PALLIATIVE CARE RESEARCH COOPERATIVE

NATIONAL Palliative Care RESEARCH CENTER

The Palliative Care Research Cooperative and The National Palliative Care Research Center

Comparing Apples, Oranges…and Bacon Bits:
Systematic Review and Meta-Analysis in Palliative Care

a webinar in the Investigator Development series

January 29, 2018

Host: Dio Kavalieratos, PhD
Assistant Professor of Medicine
Director of Implementation Research, UPMC Palliative & Supportive Institute
Associate Director of Palliative Care Research, Section of Palliative Care and Medical Ethics
Division of General Internal Medicine, University of Pittsburgh
DioK@pitt.edu

Overview

- What is “evidence synthesis?”
  - Systematic review vs meta-analysis
  - Why is evidence synthesis important?
- Three key questions to consider in evidence synthesis
  - WHAT kinds of studies were included?
  - HOW did authors critically evaluate study bias/quality?
  - WHO: Are the interventions and outcomes homogeneous?

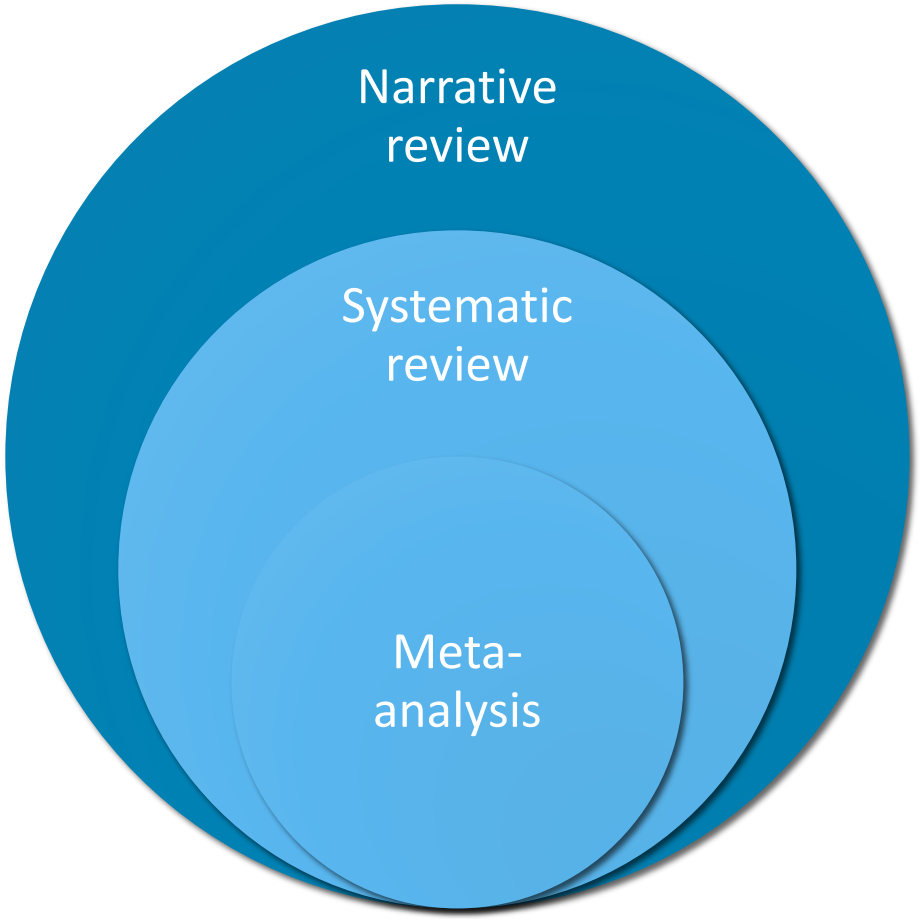
Association Between Palliative Care and Patient and Caregiver Outcomes

A Systematic Review and Meta-analysis

Dio Kavalieratos, PhD; Jennifer Corbelli, MD, MS; Di Zhang, BS; J. Nicholas Dionne-Odom, PhD, RN; Natalie C. Ernecoff, MPH; Janel Hanmer, MD, PhD; Zachariah P. Hoydich, BS; Dara Z. Ikejiani; Michele Klein-Fedyshin, MSLS, BSN, RN, BA; Camilla Zimmermann, MD, PhD; Sally C. Morton, PhD; Robert M. Arnold, MD; Lucas Heller, MD; Yael Schenker, MD, MAS

What are the challenges in synthesizing the palliative care evidence base?

