Bispebjerg og
Frederiksberg Hospitaler

UNIVERSITY OF
COPENHAGEN

REGION

The Danish Palliative Care Trial (DanPaCT), a randomised trial of early palliative care in cancer

Results of the primary analysis

Mogens Groenvold

Head of Research Unit, Department of Palliative Medicine, Bispebjerg Hospital, Copenhagen

Professor of Palliative Care and Quality of Life Research, Department of Public Health, University of Copenhagen

Co-authors and investigators/collaborators

- Morten Aa. Petersen
- Anette Damkier
- Christian Gluud
- Irene Higginson
- Jane Lindschou
- Peter M. Fayers
- Jan B. Nielsen
- Mette A. Neergaard
- Lise Pedersen
- Per Sjøgren
- Annette S. Strömgren
- Tove Vejlgaard
- **Anna Thit Johnsen**
  Project coordinator

BACKGROUND

- **National level**

A large Danish survey (2005-2006) showed that advanced cancer patients, who were **not** in specialist palliative care (SPC) reported frequent, unrelieved palliative care needs (mean number of unrelieved needs: 2.5)

Johnsen et al. Pall Med 2009, Psycho-Oncol 2012

BACKGROUND

- **National level**

A large Danish survey (2005-2006) showed that advanced cancer patients, who were **not** in specialist palliative care (SPC) reported frequent, unrelieved palliative care needs (mean number of unrelieved needs: 2.5)

Johnsen et al. Pall Med 2009, Psycho-Oncol 2012

➞ ”***Would there be any benefit from starting SPC earlier?”***

Grant application 2009

BACKGROUND

- **National level**

A large Danish survey (2005-2006) showed that advanced cancer patients, who were **not** in specialist palliative care (SPC) reported frequent, unrelieved palliative care needs (mean number of unrelieved needs: 2.5)

Johnsen et al. Pall Med 2009, Psycho-Oncol 2012

→ ”***Would there be any benefit from starting SPC earlier?”***

Grant application 2009

- **International level**

Promising results from North American trials of early SPC

- Bakitas (JAMA, 2009)
- Temel (NEJM, 2010)
- Zimmermann (Lancet, 2014)
- Bakitas + Dionne-Odom (JCO, 2015)

ASCO 2012

American Society of Clinical Oncology Provisional Clinical Opinion: The Integration of Palliative Care Into Standard Oncology Care

Recent Data

Seven published RCTs form the basis of this PCO.

Provisional Clinical Opinion

Based on strong evidence from a phase III RCT, patients with metastatic non–small-cell lung cancer should be offered concurrent palliative care and standard oncologic care at initial diagnosis. While a survival benefit from early involvement of palliative care has not yet been demonstrated in other oncology settings, substantial evidence demonstrates that palliative care—when combined with standard cancer care or as the main focus of care—leads to better patient and caregiver outcomes. These include improvement in symptoms, QOL, and patient satisfaction, with reduced caregiver burden. Earlier involvement of palliative care also leads to more appropriate referral to and use of hospice, and reduced use of futile intensive care. While evidence clarifying optimal delivery of palliative care to improve patient outcomes is evolving, no trials to date have demonstrated harm to patients and caregivers, or excessive costs, from early involvement of palliative care. Therefore, it is the Panel's expert consensus that 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. Strategies to optimize concurrent palliative care and standard oncology care, with evaluation of its impact on important patient and caregiver outcomes (eg, QOL, survival, health care services utilization, and costs) and on society, should be an area of intense research.

ASCO 2012

American Society of Clini
Opinion: The In
Oncolo

Published Ahead of Print on March 23, 2015 as 10.1200/JCO.2014.60.5386
The latest version is at http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2014.60.5386

JOURNAL OF CLINICAL ONCOLOGY

EDITORIAL

Palliative Care: If It Makes a Difference, Why Wait?

Barbara Gomes, King's College London, Cicely Saunders Institute, London, United Kingdom

ancer should
s. While a survival
d in other oncology settings,
ed with standard cancer care or as
outcomes. These include improvement in
caregiver burden. Earlier involvement of palliative
nd use of hospice, and reduced use of futile intensive care.
ery of palliative care to improve patient outcomes is evolving, no
ted harm to patients and caregivers, or excessive costs, from early
e care. Therefore, it is the Panel's expert consensus that combined standard
onc nd palliative care should be considered early in the course of illness for any patient with
met c cancer and/or high symptom burden. Strategies to optimize concurrent palliative care and
standard oncology care, with evaluation of its impact on important patient and caregiver outcomes (eg,
QOL, survival, health care services utilization, and costs) and on society, should be an area of intense
research.

