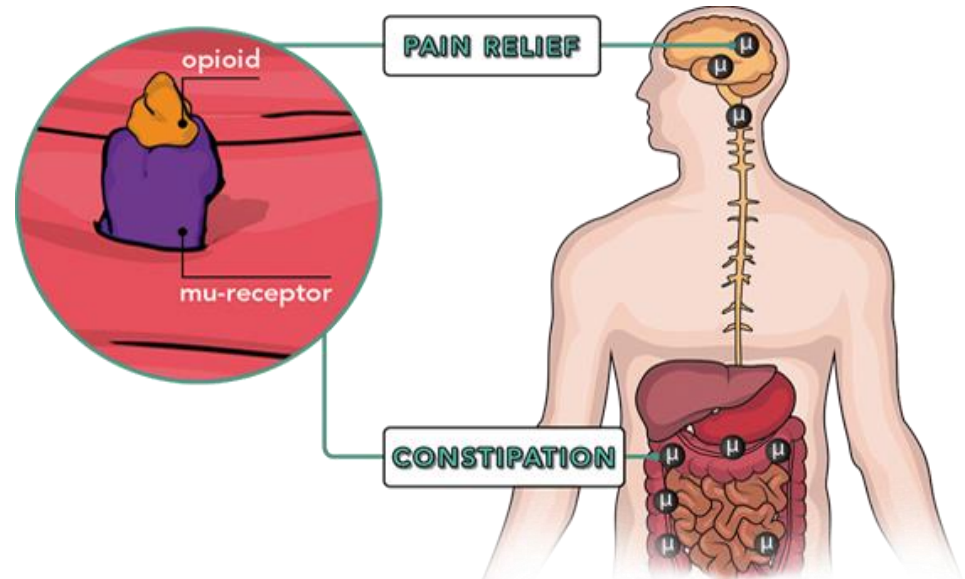
Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy. Arch Intern Med. 2010 Oct 11;170(18):1648-54.

Medications Associated with Constipation

- Opioids/tramadol
- (methadone and fentanyl are the least constipating)
- Amiodarone
- Antacids (Tums)
- Antidepressants
- Antihistamines (Benadryl)
- Calcium
- Calcium Channel Blockers (Norvasc, Diltiazem, Verapamil)
- Iron
- Zofran

9) Opiate-induced Constipation

- “the passage of small, hard feces infrequently and with difficulty”
- 10% of all people > 65
- 50% of all patients on admission to hospice
- Up to 90% of patients on opioids will experience constipation at some point!



Randomized, Double-Blind, Placebo-Controlled Trial of Oral Docusate in the Management of Constipation in Hospice Patients

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Abstract

Context. The stool softener docusate is widely used in the management of constipation in hospice patients. There is little experimental evidence to support this practice, and no randomized trials have been conducted in the hospice setting.








Objectives. To assess the efficacy of docusate in hospice patients.

Methods. This was a 10-day, prospective, randomized, double-blind, placebo-controlled trial of docusate and sennosides vs. placebo and sennosides in hospice patients in Edmonton, Alberta. Patients were included if they were age 18 years or older, able to take oral medications, did not have a gastrointestinal stoma, and had a Palliative Performance Scale score of 20% or more. The primary outcome measures were stool frequency, volume, and consistency. Secondary outcomes were patient perceptions of bowel movements (difficulty and completeness of evacuation) and bowel-related interventions.

Results. A total of 74 patients were randomized into the study (35 to the docusate group and 39 to the placebo group). There were neither significant differences between the groups in stool frequency, volume, or consistency, nor in difficulty or completeness of evacuation. On the Bristol Stool Form Scale, more patients in the placebo group had Type 4 (smooth and soft) and Type 5 (soft blobs) stool, whereas in the docusate group, more had Type 3 (sausage like) and Type 6 (mushy) stool ($P=0.01$).