Types of evidence syntheses



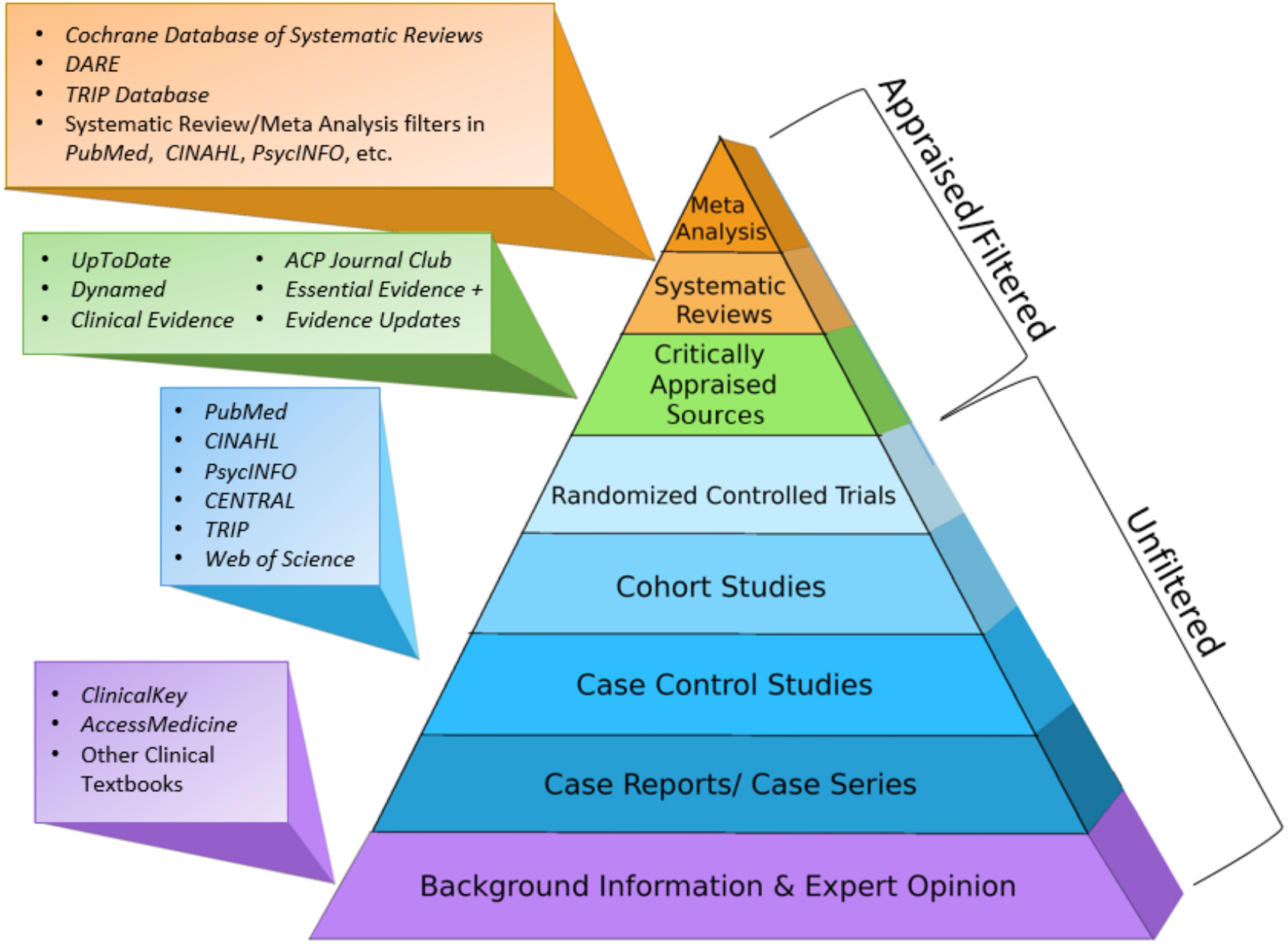
Broad summaries
Not replicable
Inclusion/exclusion unclear

Focused, comprehensive, structured
Methods clearly specified

Statistical method of pooling results from multiple studies

W

- Hig
- Pro
  - G
    -


Cochrane Database of Systematic Reviews
DARE
TRIP Database
Systematic Review/Meta Analysis filters in PubMed, CINAHL, PsycINFO, etc.
UpToDate
Dynamed
Clinical Evidence
ACP Journal Club
Essential Evidence +
Evidence Updates
PubMed
CINAHL
PsycINFO
CENTRAL
TRIP
Web of Science
ClinicalKey
AccessMedicine
Other Clinical Textbooks
Meta Analysis
Systematic Reviews
Critically Appraised Sources
Randomized Controlled Trials
Cohort Studies
Case Control Studies
Case Reports/ Case Series
Background Information & Expert Opinion
Appraised/Filtered
Unfiltered

What is the evidence for palliative care?

REVIEW

CLINICIAN'S CORNER

Effectiveness of Specialized Palliative Care
A Systematic Review

Camilla Zimmermann, MD, MSc
Rachel Riechelmann, MD
Monika Krzyzanowska, MD, MPH
Gary Rodin, MD
Ian Tannock, MD, PhD

Context Specialized palliative care teams are increasingly providing care for the terminally ill. However, the impact of such teams on quality of life, satisfaction with care, and economic cost has not been examined systematically using detailed criteria for study quality.

Objective To systematically review the evidence for effectiveness of specialized palliative care.

Data Sources We performed a keyword search of the following databases from their inception to January 2008: MEDLINE, Ovid Healthstar, CINAHL, EMBASE, and the Cochrane Central Register of Controlled Trials.

Study Selection We included all randomized controlled trials in which specialized palliative care was the intervention and for which outcomes included quality of life, satisfaction with care, or economic cost.

Data Extraction Data on population, intervention, outcome, methods, and methodological quality were extracted by 2 investigators using standardized criteria.