In 2009, specialized palliative care (SPC) in Denmark…

- Was newly established
- Was almost entirely used for end-of-life PC
- Had insufficient capacity

It was therefore **unrealistic to offer early SPC to all** advanced cancer patients

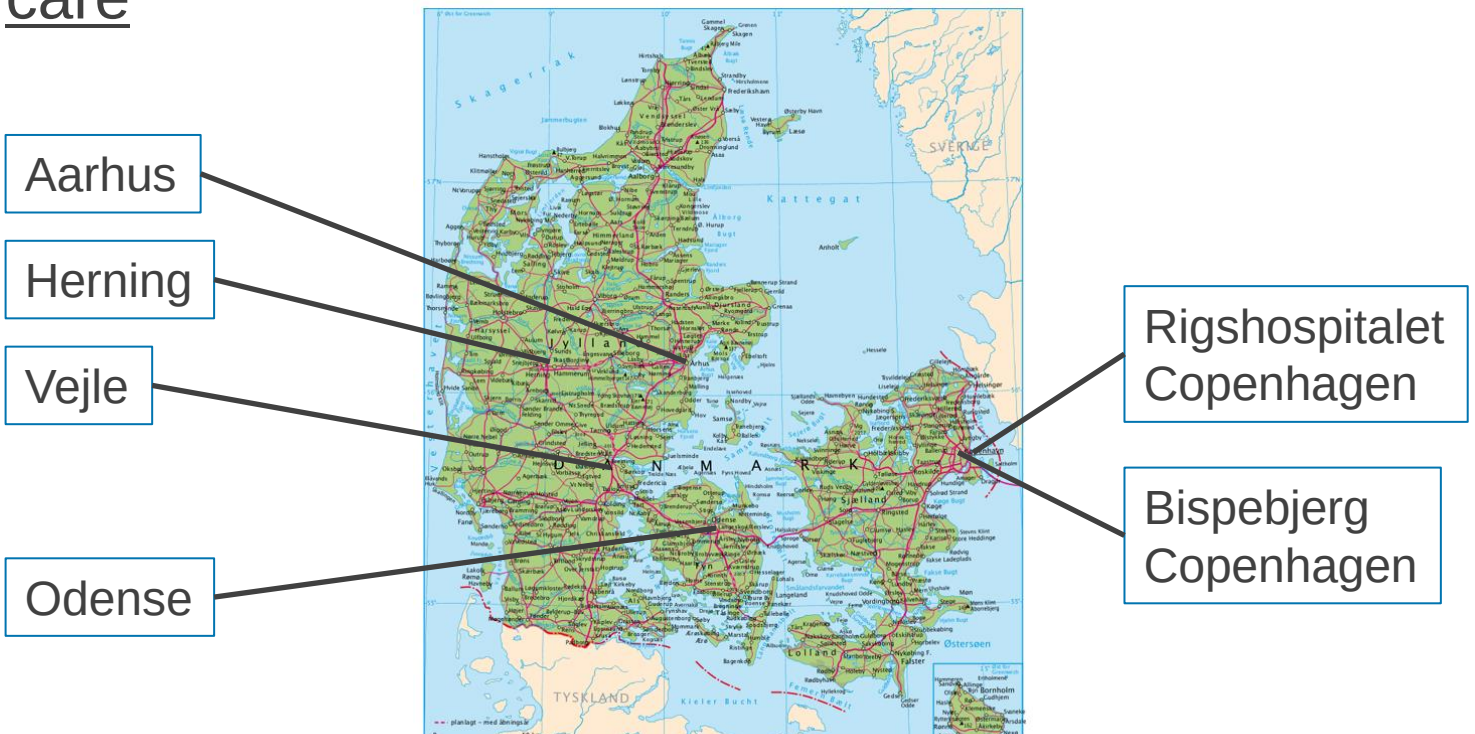
AIM

To determine whether patients with metastatic cancer, **who reported palliative needs in a screening**, would benefit from early SPC (i.e. referral to a palliative care team).