Conclusion. There was no significant benefit of docusate plus sennosides compared with placebo plus sennosides in managing constipation in hospice patients. Docusate use should be considered on an individual basis. *J Pain Symptom Manage* 2013;45:2–13. © 2013 U.S. Cancer Pain Relief Committee. Published

Bristol Poop Chart

BRISTOL STOOL CHART			
	Type 1	Separate hard lumps	Very constipated
	Type 2	Lumpy and sausage like	Slightly constipated
	Type 3	A sausage shape with cracks in the surface	Normal
	Type 4	Like a smooth, soft sausage or snake	Normal
	Type 5	Soft blobs with clear-cut edges	Lacking fibre
	Type 6	Mushy consistency with ragged edges	Inflammation
	Type 7	Liquid consistency with no solid pieces	Inflammation



Lubiprostone vs Senna in postoperative orthopedic surgery patients with opioid-induced constipation: A double-blind, active-comparator trial

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Author contributions: Marciniak CM, Toledo S, Jesselson M, Bateman J and Lee J designed the research project; Marciniak

day or Senna (generic) two capsules administered daily for six days. Subjects were assessed using the patient assessment of constipation (PAC)-symptoms (PAC-SYM) and the PAC-quality of life (PAC-QOL) scales measured at baseline and Day 7; Subjects were assessed daily for secondary measures included the Bristol stool scale bowel consistency, specific bowel symptom score (Nausea, cramping, straining, completeness, abdominal pain, time per lavatory attempt, assistance needed), adverse events and rescue medications required. Function was measured using the functional independence measure (FIM) at admission and discharge; length of stay (LOS) and missed treatments due to gastrointesti-

[World J Gastroenterol.](http://www.wjgnet.com) 2014 Nov 21;20(43):16323-33

10) Pearls for Treating Depression at End-of-life

- SSRIs often have a considerable time to action in patients with significant comorbid illness
 - (median time of 6+ weeks for a 50% reduction in the symptoms in Star*D trial.)
- Mirtazapine
 - Advantages include quicker relief, appetite stimulation and reduction in insomnia
- Ritalin offers quick relief for many refractory patients but trials are mixed
- Ketamine has demonstrated very encouraging preliminary results
 - Earliest studies IV and intranasal

Mirtazapine for Treating Depression in Patients with Advanced Cancer



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Rapid response to methylphenidate as an add-on therapy to mirtazapine in the treatment of major depressive disorder in terminally ill cancer patients: A four-week, randomized, double-blinded, placebo-controlled study



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KEYWORDS

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Pharmacotherapy;
Mirtazapine;
Palliative;
Cancer

Abstract

This is a 4 week, randomized, double-blind, placebo-controlled study to examine the effects of methylphenidate as add-on therapy to mirtazapine compared to placebo for treatment of depression in terminally ill cancer patients. It involved 88 terminally ill cancer patients from University of Malaya Medical Centre, Kuala Lumpur, Malaysia. They were randomized and treated with either methylphenidate or placebo as add on to mirtazapine. The change in Montgomery-Åsberg Depression Rating Scale (MADRS) score from baseline to day 3 was analyzed by linear regression. Changes of MADRS and Clinical Global Impression-Severity Scale (CGI-S) over 28 days were analyzed using mixed model repeated measures (MMRM). Secondary analysis of MADRS response rates, defined as 50% or more reduction from baseline score. A significantly larger reduction of Montgomery-Åsberg Depression Rating Scale (MADRS) score in the methylphenidate group was observed from day 3 (B=4.14; 95% CI=1.83-6.45). Response rate (defined as 50% or more reduction from baseline MADRS score) in the methylphenidate treated

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Methylphenidate for Treating Depression in Patients with Advanced Cancer

68 *Journal of Pain and Symptom Management*

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Original Article

Effects of Methylphenidate on Fatigue and Depression: A Randomized, Double-Blind, Placebo-Controlled Trial

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Abstract

Context. Fatigue is highly prevalent in populations with advanced illness and is often associated with depressed mood. The role of psychostimulant therapy in the treatment of these conditions remains ill defined.

Objectives. To evaluate the response of fatigue and depression in patients with advanced illness to titrated doses of methylphenidate (MP) as compared with placebo.