Results Of 396 reports of randomized controlled trials, 22 met our inclusion criteria. There was most consistent evidence for effectiveness of specialized palliative care in improvement of family satisfaction with care (7 of 10 studies favored the intervention). Only 4 of 13 studies assessing quality of life and 1 of 14 assessing symptoms showed a significant benefit of the intervention; however, most studies lacked statistical power to report conclusive results, and quality-of-life measures were not specific for terminally ill patients. There was evidence of significant cost savings of specialized palliative care in only 1 of the 7 studies that assessed this outcome. Methodological limitations were identified in all trials, including contamination of the control group, failure to account for clustering in cluster randomization studies, and substantial problems with recruitment, attrition, and adherence.

Conclusions The evidence for benefit from specialized palliative care is sparse and limited by methodological shortcomings. Carefully planned trials, using a standardized palliative care intervention and measures constructed specifically for this population, are needed.

JAMA. 2008;299(14):1698-1709

THERE IS INCREASING AWARENESS of the suffering of patients with terminal illnesses, including pain, other physical symptoms, and psychosocial distress, which may arise many months before the patient's death.[1-3] Specialized palliative care services have proliferated worldwide, initially focusing on terminal cancer care,[4] but increasingly expanding to include patients with cancer and other terminal diseases who are at earlier stages of their disease trajectory.[5] The objective of such services is to improve the symptom control and quality of life of patients with terminal illnesses and to coordinate care of the patient and support for the family.[6] With the increasing development of such services, it is important to determine their effectiveness compared with other models of care.

There have been previous reviews

ORIGINAL CONTRIBUTION

Effects of a Palliative Care Intervention on Clinical Outcomes in Patients With Advanced Cancer
The Project ENABLE II Randomized Controlled Trial

Marie Bakitas, DNSc, APRN

Context There are few randomized controlled trials on the effectiveness of palli-

ORIGINAL ARTICLE

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

Jennifer S. Temel, M.D., Joseph A. Greer, Ph.D., Alona Muzikansky, M.A., Emily R. Gallagher, R.N., Sonal Admane, M.B., B.S., M.P.H., Vicki A. Jackson, M.D., M.P.H., Constance M. Dahlin, A.P.N., Craig D. Blinderman, M.D., Juliet Jacobsen, M.D., William F. Pirl, M.D., M.P.H.,

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Early Versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial

Marie A. Bakitas, Tor D. Tosteson, Zhigang Li, Kathleen D. Lyons, Jay G. Hull, Zhongze Li, J. Nicholas Dionne-Odom, Jennifer Frost, Konstantin H. Dragnev, Mark T. Hegel, Andres Azuero, and Tim A. Ahles

See accompanying editorial doi: 10.1200/JCO.2014.60.5386 and article doi: 10.1200/JCO.2014.58.7824

ABSTRACT

Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial

Camilla Zimmermann, Nadia Swami, Monika Krzyzanowska, Breffni Hannon, Natasha Leighl, Amit Oza, Gary Rodin, Ian Tannock, Allan Donner, Christopher Lo

Summary

Background Patients with advanced cancer have reduced quality of life, which tends

An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial

Irene J Higginson, Claudia Bausewein, Charles C Reilly, Wei Gao, Marjolein Gysels, Mendwas Dzingina, Paul McCrone, Sara Booth, ohn Moxham

reathlessness is a common and distressing symptom, which increases in many diseases as they progress to manage. We assessed the effectiveness of early palliative care integrated with respiratory services for

Lancet Respir Med 2014; 2: 979-87

Original Investigation

Emergency Department–Initiated Palliative Care in Advanced Cancer
A Randomized Clinical Trial

Corita R. Grudzen, MD, MSHS; Lynne D. Richardson, MD; Pauline N. Johnson, BS; Ming Hu, PhD; Binhuan Wang, PhD; Joanna M. Ortiz, BA; Emmett A. Kistler, MD; Angela Chen, MD; R. Sean Morrison, MD

Why conduct evidence synthesis?

- Highest level of evidence
- Provides a succinct and digestible summary of evidence
  - Great in disciplines with multiple sources of evidence
    - ”Palliative care”
      - By setting
      - By population
      - By modality
      - By specialization
      - By outcome
- Highly influential for policy and practice change; encouraged by funders
- Great tool for early career investigators

Three key questions to consider

- **WHAT kinds of studies were included?**
- HOW did authors critically evaluate study bias/quality?
- WHO: Are the interventions and outcomes homogeneous?

What is the evidence for palliative care?

REVIEW CLINICIAN'S CORNER

Effectiveness of Specialized Palliative Care
A Systematic Review

Camilla Zimmermann, MD, MSc
Rachel Riechelmann, MD
Monika Krzyzanowska, MD, MPH
Gary Rodin, MD
Ian Tannock, MD, PhD

Context Specialized palliative care teams are increasingly providing care for the terminally ill. However, the impact of such teams on quality of life, satisfaction with care, and economic cost has not been examined systematically using detailed criteria for study quality.

Objective To systematically review the evidence for effectiveness of specialized palliative care.

Data Sources We performed a keyword search of the following databases from their inception to January 2008: MEDLINE, Ovid Healthstar, CINAHL, EMBASE, and the Cochrane Central Register of Controlled Trials.

Study Selection We included all randomized controlled trials in which specialized palliative care was the intervention and for which outcomes included quality of life, satisfaction with care, or economic cost.

Data Extraction Data on population, intervention, outcome, methods, and methodological quality were extracted by 2 investigators using standardized criteria.