METHODS

Design

Multicentre randomized controlled trial (RCT) comparing early SPC plus standard care vs. standard care



Patients

- **Consecutive metastatic cancer patients in oncological departments with no prior contact with SPC**
- Screened for palliative care needs
- Planned N=300

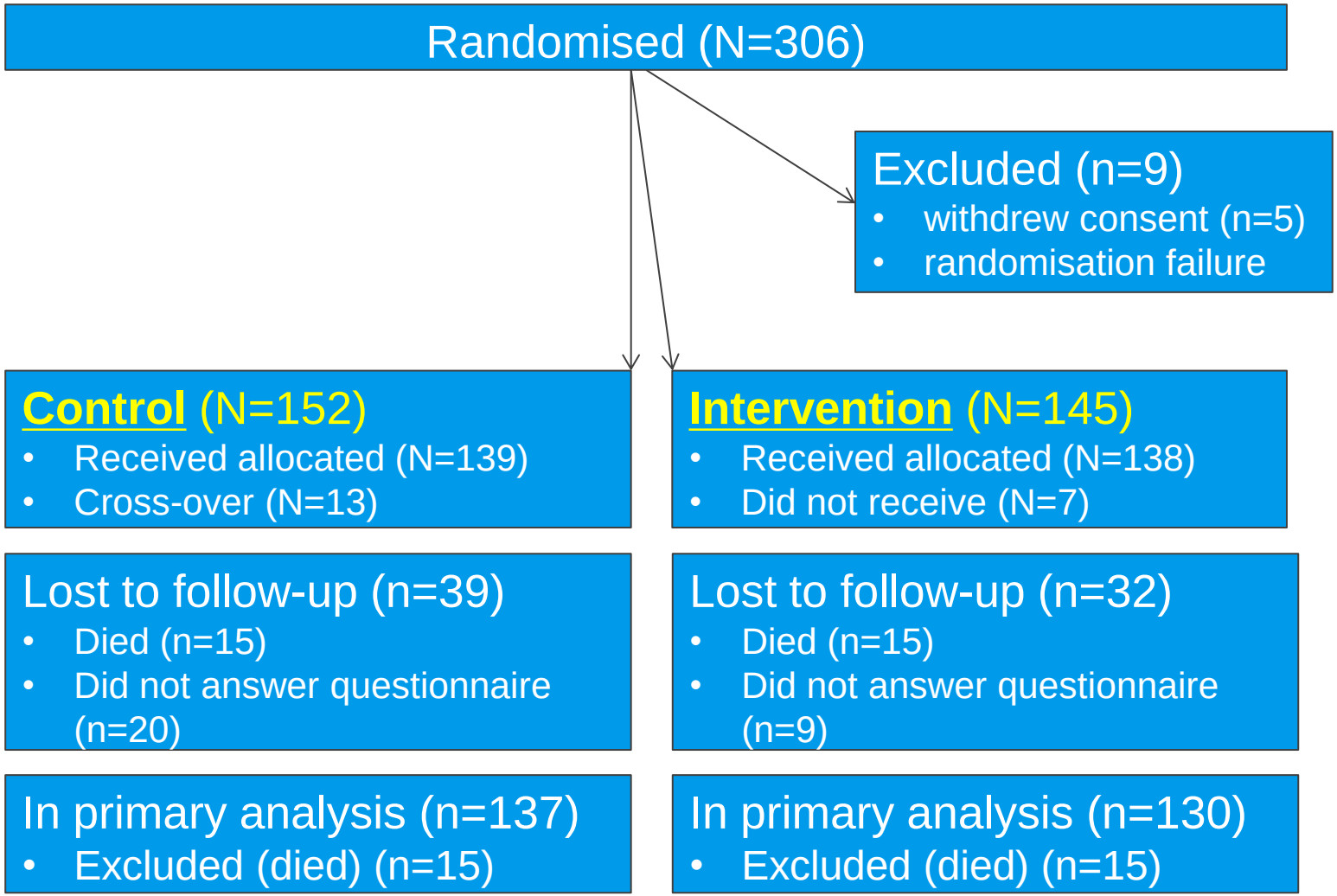
Methods: outcomes and assessments

- For screening, seven scales in EORTC QLQ-C30 questionnaire selected:
  - Physical, role or emotional function
  - Nausea/vomiting, pain, dyspnea, lack of appetite
- Inclusion criterion:
  - A score of **of at least 50** (100= maximal symptomatology) in at least one of these seven scales
  - At least 4 other symptoms (≥ 33)
- Eight week trial period with assessments
  - Baseline
  - 3 weeks
  - 8 weeks

Primary/secondary outcomes

- The classical paradox in palliative care trials:
  - If the patient doesn't have the problem, it probably doesn't improve even if we help – this may weaken the outcome measurement ('dilution')
- Our solution, a patient-individualised primary outcome:
  - For each patient, **the scale** (among the seven selected scales in QQL-C30) **having the highest score** (100= maximal symptomatology) **was used as primary outcome**
- As secondary outcomes, the usual approach:
  - The seven scales
- Analysis of all outcomes: the change from baseline to the weighted mean of the 3 and 8 weeks follow-up
- Linear regression with multiple imputation and five additional sensitivity analyses

