

**Cochrane** Database of Systematic Reviews

# Early palliative care for adults with advanced cancer (Review)

Haun MW, Estel S, Rücker G, Friederich HC, Villalobos M, Thomas M, Hartmann M

Haun MW, Estel S, Rücker G, Friederich HC, Villalobos M, Thomas M, Hartmann M. Early palliative care for adults with advanced cancer. *Cochrane Database of Systematic Reviews* 2017, Issue 6. Art. No.: CD011129. DOI: 10.1002/14651858.CD011129.pub2.

www.cochranelibrary.com

**Early palliative care for adults with advanced cancer (Review)** Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.



# [Intervention Review]

# Early palliative care for adults with advanced cancer

Markus W Haun<sup>1</sup>, Stephanie Estel<sup>1</sup>, Gerta Rücker<sup>2</sup>, Hans-Christoph Friederich<sup>3</sup>, Matthias Villalobos<sup>4</sup>, Michael Thomas<sup>4</sup>, Mechthild Hartmann<sup>1</sup>

<sup>1</sup>Department of General Internal Medicine and Psychosomatics, Im Neuenheimer Feld 410, Heidelberg University Hospital, Heidelberg, Germany. <sup>2</sup>Institute for Medical Biometry and Statistics, Faculty of Medicine and Medical Center – University of Freiburg, Freiburg, Germany. <sup>3</sup>Psychosomatic Medicine and Psychotherapy, University Hospital Düsseldorf, Düsseldorf, Germany. <sup>4</sup>Department of Thoracic Oncology, Thoraxklinik at Heidelberg University Hospital, Heidelberg, Germany

**Contact address:** Markus W Haun, Department of General Internal Medicine and Psychosomatics, Im Neuenheimer Feld 410, Heidelberg University Hospital, Heidelberg, D-69120, Germany. Markus.Haun@med.uni-heidelberg.de.

**Editorial group:** Cochrane Pain, Palliative and Supportive Care Group. **Publication status and date:** New, published in Issue 6, 2017.

**Citation:** Haun MW, Estel S, Rücker G, Friederich HC, Villalobos M, Thomas M, Hartmann M. Early palliative care for adults with advanced cancer. *Cochrane Database of Systematic Reviews* 2017, Issue 6. Art. No.: CD011129. DOI: 10.1002/14651858.CD011129.pub2.

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

# ABSTRACT

#### Background

Incurable cancer, which often constitutes an enormous challenge for patients, their families, and medical professionals, profoundly affects the patient's physical and psychosocial well-being. In standard cancer care, palliative measures generally are initiated when it is evident that disease-modifying treatments have been unsuccessful, no treatments can be offered, or death is anticipated. In contrast, early palliative care is initiated much earlier in the disease trajectory and closer to the diagnosis of incurable cancer.

#### Objectives

To compare effects of early palliative care interventions versus treatment as usual/standard cancer care on health-related quality of life, depression, symptom intensity, and survival among adults with a diagnosis of advanced cancer.

#### Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, OpenGrey (a database for grey literature), and three clinical trial registers to October 2016. We checked reference lists, searched citations, and contacted study authors to identify additional studies.

#### Selection criteria

Randomised controlled trials (RCTs) and cluster-randomised controlled trials (cRCTs) on professional palliative care services that provided or co-ordinated comprehensive care for adults at early advanced stages of cancer.

#### Data collection and analysis

We used standard methodological procedures as expected by Cochrane. We assessed risk of bias, extracted data, and collected information on adverse events. For quantitative synthesis, we combined respective results on our primary outcomes of health-related quality of life, survival (death hazard ratio), depression, and symptom intensity across studies in meta-analyses using an inverse variance random-effects model. We expressed pooled effects as standardised mean differences (SMDs, or Hedges' adjusted *g*). We assessed certainty of evidence at the outcome level using GRADE (Grading of Recommendations Assessment, Development, and Evaluation) and created a 'Summary of findings' table.

#### **Main results**

We included seven randomised and cluster-randomised controlled trials that together recruited 1614 participants. Four studies evaluated interventions delivered by specialised palliative care teams, and the remaining studies assessed models of co-ordinated care. Overall, risk of bias at the study level was mostly low, apart from possible selection bias in three studies and attrition bias in one study, along with insufficient information on blinding of participants and outcome assessment in six studies.