Results Of 396 reports of randomized controlled trials, 22 met our inclusion criteria. There was most consistent evidence for effectiveness of specialized palliative care in improvement of family satisfaction with care (7 of 10 studies favored the intervention). Only 4 of 13 studies assessing quality of life and 1 of 14 assessing symptoms showed a significant benefit of the intervention; however, most studies lacked statistical power to report conclusive results, and quality-of-life measures were not specific for terminally ill patients. There was evidence of significant cost savings of specialized palliative care in only 1 of the 7 studies that assessed this outcome. Methodological limitations were identified in all trials, including contamination of the control group, failure to account for clustering in cluster randomization studies, and substantial problems with recruitment, attrition, and adherence.

Conclusions The evidence for benefit from specialized palliative care is sparse and limited by methodological shortcomings. Carefully planned trials, using a standardized palliative care intervention and measures constructed specifically for this population, are needed.

THERE IS INCREASING AWARENESS of the suffering of patients with terminal illnesses, including pain, other physical symptoms, and psychosocial distress, which may arise many months before the patient's death.[1-3] Specialized palliative care services have proliferated worldwide, initially focusing on terminal cancer care,[4] but increasingly expanding to include patients with cancer and other terminal diseases who are at earlier stages of their disease trajectory.[5] The objective of such services is to improve the symptom control and quality of life of patients with terminal illnesses and to coordinate care of the patient and support for the family.[6] With the increasing development of such services, it is important to determine their effectiveness compared with other models of care.

There have been previous reviews

JAMA. 2008;299(14):1698-1709 www.jama.com

ORIGINAL CONTRIBUTION

Effects of a Palliative Care Intervention on Clinical Outcomes in Patients With Advanced Cancer
The Project ENABLE II Randomized Controlled Trial

Marie Bakitas, DNSc, APRN

Context There are few randomized controlled trials on the effectiveness of palli-

ORIGINAL ARTICLE

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

Jennifer S. Temel, M.D., Joseph A. Greer, Ph.D., Alona Muzikansky, M.A., Emily R. Gallagher, R.N., Sonal Admane, M.B., B.S., M.P.H., Vicki A. Jackson, M.D., M.P.H., Constance M. Dahlin, A.P.N., Craig D. Blinderman, M.D., Juliet Jacobsen, M.D., William F. Pirl, M.D., M.P.H.,

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Early Versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial

Marie A. Bakitas, Tor D. Tosteson, Zhigang Li, Kathleen D. Lyons, Jay G. Hull, Zhongze Li, J. Nicholas Dionne-Odom, Jennifer Frost, Konstantin H. Dragnev, Mark T. Hegel, Andres Azuero, and Tim A. Ahles

See accompanying editorial doi: 10.1200/JCO.2014.60.5386 and article doi: 10.1200/JCO.2014.58.7824

ABSTRACT

Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial

Camilla Zimmermann, Nadia Swami, Monika Krzyzanowska, Breffni Hannon, Natasha Leighl, Amit Oza, Gary Rodin, Ian Tannock, Allan Donner, Christopher Lo

Summary
Background Patients with advanced cancer have reduced quality of life, which tends

An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial

Irene J Higginson, Claudia Bausewein, Charles C Reilly, Wei Gao, Marjolein Gysels, Mendwas Dzingina, Paul McCrone, Sara Booth, ohn Moxham

reathlessness is a common and distressing symptom, which increases in many diseases as they progress to manage. We assessed the effectiveness of early palliative care integrated with respiratory services for