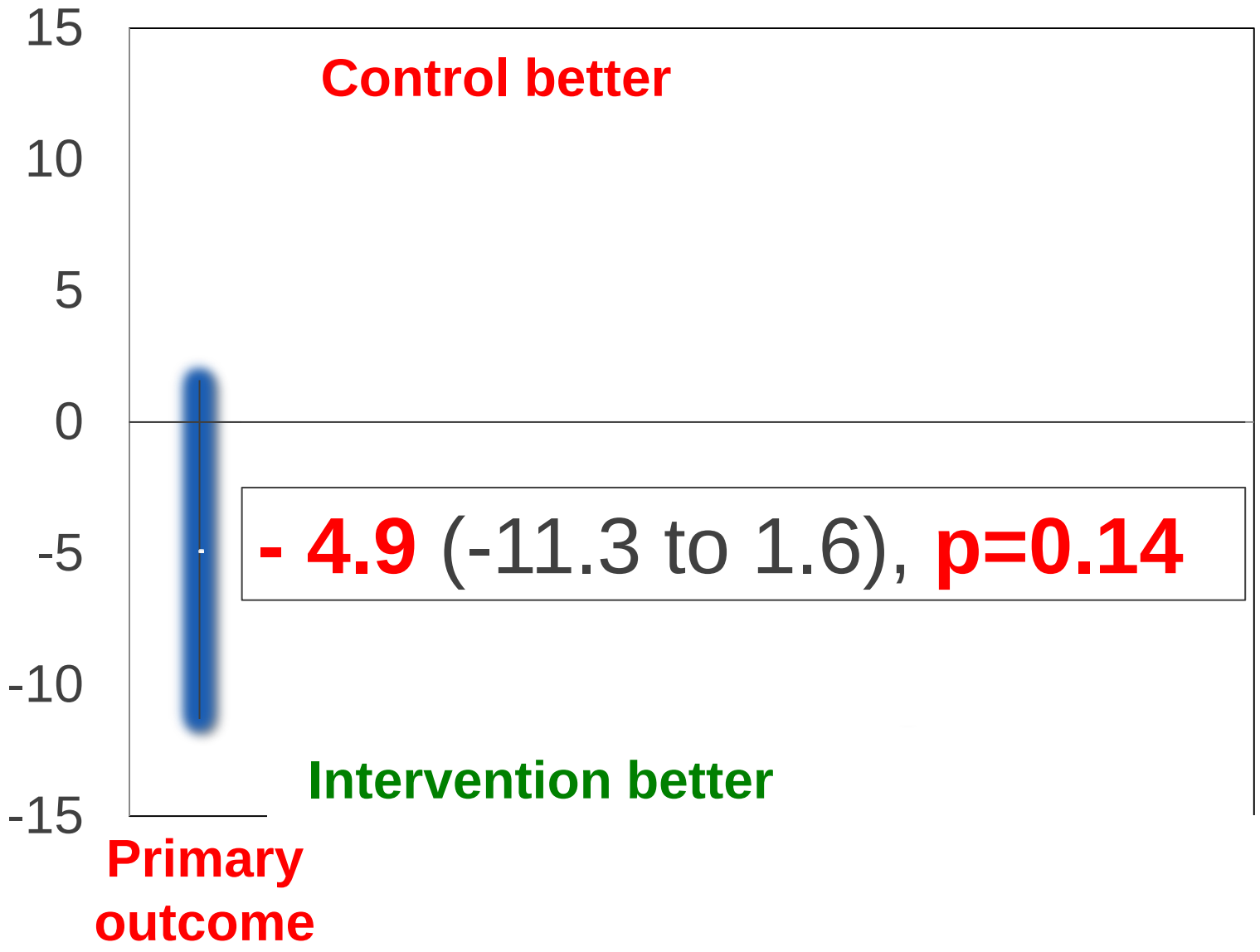
RESULTS


Randomised (N=306)
Excluded (n=9)
• withdrew consent (n=5)
• randomisation failure
Control (N=152)
• Received allocated (N=139)
• Cross-over (N=13)
Intervention (N=145)
• Received allocated (N=138)
• Did not receive (N=7)
Lost to follow-up (n=39)
• Died (n=15)
• Did not answer questionnaire (n=20)
Lost to follow-up (n=32)
• Died (n=15)
• Did not answer questionnaire (n=9)
In primary analysis (n=137)
• Excluded (died) (n=15)
In primary analysis (n=130)
• Excluded (died) (n=15)

