

Early Palliative Care Trials: From Research to Practice

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WHO definition of palliative care

- “an approach that improves the **quality of life** of patients and their families...

...by means of **early identification** and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.”

WHO, 2002

Effectiveness of Specialized Palliative Care: A Systematic Review

Camilla Zimmermann, Rachel Froehelmann, Monika Krzyzanowska, et al.
JGIM. 2008;23(6):141-148. doi:10.1001/jama.299.14.1408
<http://jama.ama-assn.org/cgi/content/full/299/14/1408>

- 22 RCTs, 19 including patients with cancer
- Many were underpowered
- Strong evidence for family satisfaction with care
- Challenges with recruitment, attrition, and co-intervention
- 4/13 studies assessing QOL had significant results
- None specifically assessed early palliative care in patients with cancer

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

Objective: To determine the effect of a nursing-led intervention on quality of life, symptom severity, clinical, and treatment use in patients with advanced cancer.

Design, Setting, and Participants: Randomized controlled trial conducted from November 2006 through May 2008 at 112 tertiary care palliative care or oncology inpatient units across 10 general oncology centers in the United States and one cancer center in the United Kingdom.

Interventions: A multidimensional, psychosocial intervention (Project ENABLE II) (ENABLE II) versus usual care (UC).

Main Results and Measures: Quality of life was measured by the Functional Assessment of Chronic Illness Therapy (FACT) Palliative Care Subscale (FACT-P) at baseline, 1, 3, and 6 months. Symptom severity was measured by the EORTC QLQ-C15-Pal. Clinical outcomes were measured as the number of days in the hospital and the number of emergency department visits recorded in the electronic medical record.

Results: A total of 1122 participants with cancer of the gastrointestinal tract (61%), lung (22%), breast (13%), and other (2%) were randomized to the ENABLE II intervention group (n = 561) or to the UC group (n = 561). The ENABLE II intervention group had significantly better quality of life (FACT-P) at baseline (mean [SD], 48.8 [10.1] vs 46.8 [10.1], P = .001), at 1 month (mean [SD], 50.8 [10.1] vs 48.8 [10.1], P = .001), at 3 months (mean [SD], 50.8 [10.1] vs 48.8 [10.1], P = .001), and at 6 months (mean [SD], 50.8 [10.1] vs 48.8 [10.1], P = .001). The ENABLE II intervention group had significantly fewer hospital days (mean [SD], 10.1 [10.1] vs 11.1 [10.1], P = .001) and fewer emergency department visits (mean [SD], 1.1 [1.1] vs 1.1 [1.1], P = .001) compared with the UC group.

Conclusions: Compared with patients receiving usual oncology care, those receiving a nurse-led, palliative care-focused intervention addressing physical, psychosocial, and spiritual needs demonstrated significantly better quality of life and fewer hospital days and emergency department visits.

Effects of a Palliative Care Intervention on Clinical Outcomes in Patients With Advanced Cancer

The Project ENABLE II Randomized Controlled Trial

Scott R. Decker, MD, MPH, APN*

Abstract. From the International Palliative Care in the Elderly Study of Life

2009, JAMA 302;7:741-749

- Early PC: telephone problem-solving intervention by APNs
- 322 pts, newly-diagnosed advanced GI, GU, lung, breast cancer
- prognosis of one year
- outcomes FACIT-Pal, ESAS, CES-D (every 3 months)
- **Results: Improved QOL, mood, but not symptom intensity or reduced days in hospital, ICU, emergency department**

Background and objectives: Telephone-based palliative care interventions have been shown to improve quality of life and reduce symptom burden in advanced cancer patients. However, the impact of such interventions on clinical outcomes remains unclear. This study examined the effects of a telephone-based palliative care intervention on clinical outcomes in patients with advanced cancer.

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

Jennifer S. Temel, M.D., Joseph A. Greer, Ph.D., Aloia Muzikansky, M.A., Emily R. Gallagher, R.N., Sarah Admane, M.S., E.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. Pivl, M.D., M.P.H., J. Andrew Billings, M.D., and Thomas J. Lynch, M.D.

ABSTRACT

BACKGROUND

Patients with metastatic non-small-cell lung cancer have a substantial symptom burden and may receive aggressive care at the end of life. We examined the effect of introducing palliative care early after diagnosis on patient-reported outcomes and end-of-life care among ambulatory patients with newly diagnosed disease.