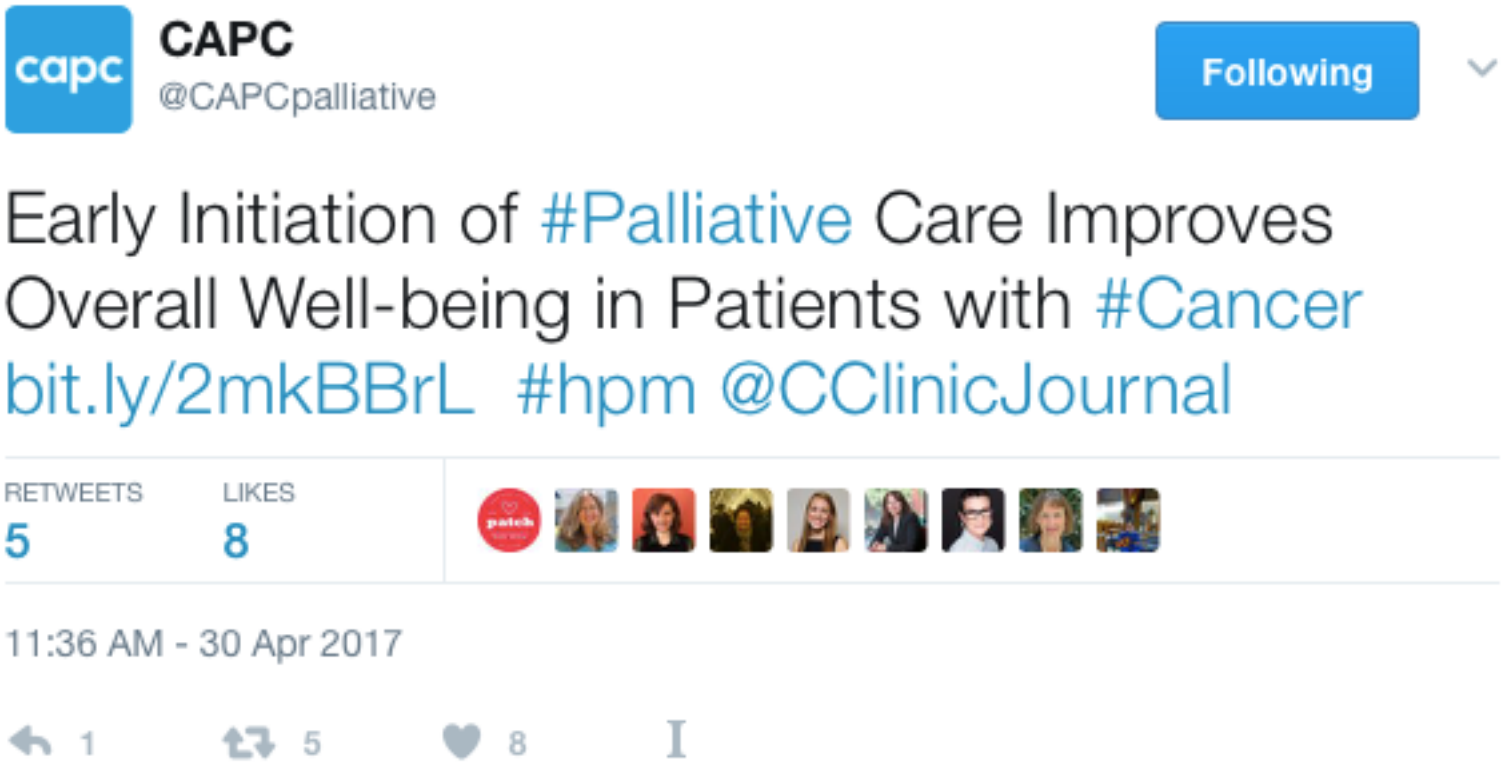
Lancet Respir Med 2014; 2: 979-87

Original Investigation

Emergency Department–Initiated Palliative Care in Advanced Cancer
A Randomized Clinical Trial

Corita R. Grudzen, MD, MSHS; Lynne D. Richardson, MD; Pauline N. Johnson, BS; Ming Hu, PhD; Binhuan Wang, PhD; Joanna M. Ortiz, BA; Emmett A. Kistler, MD; Angela Chen, MD; R. Sean Morrison, MD

What is “palliative care?”



What is “palliative care?”

- WHO
  - “Palliative care is an **approach** that **improves the quality of life** of patients and their families facing the problem associated with life-threatening illness, through the **prevention and relief of suffering** by means of early identification and impeccable assessment and treatment of **pain** and **other problems, physical, psychosocial and spiritual**.”
- CAPC
  - “Palliative care, **and the medical sub-specialty** of palliative medicine, is **specialized medical care** for people living with serious illness. It focuses on providing relief from the symptoms and stress of a serious illness. The goal is to improve quality of life for both the patient and the family.
  - Palliative care is provided **by a team** of palliative care doctors, nurses, social workers and others who work together with a patient’s other doctors to provide an **extra layer of support**. It is appropriate at any age and at any stage in a serious illness and can be provided along with curative treatment.”
- What is the conceptual framework/model for palliative care?

JAMA @JAMA_current Jul 6, 2016

No need for routine #palliativecare meetings for families of pts w chronic #criticalillness ja.ma/28Z6xnp

Alex K. Smith
@AlexSmithMD

Re-phrase: No need for routine "fast food style" #palliativecare meetings for families of pts w chronic #criticalillness @JAMA_current #hpm

3:44 PM - Jul 6, 2016

7 6

WHAT kinds of studies were included?

Do the authors provide information needed to recreate review?

- A HQ review should specify ***explicit inclusion/exclusion criteria***
- Key constructs must be ***defined*** in a ***tangible*** way
  - What is a "Palliative care intervention?"
- ***Search string(s)*** should be provided
  - Are there obvious gaps in the search terms?

PubMed/MEDLINE Search strategy

((((((((("Palliative Care"[Mesh] OR "Terminal Care"[Mesh] OR "Terminally Ill"[Mesh] OR "Hospices"[Mesh] OR "Hospice Care"[Mesh] OR "Hospice and Palliative Care Nursing"[Mesh] OR palliat* OR "End of life" OR EOL[tiab] OR "terminal care" OR "terminal illness" OR "terminally ill" OR "Terminal phase" OR "terminal stage" OR hospice*[tiab] OR hospice*[ot] OR "Stage IV cancer" OR "Life-limiting"[tiab] OR "Actively dying" OR "terminal stage" OR "limited survival" OR terminal patient* OR "Advance Care Planning"[Mesh] OR "Advance Care Planning"[ot] OR "Advance care planning"[tiab] OR "life-threatening illness" OR life-threatening diagnos* OR "Bereavement"[Majr] OR bereavement[ot] OR bereave*[title])) OR ((((("Caregivers"[Mesh]) OR "supportive care")) AND ("life-threatening illness" OR "life-threatening diagnoses" OR "progressive lung cancer" OR "Last year of life" OR "advanced illness" OR "advanced cancer" OR "advanced cancer"[ot] OR "advanced disease" OR "advanced lung cancer" OR "advanced dementia" OR "advanced transitional cell carcinoma" OR "advanced stages" OR "advanced heart" OR "limited survival"[tiab] OR Inoperable OR Incurable OR unresectable))) OR