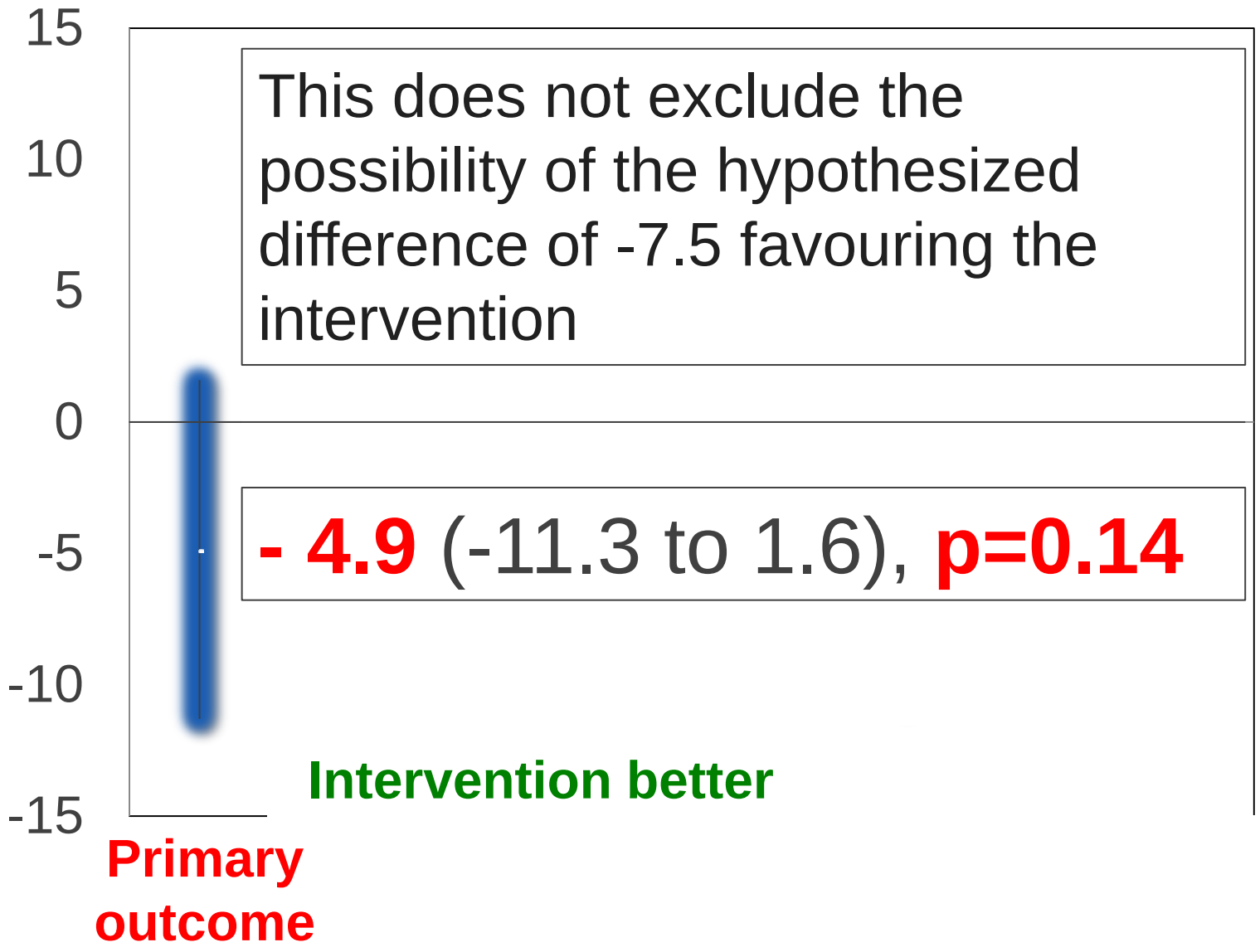
MAIN RESULT

Primary analysis of the primary outcome

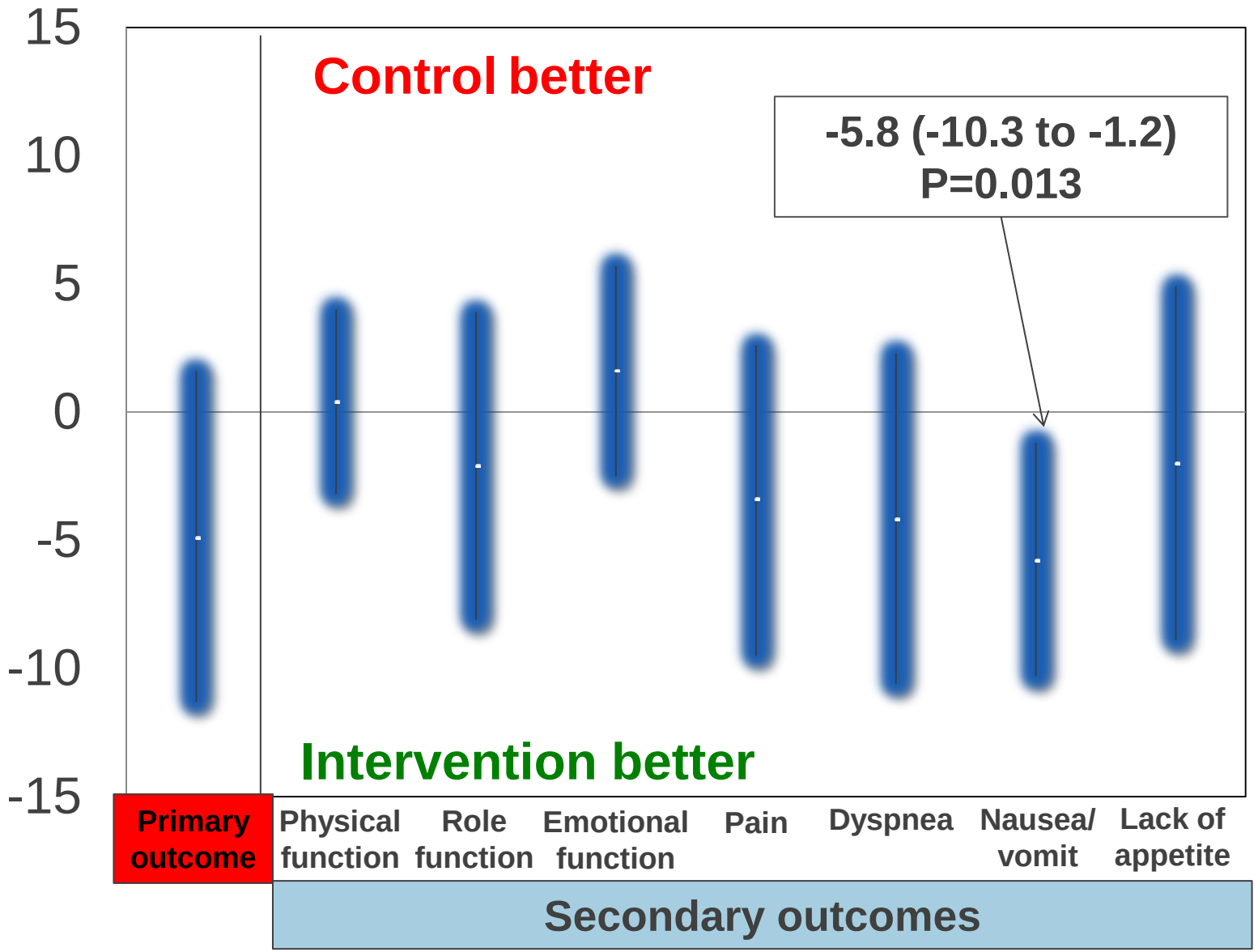
Intervention effect:
Mean weighted change over time (0-100 scale)



Intervention effect:
Mean weighted change over time (0-100 scale)