METHODS

We randomly assigned patients with newly diagnosed metastatic non-small-cell lung cancer to receive either early palliative care integrated with standard oncologic care or standard oncologic care alone. Quality of life and mood were assessed at baseline and at 12 weeks with the use of the Functional Assessment of Cancer

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

Temel et al, 2010, NEJM 363;8:733-742

- Early PC: palliative care physician or APN
- 151 pts, newly-diagnosed advanced non-small cell lung cancer
- ECOG 0, 1, 2
- Outcomes: FACT-Lung, HADS, PHQ-9 at 12 weeks
- **Results: improved QOL, mood; longer survival (11.6 vs. 8.9 months), despite less aggressive treatment**

THE LANCET

2014, 383, 1713-19

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

Carola Zimmerman, Nadia Swart, Monika Ryznarowska, Beffert Hansen, Ineke de Jongh, Anni Eise, Malène Meier, AnneHyatt, Gary Rude, Ann Turrell, Alan Evans, Christopher Lin

Early palliative care: palliative care team (MD and nurse)

24 clinics, randomized 1:1 to EPC or standard care

461 patients, GU, GI, breast, gyne, lung cancer
prognosis 6-24 mo, ECOG 0,1,2

Outcomes: monthly for 4 months

- patient quality of life (FACIT-Sp*, QUAL-E)
- patient satisfaction with care (FAMCARE-P)
- symptom control (ESAS)
- difficulty with clinician-patient interactions (CARES-MIS)

*primary outcome: FACIT-Sp at 3 months

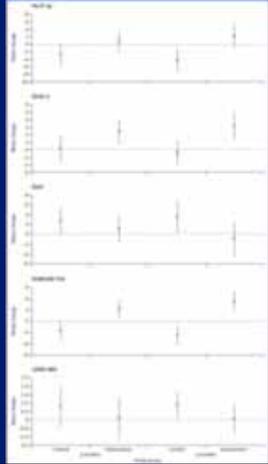
Results (n=461):

3 months:

FACIT-Sp: p=0.07
QUAL-E: p=0.05
FAMCARE-P-16: p=0.0003
ESAS: p=0.33
CARES-MIS: p=0.40

4 months:

FACIT-Sp: p=0.006
QUAL-E: p=0.003
ESAS: p=0.05
FAMCARE-P-16: p<0.0001
CARES-MIS: p=0.11



Further EPC trials

- Bakitas et al. J Clin Oncol 2015 (early vs delayed)
- Temel et al. ASCO 2016 (non-colon GI and lung)
- Maltoni et al. Eur J Cancer 2016 (pancreatic cancer)
- El-Jawahri et al. JAMA 2016 (hematological cancers, hospitalized for stem cell transplantation)

JAMA | Original Investigation

Association Between Palliative Care and Patient and Caregiver Outcomes A Systematic Review and Meta-analysis

Diei Kavaleratos, PhD; Jennifer Corbelli, MD, MS; Di Zhang, BS; J. Nicholas Deonno-Odom, PhD, RN; Natalie C. Ezzaveff, MPH; Jamel Hammer, MD, PhD; Zachariah P. Heydich, BS; Dana Z. Ikejiani; Michele Klein Fendyshon, MS, S, BSN, RN, BA; Camilla Zimmerman, MD, PhD; Sally C. Morton, PhD; Robert M. Arnold, MD; Lucas Heller, MD; Yael Schenker, MD, MMS

- 43 RCTs, 19 including only patients with cancer
- Meta-analysis:
 - Statistically and clinically significant improvement in patient QOL and symptom burden at 1-3 mo
 - No association between palliative care and survival
- Narrative synthesis
 - Palliative care consistently associated with improvements in advance care planning, patient and caregiver satisfaction, and lower health care utilization

ASCO Clinical Guideline

Combined standard oncology care and palliative care should be considered early in the course of illness for any patient with metastatic cancer and/or high symptom burden.

ASCO Provisional Opinion
Smith et al. J Clin Oncol 2012

Inpatients and outpatients with advanced cancer should receive dedicated palliative care services, early in the disease course, concurrent with active treatment.

ASCO Clinical Guideline
Ferrell et al. J Clin Oncol 2016



Surveyed Canadian Medical, Radiation and Surgical Oncologists

- response rate >70%
- 85% referred "usually" or "always", but 1/3 referred only after stopping all treatment

Factors influencing early referral (at diagnosis or during chemo):

- Satisfaction with availability of PC service
- Acceptance by PC service of patients on chemotherapy
- Completing a rotation in palliative care
- 1/3 agreed they would refer earlier if palliative care was renamed supportive care

Perceptions of palliative care

- **Initial perceptions:**
 - "Death", "plots waiting", "end of the road", preparing to die", "nothing to be done", "no hope left", "places that you never get out of again"
- **Sources of perceptions:**
 - Caring for a dying relative or friend; personal experience
- **After receiving early palliative care:**
 - Broadened understanding, deep appreciation for care, but still uncomfortable with term "palliative"
- **Reframing and/or renaming palliative care:**
 - "That shell of meaning that surrounds palliative care has to somehow change..."
 - "I think you have to think about a name outlining what you're trying to do..."