Inclusion Criteria	Exclusion Criteria
☐ Sample: Life-limiting illness (defined by classifications of disease severity, such as tumor stage or New York Heart Association class) ☐ ~~Sample: Ages 18 and older~~ ☐ Intervention: Self-described as "palliative care" and/or comprises at least two domains of palliative care, as defined by the National Consensus Project for Quality Palliative Care[1] ☐ Study design: randomization ☐ Comparators: usual care, enhanced usual care, attention control ☐ Outcomes: study reports on at least one of pre-specified review outcomes (i.e., patient quality of life, symptom burden, mood, advance care planning, survival, resource utilization, satisfaction with care, healthcare expenditures, site of death)	☐ Sample: Indication for palliative care is not related to life-limiting illness (e.g., chronic, non-malignant pain) ☐ Intervention: single-focus intervention (e.g., advance care planning only, opioid therapy only), or study does not otherwise meet our definition of "palliative care" based on National Consensus Project for Quality Palliative Care[1] ☐ Intervention: patient is not the target of intervention ☐ Intervention: caregiver is the exclusive or primary target of intervention ☐ Study design: non-randomized

PubMed Inception to June 2016

1. "Heart failure"[Mesh] OR "heart failure"[tiab]
2. "Palliative Care"[Mesh] OR "Hospice Care"[Mesh] OR "Hospices"[Mesh] OR palliat*[tiab] OR hospice*[tiab]
3. #1 AND #2

Diop M, et al. *J Palliat Med* 2017.

Three key questions to consider

- WHAT kinds of studies were included?
- **HOW did authors critically evaluate study bias/quality?**
- WHO: Are the interventions and outcomes homogeneous?

HOW was study quality evaluated?

Strength of evidence should be based on quality, not quantity, of studies.

- Bias: Factors that +/- lead to “systematic deviations from underlying truth”
  - “Systematic” implies that bias is predictable; not random error or chance
- Cochrane Risk of Bias Tool is the gold standard for evaluating risk bias
  - ***Risk of bias does not confirm the presence of bias***
- Palliative care trials will always have some bias, but can still be high-quality
  - What are some examples of unavoidable risk of bias in palliative care?

Katherine Sleeman
@kesleeman

Follow

Interesting - answer is survival was not specified a priori as outcome of interest in Temel trial protocol. Thanks 4 email @diokavalieratos!

> **Katherine Sleeman** @kesleeman
> Systematic review on effectiveness of palliative care. Why is Temel RCT 'high bias' for survival but not for PROMs? jamanetwork.com/journals/jama/…

9:58 AM - 17 Jan 2017

Example Risk of Bias table

Entry	Judgement	Description
Adequate sequence generation?	Yes.	Quote: "patients were randomly allocated." Comment: Probably done, since earlier reports from the same investigators clearly describe use of random sequences (Cartwright 1980).
Allocation concealment?	No.	Quote: "...using a table of random numbers." Comment: Probably not done.
Blinding? (Patient-reported outcomes)	Yes.	Quote: "double blind, double dummy"; "High and low dose tablets or capsules were indistinguishable in all aspects of their outward appearance. For each drug an identically matched placebo was available (the success of blinding was evaluated by examining the drugs before distribution)." Comment: Probably done.
Blinding? (Mortality)	Yes.	Obtained from medical records; review authors do not believe this will introduce bias.
Incomplete outcome data addressed? (Short-term outcomes (2-6 wks))	No.	4 weeks: 17/110 missing from intervention group (9 due to 'lack of efficacy'); 7/113 missing from control group (2 due to 'lack of efficacy').
Incomplete outcome data addressed? (Longer-term outcomes (>6 wks))	No.	12 weeks: 31/110 missing from intervention group; 18/113 missing from control group. Reasons differ across groups.
Free of selective reporting?	No.	Three rating scales for cognition listed in Methods, but only one reported.
Free of other bias?	No.	Trial stopped early due to apparent benefit.

Box. Quality Criteria[a]

Participants

Reported

1. Clear description of inclusion and exclusion criteria[7,17,18]

Adequate

2. Comprehensive strategy for identification of potential cases[12]
3. Patient recruitment rate >70%[12]
4. Evaluation of nonparticipants to judge generalizability[12]

Objectives and Outcome Measures

Reported

5. Specific objectives and hypotheses[17,18]
6. Clearly defined primary and secondary outcome measure(s)[17,18]

Adequate

7. Use of validated outcome measures[12]
8. Blinding to group assignment of those assessing outcome measures[7,16]

Baseline Measurement and Homogeneity

Reported

9. Baseline demographics and clinical characteristics of each group prior to intervention[12,18]
10. Baseline outcome measures of each group prior to the intervention[16]

Adequate

11. No significant differences present across study groups[7,16]

Randomization and Concealment of Allocation

Reported

12. Study design and method of randomization, including details of any restriction (eg, blocking, stratification, matching)[7,12,18]

Adequate

13. Method to generate the randomization sequence explicitly described and adequate[16]

14a. Unit of allocation was by institution, team, or professional, and the number of clusters was adequate (cluster randomization only)[19-21]