Compared with usual/standard cancer care alone, early palliative care significantly improved health-related quality of life at a small effect size (SMD 0.27, 95% confidence interval (CI) 0.15 to 0.38; participants analysed at post treatment = 1028; evidence of low certainty). As reexpressed in natural units (absolute change in Functional Assessment of Cancer Therapy-General (FACT-G) score), health-related quality of life scores increased on average by 4.59 (95% CI 2.55 to 6.46) points more among participants given early palliative care than among control participants. Data on survival, available from four studies enrolling a total of 800 participants, did not indicate differences in efficacy (death hazard ratio 0.85, 95% CI 0.56 to 1.28; evidence of very low certainty). Levels of depressive symptoms among those receiving early palliative care did not differ significantly from levels among those receiving usual/standard cancer care (five studies; SMD -0.11, 95% CI -0.26 to 0.03; participants analysed at post treatment = 762; evidence of very low certainty). Results from seven studies that analysed 1054 participants post treatment suggest a small effect for significantly lower symptom intensity in early palliative care compared with the control condition (SMD -0.23, 95% CI -0.35 to -0.10; evidence of low certainty). The type of model used to provide early palliative care did not affect study results. One RCT reported potential adverse events of early palliative care, such as a higher percentage of participants with severe scores for pain and poor appetite; the remaining six studies did not report adverse events in study publications. For these six studies, principal investigators stated upon request that they had not observed any adverse events.

# **Authors' conclusions**

This systematic review of a small number of trials indicates that early palliative care interventions may have more beneficial effects on quality of life and symptom intensity among patients with advanced cancer than among those given usual/standard cancer care alone. Although we found only small effect sizes, these may be clinically relevant at an advanced disease stage with limited prognosis, at which time further decline in quality of life is very common. At this point, effects on mortality and depression are uncertain. We have to interpret current results with caution owing to very low to low certainty of current evidence and between-study differences regarding participant populations, interventions, and methods. Additional research now under way will present a clearer picture of the effect and specific indication of early palliative care. Upcoming results from several ongoing studies (N = 20) and studies awaiting assessment (N = 10) may increase the certainty of study results and may lead to improved decision making. In perspective, early palliative care is a newly emerging field, and well-conducted studies are needed to explicitly describe the components of early palliative care and control treatments, after blinding of participants and outcome assessors, and to report on possible adverse events.

# PLAIN LANGUAGE SUMMARY

# Early palliative care for adults with advanced cancer

# **Review question**

What is the evidence for the effects of early palliative care on quality of life, survival, depression, and symptom intensity in people with advanced cancer?

#### Background

Frequently, cancer is diagnosed at a late stage, and the disease might have progressed through anticancer treatment. Patients can choose to start or continue anticancer treatment at the potential cost of side effects. Standard care means that all patients are offered palliative care towards the end of life. However, patients may be able to receive palliative care a lot earlier. This approach, which is known as early palliative care, begins at the time of, or shortly after, the diagnosis of advanced cancer. Often, early palliative care is combined with anticancer treatment such as chemotherapy or radiotherapy. Early palliative care, whether provided by the attending oncologist or by specialist teams, involves empathetic communication with patients about their prognosis, advance care planning, and symptom assessment and control.

#### Study characteristics

In October 2016, we searched for clinical trials on early palliative care in adults with advanced cancer. We included seven studies and found 20 ongoing studies. Most of the studies included participants older than 65 years of age on average, diagnosed with different tumour types and receiving treatment in tertiary care centres in North America. Most of these studies compared early palliative care with standard oncological (cancer) care. All studies were funded by government agencies.

# **Key results**

When evaluated together in a meta-analysis, studies showed that in patients with advanced cancer, early palliative care may slightly increase quality of life. It may also decrease symptom intensity to a small degree. Effects on survival and depression are uncertain. A single



study reported side effects (adverse events), for example, more pain and reduced appetite. For the remaining six studies, information about side effects was not published, but trial authors told us they had not observed any.

#### Certainty of the evidence

We rated the certainty of the evidence using four levels: very low, low, moderate, and high. Evidence of very low certainty means that we have little confidence in the results. Evidence of high certainty means that we are very confident in the results. We found that certainty of the evidence was low for health-related quality of life and symptom intensity, and was very low for depression and survival. We downgraded certainty of the evidence for various reasons, for example, problems in the way studies were carried out, differences between studies, and the small number of studies. We remain uncertain about the effects of early palliative care; therefore we have to interpret the results with caution. When published, ongoing studies may provide more evidence, and this may affect the certainty of the results.