Zimmermann et al. CMAJ 2016

*71 patients/caregivers participating in EPC trial

Qualitative study: Patient/caregiver perceptions

- **Prompt, personalized symptom management**
 - "You're never panicked really about the pain, because you know you've got somebody there that's going to help you deal with it"
- **Holistic support of patients and caregivers**
 - "Well I can say anything pretty well to [palliative care physician], I can say anything -- if something is really bothering me, I can say it to her."
- **Guidance in decision-making**
 - "...because there are many things that happened to [her] along the way that maybe her and I together might not have been able to deal with unless we had his knowledge, or his expertise, or his suggestion or advice"
- **Preparation for the future**
 - "It's just such an unknown and to have it explained as nicely as it was by [palliative care physician], so it was very good"

Hannon et al. Palliat Med. 2016

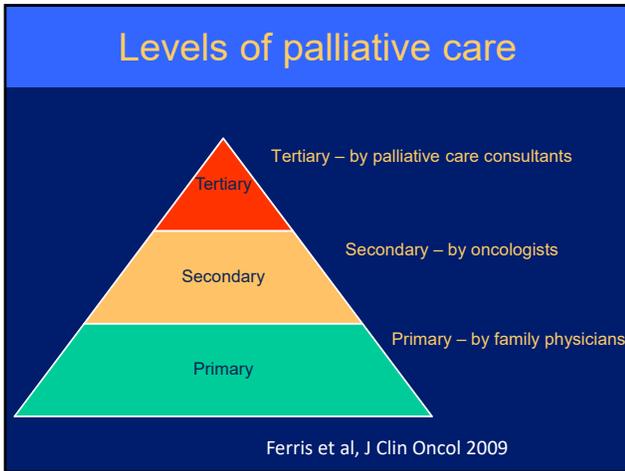
*40 patients and caregivers in EPC intervention arm

Perception of oncologist vs. pc roles

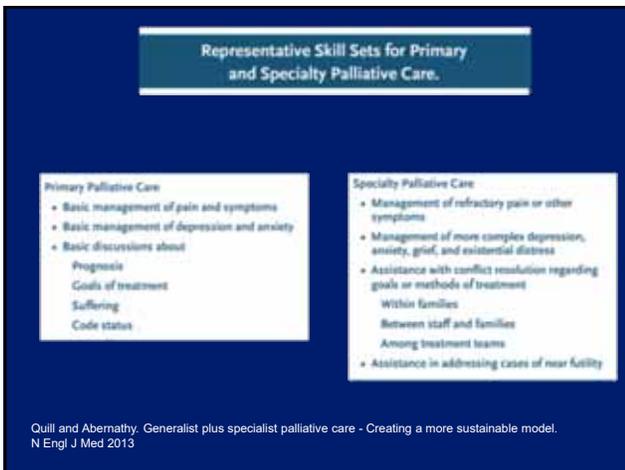
Category	Oncology theme	EPC Theme
Focus of care	Cancer control, disease-focused care	Symptom control, holistic, family-focused care
Care delivery	Structured, time-limited visits based on protocol	Flexible, personalized, unstructured visits
Complementary care (intervention group)	I do see them as different. I think [oncologist] is there...He's the guy who's mapping the way. He's saying, "Okay, these tests and based on my experience and my understanding of this disease indicates that we should go this way and there are side effects as a result of that". [Palliative care physician]'s role is understanding what the path is doing (...) As well as being there just as another ear and looking at you from a more holistic perspective, as a whole person. So I think they're both necessary and I think they're both really beneficial.	

Hannon et al, Oncologist 2016

* 71 interviews with patients and caregivers



- ## Primary PC: Family Physician involvement
- Wide range of involvement internationally in palliative care
 - UK, Netherlands, Australia: 75-85% of GPs involved in primary care
 - Canada, Denmark, Japan: <50% of family physicians/GPs provide palliative care
 - Varies by setting
 - Urban – low level of involvement, with frequent sign-over to specialized services
 - Rural – most family physicians provide palliative care
- Rubin et al, The expanding role of primary care in cancer control Lancet Oncol. 2015



- ## Ongoing trials
- ClinicalTrials.gov: “early palliative care”
 - 112 entries (35 Europe, 41 US, 12 Canada)
 - 42 specifically early palliative care interventions
 - Cancer: Lung, GI, Esophageal, HCC, Gastric/pancreatic, Stem cell transplant, Gynaecologic, Breast, Leukemia
 - Non-cancer: COPD, AIDS, Renal failure, CHF

Further research needed

- Other models of early palliative care (primary, secondary)
- Identifying high-need patients who should receive tertiary palliative care: e.g. by referral guidelines, symptom-screening, prognostic modeling or other means
- Studies specifically assessing economic cost at system and patient/family level

Thank-you

PM palliative care research and clinical team

Medical oncologists at PM

Patients and families participating in research

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Long Term Care