14b. Unit of allocation was by patient and a centralized randomization scheme was implemented by calling a central number, an on-site computer system, or sealed opaque envelopes (individual randomization only)[16]

Sample Size and Attrition

Reported

15. How sample size was determined and, when applicable, explanation of interim analyses[17,18]
16. Flow of participants through each stage[17,18]

Adequate

17. Intended sample size attained at baseline and based on an adequate sample size calculation[12]
18. Outcome measures obtained for 90% to 100% of participants ("yes") or 70% to 89% ("partial") randomized (stated explicitly)[7,12,16]

Intervention, Control, and Protection Against Contamination

Reported

19. Precise details of the intervention and how and when it was administered[7,12,17,18]
20. Precise details of the control (contrast between intervention and control clearly defined)[12]

Adequate

21. It is unlikely that control patients received the study intervention or a similar intervention[7,12,16]
22. It is documented that intervention patients actually received the intervention[12]

Analyses

Reported

23. Statistical methods used to compare groups for primary and secondary outcomes and for subgroup analyses, if relevant[17,18]
24. For each primary and secondary outcome, a summary of results for each group and estimated effect size and precision (eg, *P* value or 95% confidence interval)[18]

Adequate

25. Analysis by "intention to treat" (analysis is performed on groups initially produced by the randomization process) and, in cluster trials, accounting for between-cluster variation[18,20,22]

[a]Each of the 25 items is scored 4 (complete marks), 2 (partial marks), or 0.

Zimmermann et al. JAMA 2008

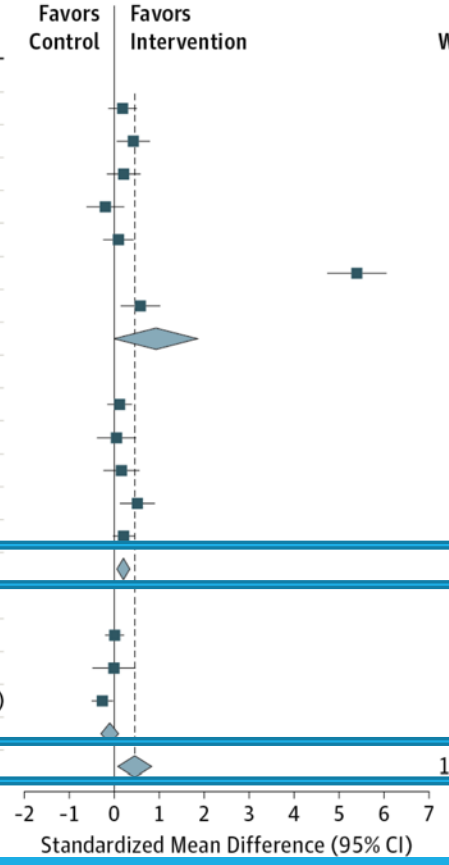
Three key questions to consider

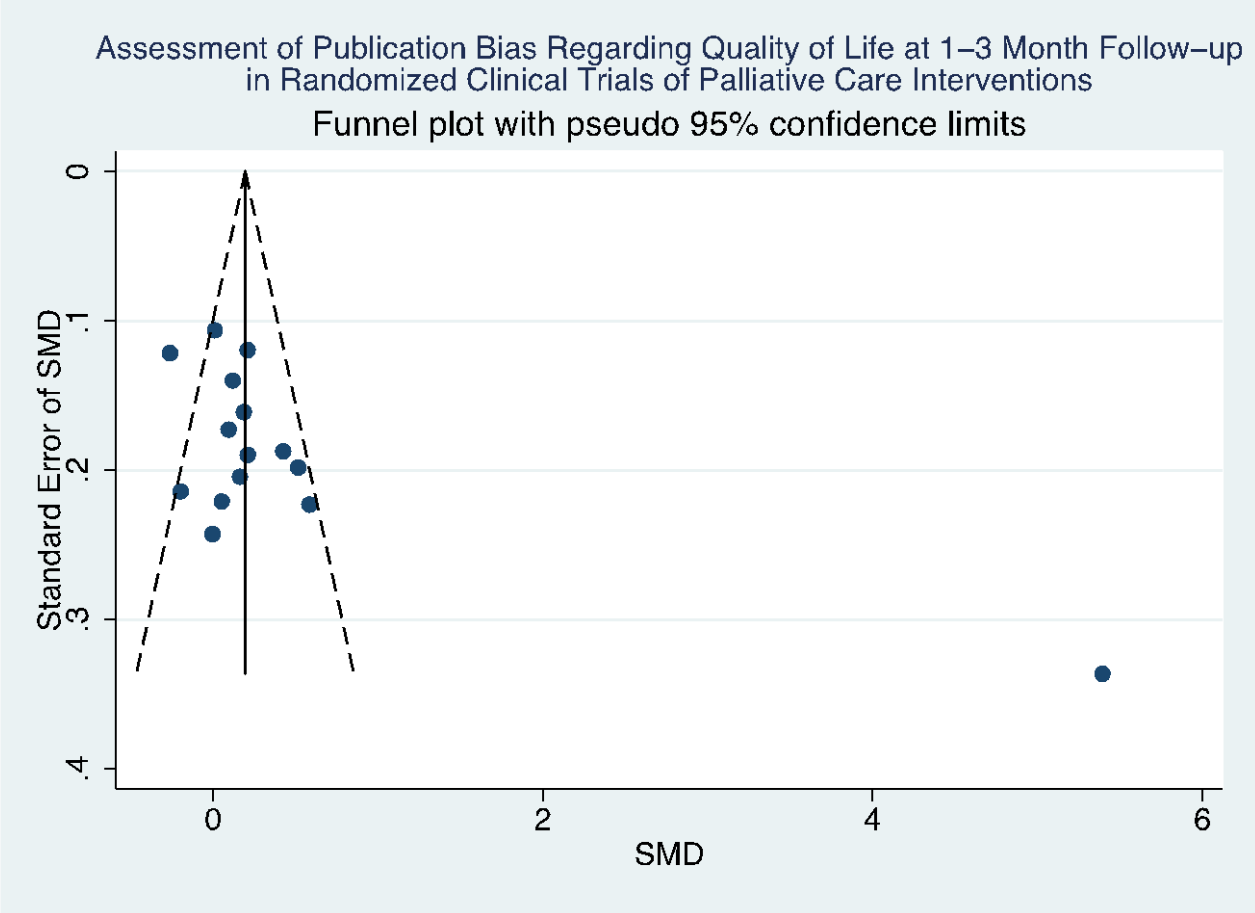
- WHAT kinds of studies were included?
- HOW did authors critically evaluate study bias/quality?
- **WHO: Are the interventions and outcomes homogeneous?**