Methods. In a randomized, double-blind, placebo-controlled trial, 30 hospice patients, both inpatients and outpatients, who had fatigue scores of at least four on a scale of zero to 10 (0 = no fatigue and 10 = worst fatigue), were randomly assigned to receive either 5 mg of MP at 8 AM and 1 PM or placebo. Doses of MP were titrated every three days according to response and adverse effects. Home care patients were monitored daily by telephone and visited by a research nurse on Study Days 0 (baseline), 3, 7, and 14. Fatigue was assessed using the Piper Fatigue Scale as the primary outcome measure and validated by the Visual Analogue Scale for Fatigue and the Edmonton Symptom Assessment Scale (ESAS) fatigue score. Subjects in inpatient facilities were interviewed or assessed by staff on an identical schedule. Depressive symptoms were assessed by the Beck Depression Inventory-II, Center for Epidemiologic Studies Depression Scale, and the ESAS depression score. Primary statistical analysis was conducted using repeated-measures multivariate analysis of the variance.

Results. Both MP- and placebo-treated groups had similar measures of fatigue at baseline. Patients taking MP were found to have significantly lower fatigue scores (Piper Fatigue Scale, Visual Analogue Scale for Fatigue, and ESAS) at Day 14 compared with baseline. The improvement in fatigue with MP treatment was dose-dependent; the mean average effective dose was 10 mg on Day 3 and 20 mg on Day 14 (dose range of 10–40 mg). Placebo-treated individuals showed no

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Comparison of Mean ESAS Scores for Placebo- and MP-Treated Groups at Baseline (Day 0) and Day 14

Variable	Placebo		MP Treatment	
	Mean ± SD			
	Day 0	Day 14	Day 0	Day 14
Fatigue	6.93 ± 2.37	6.58 ± 2.31	7.40 ± 2.03	2.69 ± 1.32
Depression	3.93 ± 3.06	3.58 ± 2.57	2.93 ± 3.12	1.92 ± 1.98
Well-Being	5.07 ± 1.77	4.82 ± 2.09	6.00 ± 2.04	3.67 ± 2.06
Anxiety	2.60 ± 2.20	3.42 ± 2.87	3.13 ± 2.33	1.69 ± 2.21
Pain	2.07 ± 1.44	1.75 ± 1.86	2.07 ± 2.15	1.08 ± 1.50
Appetite	3.13 ± 2.26	2.25 ± 2.34	4.13 ± 2.70	4.08 ± 3.40
Nausea	1.73 ± 2.81	1.67 ± 2.06	0.87 ± 0.99	1.54 ± 3.36

SD = standard deviation.
Scores: 0 = best; 10 = worst.

Interesting New Therapies!

Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. J Psychopharmacol. 2016; 30(12):1181-1197.