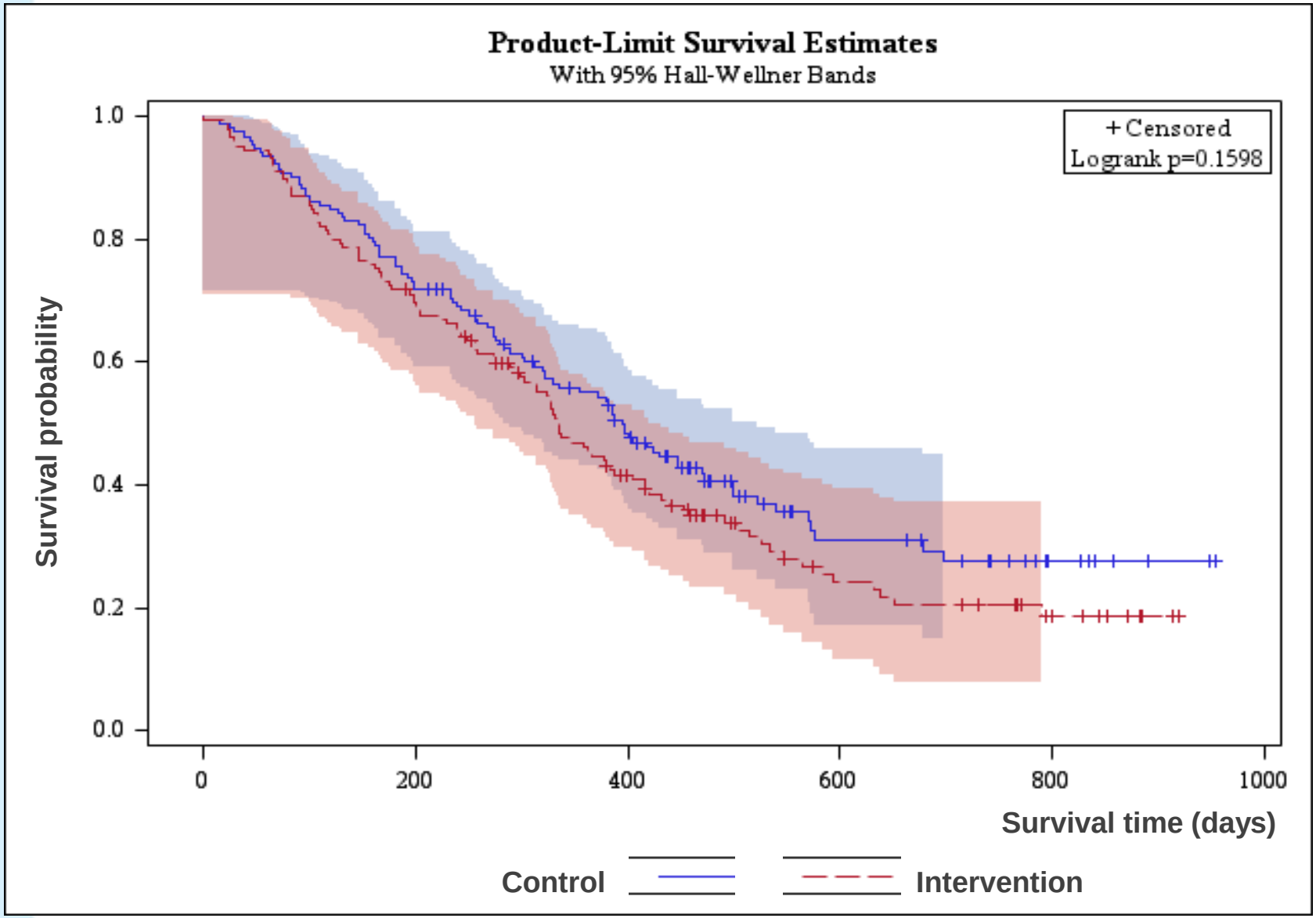


Intervention effect:
Mean weighted change over time (0-100 scale)



No difference in survival

Intervention group: median 345 days
Control group: median 365 days
Cox regression analysis: **P=0.39**



Five sensitivity analyses

- Similar results

CONCLUSIONS

- No effect of early SPC on
  - primary outcome (patient-individualised)
  - Secondary outcomes:
    - Physical, role or emotional function, nausea/vomiting, pain, dyspnea, lack of appetite
    - Survival

- except maybe on nausea/vomiting

CONCLUSIONS

- No effect of early SPC on
  - primary outcome (patient-individualised)
  - Secondary outcomes:
    - Physical, role or emotional function, nausea/vomiting, pain, dyspnea, lack of appetite
    - Survival

- except maybe on nausea/vomiting

- Positive effects of early SPC in four North-American trials
  - Bakitas (JAMA, 2009), Temel (NEJM, 2010, Zimmermann (Lancet, 2014), Bakitas + Dionne-Odom (JCO, 2015)

Was the trial adequately conducted?

- Adequate outcomes?
  - Our new, patient-individualised outcome may be questioned
  - However, the same results in traditional outcomes (seven EORTC QLQ-C30 scales)
- Adequate analyses?
  - State of the art main analysis with multiple imputation
  - Five sensitivity analyses, consistent results
- Adequate power?
  - One of the larger trials (N=297, 2 times Temel study)
  - High completeness of data



Maybe insufficient exposure contrast between arms?

- **Cross-over between allocated arms**
  - Intervention arm: 7 patients did not establish contact to SPC
  - Control arm: 13 patients crossed over to early SPC
- **Maybe insufficient SPC activity in intervention arm?**
  - Only 51% had more than one contact during the 8 weeks
  - Only 62% in had one or more interventions documented in their medical records
    - See poster by Nete Skjødt et al.
- **Were SPC teams ready and able to deliver 'early SPC'?**
  - Maybe they felt that there was no urgency and less alarming needs than in their usual patients
- **Was there compensation in the control arm?**
  - Maybe trial staff or oncology department staff felt morally oblige to care for the most obvious palliative care needs in control patients (needs that were carefully exposed via the initial screening)?