WHO: Study heterogeneity

Are the included studies and their results consistent?

Source	No. of Patients: Intervention	Control	Setting	Instrument	Disease	Standardized Mean Difference (95% CI)	Weight, %
High risk of bias							
Bakitas et al,[20] 2015	72	83	Home	FACIT-Pal	Cancer[a]	0.19 (-0.13 to 0.50)	6.81
Clark et al,[35] 2013	54	63	Ambulatory	FACT-G	Cancer[b]	0.42 (0.06 to 0.79)	6.70
Given et al,[54] 2002	53	59	Home	SF-36	Cancer[c]	0.21 (-0.16 to 0.58)	6.69
McCorkle et al,[51] 2015	36	56	Ambulatory	FACT-G	Cancer[d]	-0.20 (-0.62 to 0.22)	6.57
Northouse et al,[32] 2005	69	65	Ambulatory	SF-36	Cancer[e]	0.09 (-0.25 to 0.43)	6.77
Sidebottom et al,[9] 2015	79	88	Hospital	MLHFQ	Heart failure	5.39 (4.74 to 6.05)	5.87
Wong et al,[10] 2016	43	41	Home	MQOL-HK	Heart failure	0.58 (0.15 to 1.02)	6.53
Subtotal (I^2 = 97.4%, P = .000)						0.93 (-0.00 to 1.85)	45.94
Low risk of bias							
Bakitas et al,[57] 2009	108	97	Home	FACIT-Pal	Cancer[f]	0.12 (-0.16 to 0.39)	6.90
Higginson et al,[12] 2014	42	40	Ambulatory	EQ5D	Mixed[g]	0.05 (-0.38 to 0.49)	6.54
Rummans et al,[59] 2006	47	49	Ambulatory	Spitzer	Cancer[d]	0.16 (-0.24 to 0.56)	6.62
Temel et al,[60] 2010	60	47	Ambulatory	FACT-L TOI	Cancer[h]	0.52 (0.13 to 0.90)	6.65
Zimmermann et al,[8] 2014	140	141	Ambulatory	FACIT-Sp	Cancer[i]	0.21 (-0.03 to 0.44)	6.96
Subtotal (I^2 = 0.0%, P = .500)						0.20 (0.06 to 0.34)	33.67
Unclear risk of bias							
Bekelman et al,[13] 2015	172	180	Home	KCCQ	Heart failure	0.01 (-0.20 to 0.22)	7.00
Grudzen et al,[11] 2016	39	30	Hospital	FACT-G	Cancer[j]	-0.01 (-0.48 to 0.47)	6.42
Northouse et al,[31] 2013	198	104	Ambulatory	FACT-G	Cancer[k]	-0.26 (-0.50 to -0.02)	6.96
Subtotal (I^2 = 33.3%, P = .223)						-0.10 (-0.30 to 0.09)	20.39
Overall (I^2 = 94.8%, P <.001)						0.46 (0.08 to 0.83)	100.00





Note: Egger's test bias estimate (SE): 8.25 (3.39), P=0.03.
Legend: Dotted lines indicate pseudo 95% confidence intervals around the overall summary estimate.
Abbreviation: SMD, standardized mean difference.

Limitations in the PC evidence base

- Of 43 trials, 12% (n=5) deemed at low risk of bias
- Heterogeneity of outcome assessment
- Inadequately defined interventions

Three key questions to consider

- WHAT kinds of studies were included?
- HOW did authors critically evaluate study bias/quality?
- WHO: Are the interventions and outcomes homogeneous?

Summary

- The scope of a review should be defined by its intent
  - Palliative care: philosophy or sub-specialty?
  - What is a “palliative care” intervention?
- Clinical practice should be guided by quality, not quantity, of evidence
  - What are mutable vs. immutable sources of bias in palliative care research?
  - How conservative should we be when discussing the impact of palliative care?
- Consistency of evidence lends confidence to our conclusions
  - Is it surprising that we see disparate findings across some palliative outcomes?

Questions?

diok@pitt.edu