11) Pearls for Treating Pain at End-of-Life

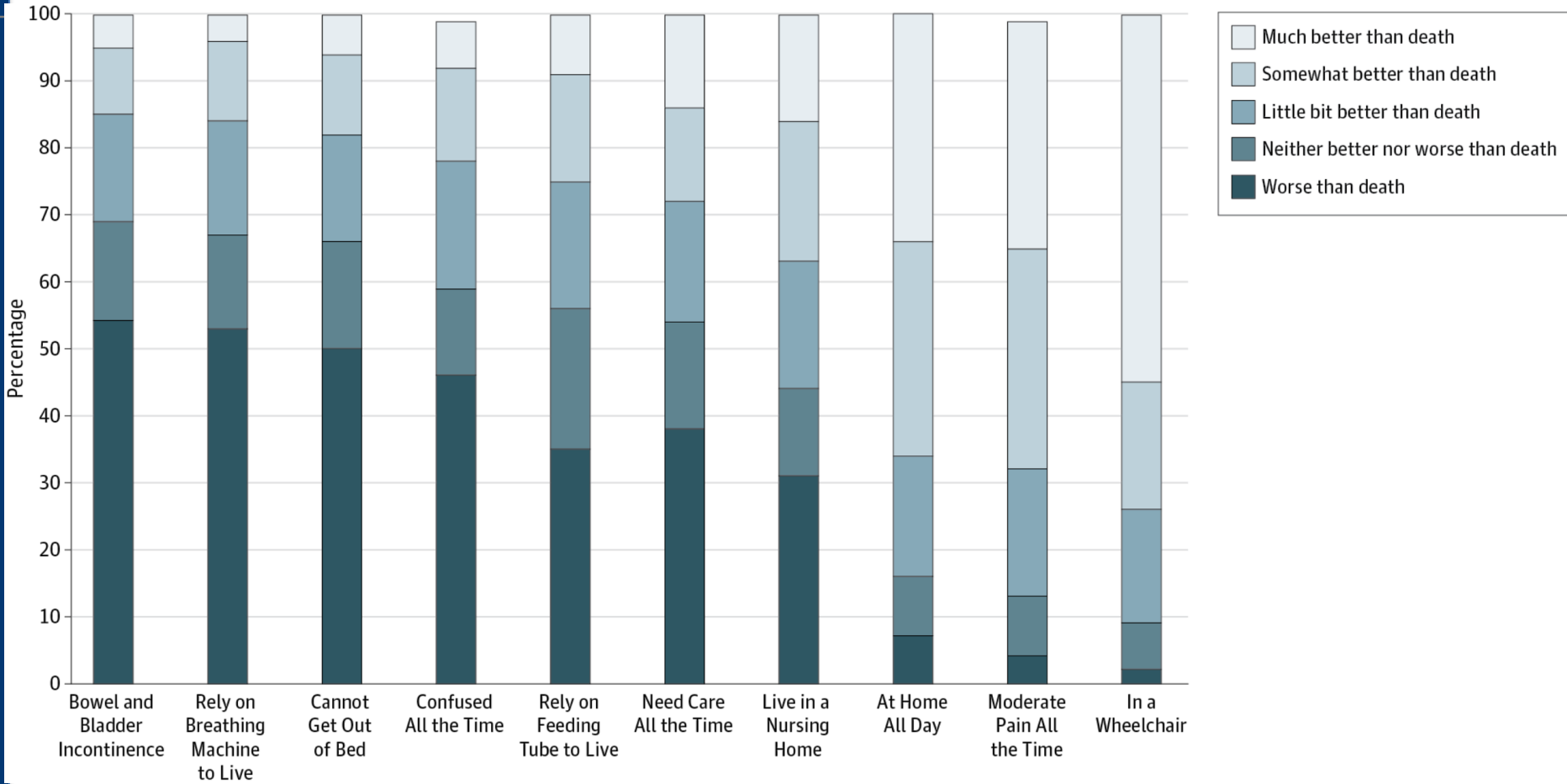
- Opiates can be titrated quickly if patients are carefully monitored
- Most typically start to schedule long-acting opioids if OME >30 mg
- Use caution in prescribing opiates in patients with renal failure
- Methadone can work wonders for patients refractory to other opioids
- If using Narcan in pt with chronic pain, dilute 0.4mg Narcan vial with 9mL of normal saline and give 1mL per minute.
- For uncomplicated painful bone metastases a single fraction of radiation can offer significant pain relief.

12) Benefits of Radiation Therapy in End-of-life

- Pain relief for uncomplicated bone metastases
 - pain relief typically starts within 2 weeks of treatment
 - partial response in 60-80% of patients at 4 weeks
 - complete relief in 30-50% of patients at 4 weeks
- Impact of early treatment of cord compression
 - Maintain ambulation and functional status
 - Maintain urinary/fecal continence and quality of life
- Some cancers respond better to radiation
 - Lymphoma, myeloma, small cell lung CA, breast CA, prostate CA, ovarian CA

[Lutz S](#), [Jones J](#), and [Chow C](#). Role of Radiation Therapy in Palliative Care of the Patient With Cancer [J Clin Oncol](#). 2014 Sep 10; 32(26): 2913–2919.

States Worse Than Death Among Hospitalized Patients With Serious Illnesses



Rubin EB, Buehler AE, Halpern SD. States Worse Than Death Among Hospitalized Patients With Serious Illnesses. JAMA Intern Med. 2016 PMID 24479808

Comparing Efficacy of Single Fraction vs Extended Courses of Radiation Therapy for Bone Metastases

- No statistically significant differences in pain control or pathologic fractures rate
- Higher increase in retreatment rate in single fraction group (20% vs 8%)
- Lower rates of toxicity in single fraction regimens
 - Appetite loss (56% vs 66%)
 - Vomiting (13 vs 23%)
 - Diarrhea (23% vs 31%)
 - Skin discoloration (14% vs 24%)

[Chow E](#), [van der Linden YM](#), [Roos D](#), [Hartsell WF](#), [Hoskin P](#), [Wu JS](#), [Brundage MD](#), [Nabid A](#), [Tissing-Tan CJ](#), [Oei B](#), [Babington S](#), [Demas WF](#), [Wilson CF](#), [Meyer RM](#), [Chen BE](#), [Wong RK](#).

Lancet Oncol. Single versus multiple fractions of repeat radiation for painful bone metastases: a randomised, controlled, non-inferiority trial.

2014 Feb;15(2):164-71.

Patient Reported Outcomes Comparing Single-fraction Vs Multi-fraction Palliative Radiotherapy

Table 5
Uncomplicated and complicated BoM PRO and pain responses for SFRT and MFRT.

Characteristic	Uncomplicated BoM			Complicated BoM		
	SFRT	MFRT	p-Value	SFRT	MFRT	p-Value
Improvement in Total score	80% (309)	83% (180)	0.41	77% (95)	84% (149)	0.12
Pain OR	75% (289)	75% (163)	0.98	71% (88)	75% (133)	0.47
Pain CR	22% (86)	21% (45)	0.65	19% (24)	33% (58)	0.01
Improvement in function	74% (213)	77% (118)	0.43	69% (62)	81% (111)	0.04
Improvement in symptom frustration	78% (264)	81% (156)	0.39	77% (85)	78% (118)	0.95

PRO = Patient Reported Outcomes; BoM = Bone Metastases; SFRT = Single Fraction Radiotherapy; MFRT = Multiple Fraction Radiotherapy; OR = Overall Response; CR = a post-RT score of zero.

Conway JL, Yurkowski E, Glazier J, et al. Comparison of patient-reported outcomes with a single versus multiple fraction palliative radiotherapy for bone metastasis in a population-based cohort. *Radiother Oncol.* 2016; 119(2):202-207.

International Variation in Practice Patterns Comparing Single-Fraction to Multi-fraction Radiotherapy

Journal of Bone Oncology 3 (2014) 96–102

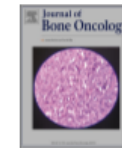


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Review Article

International patterns of practice in radiotherapy for bone metastases: A review of the literature



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ABSTRACT

Purpose: Radiation therapy is the standard treatment for symptomatic bone metastases. Several randomized control trials and meta-analyses have concluded a similar efficacy in pain relief when comparing single versus multiple fraction regimes. However, there continues to be reluctance to conform to published guidelines that recommend a single treatment for the palliation of painful bone metastases. The purpose of this literature review is to summarize international patterns of practice, and to determine if guidelines recommending single fraction treatment have been implemented in clinical care. **Methods:** A literature search was conducted in Ovid Medline, Embase, and Cochrane Central. Search words included, 'bone metastases', 'radiation therapy', 'radiotherapy', 'patterns of practice', and 'dose fractionation'. Both prospective and retrospective studies that investigated the prescription of radiotherapy to bone metastases using actual patient databases were included. Articles were excluded if they investigated hypothetical scenarios. **Results:** Six hundred and thirteen results were generated from the literature search. Twenty-six articles met the inclusion criteria. Of these, 11 were Canadian, 8 were European, 6 were American, and 1 was Australian. The use of single fraction radiotherapy (SFRT) ranged from 3% to 75%, but was generally lower in American studies. Choice of fractionation depended on a variety of factors, including patient age, prognosis, site of irradiation, and physician experience. **Conclusion:** Despite the publication of robust randomized control trials, meta-analyses, and clinical practice guidelines recommending the use of a single treatment to palliate uncomplicated bone metastasis, SFRT is internationally underutilized.

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Economic Impact of Single-fraction Versus Multi-fraction Radiotherapy

RADIATION ONCOLOGY—ORIGINAL ARTICLE

Economic evaluation of single-fraction versus multiple-fraction palliative radiotherapy for painful bone metastases in breast, lung and prostate cancer

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Abstract

Introduction: Single- and multiple-fraction external beam radiotherapy (SFX-EBRT and MFX-EBRT) are palliative treatment options for localized metastatic bone pain. MFX is the preferred choice in many developed countries. Evidence shows little difference in how effectively SFX and MFX reduce pain. However, SFX is associated with higher retreatment and (in one meta-analysis) pathological fracture rates. MFX is, however, more time-consuming and expensive. We estimated the cost-effectiveness of SFX versus MFX for metastatic bone pain in breast, prostate and lung cancer in New Zealand.

Methods: We constructed a Markov microsimulation model to estimate health gain (in quality-adjusted life-years or QALYs), health system costs (in real 2011 NZ dollars) and cost-effectiveness. The model was populated using effect estimates from randomized controlled trials and other studies, and New Zealand cancer and cost data. Disability weights from the 2010 Global Burden of Disease study were used in estimating QALYs.

Results: Across all three cancers, QALY gains were similar for SFX compared to MFX, and per patient costs were less for SFX than MFX, with a difference of NZ\$1469 (95% uncertainty interval \$1112 to \$1886) for lung cancer, \$1316 (\$810 to \$1854) for prostate cancer and \$1344 (\$855 to \$1846) for breast cancer. Accordingly, from a cost-effectiveness perspective, SFX was the preferable treatment option. Various sensitivity analyses did not overturn the clear preference for SFX.

Conclusion: For all three cancers, SFX was clearly more cost-effective than MFX. This adds to the case for desisting from offering MFX to patients with metastatic bone pain, from a cost-effectiveness angle.

Key words: bone pain; cost-effectiveness analysis; metastatic cancer; radiotherapy; single fraction.



Journal of Medical Imaging and Radiation Oncology

13) Pearls for Treating Secretions at End-of-life

- Nothing works as well as we would like
- One survey of 391 caregivers found
 - Secretions occurred in 48% of patients
 - Of those with secretions, 2/3 of families found them highly distressing
 - Female caregivers who were not prepared were at highest risk
- Mixed evidence that minimizing fluid intake reduces secretions
- Minimize deep suctioning
- Scopolamine patches can contribute to delirium while glycopyrrolate does not cross the blood barrier

Death rattle: critical review and research agenda. Support Care Cancer. 2014; 22(2):571-5.

14) Pearls for Treating Agitation at End-of-life

- Identify underlying etiology when possible
 - infections, urinary retention, hypoxia, impaction, medications, pain, electrolytes, renal failure, hepatic failure etc.
 - If reversible, mean survival 40 days compared to 17 if not reversible
- Environmental factors
 - glasses, hearing aids, etc.
- Minimize high risk medications:
 - Anticholinergics, benzodiazepines, opioids, steroids, etc.
- Recent controversy about efficacy of haloperidol / risperidone

Agitation and delirium at the end of life: "We couldn't manage him".
JAMA. 2008 Dec 24;300(24):2898-910.



THE WORLD'S BEST MEDICINE. MADE BETTER.

15) Supporting Caregivers

- 40-70% of family caregivers report clinically significant symptoms of depression
- 70% report caregiving had an impact on their employment
- One study found caregivers who reported “strain” had a 63% higher mortality rate than their non-caregiving peers



Schulz R, Beach SR. Caregiving as a risk factor for mortality: the caregiver health effects study. JAMA. 1999;282(23):2215-9.

Questions?



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