Final conclusions (1)

1. We could not show effect of early SPC, except maybe on nausea/vomiting
   a) **Overall effect -4.9** (-11.3 to 1.6) on 0-100 scale, **p=0.14**
   b) This does not exclude the possibility of the hypothesized difference of -7.5 favouring the intervention
2. We believe that
   a) The trial was **adequately powered, conducted and analysed**
   b) The magnitude of intervention may not been sufficient
      a) SPC staff had no ‘standard early SPC model’ ready and perceived many of the patients as ‘without acute palliative care needs’
   c) The effect we could measure was diluted by
      a) Insufficient retention in study arms (cross-over)
      b) Possibly compensation in control arm

Final conclusions (2)

3. Important lessons learned
4. Despite disappointing findings, we still strongly believe that early SPC may be beneficial
5. More research is needed:

Published Ahead of Print on March 23, 2015 as 10.1200/JCO.2014.60.5386
The latest version is at http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2014.60.5386

JOURNAL OF CLINICAL ONCOLOGY E D I T O R I A L

Palliative Care: If It Makes a Difference, Why Wait?

Barbara Gomes, *King's College London, Cicely Saunders Institute, London, United Kingdom*

Warm thanks to

- Patients
- Research nurses and students who helped collect data
- Co-authors
- Funding bodies:

Danish Cancer Society

TrygFonden

Johnsen et al. BMC Palliative Care 2013, 12:37
http://www.biomedcentral.com/1472-684X/12/37

BMC Palliative Care

STUDY PROTOCOL Open Access

A randomised, multicentre clinical trial of specialised palliative care plus standard treatment versus standard treatment alone for cancer patients with palliative care needs: the Danish palliative care trial (DanPaCT) protocol

Anna T Johnsen[1*], Anette Damkier[2], Tove B Vejlgaard[3], Jane Lindschou[4], Per Sjøgren[5], Christian Gluud[4], Mette A Neergaard[6], Morten Aa Petersen[1], Lena E Lundorff[7], Lise Pedersen[1], Peter Fayers[8], Annette S Strömgren[9], Irene J Higginson[10] and Mogens Groenvold[1,11]

Johnsen et al. Trials 2014, 15:376
http://www.trialsjournal.com/content/15/1/376

TRIALS

UPDATE Open Access

Detailed statistical analysis plan for the Danish Palliative Care Trial (DanPaCT)

Anna Thit Johnsen[1*], Morten Aagaard Petersen[1], Christian Gluud[2], Jane Lindschou[2], Peter Fayers[3,4], Per Sjøgren[5], Lise Pedersen[1], Mette Asbjoern Neergaard[6], Tove Bahn Vejlgaard[7], Anette Damkier[8], Jan Bjoern Nielsen[9], Annette S Strömgren[10], Irene J Higginson[11] and Mogens Groenvold[1,12]

Original Article

PALLIATIVE MEDICINE

Randomised clinical trial of early specialist palliative care plus standard care versus standard care alone in patients with advanced cancer: The Danish Palliative Care Trial

Mogens Groenvold[1,2], Morten Aagaard Petersen[1], Anette Damkier[3], Mette Asbjoern Neergaard[4], Jan Bjoern Nielsen[5], Lise Pedersen[1], Per Sjøgren[6], Annette Sand Strömgren[6], Tove Bahn Vejlgaard[7], Christian Gluud[8], Jane Lindschou[8], Peter Fayers[9,10], Irene J Higginson[11] and Anna Thit Johnsen[1,12]

Palliative Medicine
1–11

DOI: 10.1177/026921631
journals.sagepub.com/hon
SAGE

ER 1 · JANUARY 1, 2017

LINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Integration of Palliative Care Into Standard Oncology Care: American Society of Clinical Oncology Clinical Practice Guideline Update

Betty R. Ferrell, Jennifer S. Temel, Sarah Temin, Erin R. Alesi, Tracy A. Balboni, Ethan M. Basch, Janice I. Firn, Judith A. Paice, Jeffrey M. Peppercorn, Tanyanika Phillips, Ellen L. Stovall,† Camilla Zimmermann, and Thomas J. Smith

ABSTRACT

Purpose

To provide evidence-based recommendations to oncology clinicians, patients, family and friend caregivers, and palliative care specialists to update the 2012 American Society of Clinical Oncology (ASCO) provisional clinical opinion (PCO) on the integration of palliative care into standard oncology care for all patients diagnosed with cancer.

Methods

Hvad ved vi?

VOLUME 35 · NUMBER 1 · JANUARY 1, 2017

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Integration of Palliative Care Into Standard Oncology Care: American Society of Clinical Oncology Clinical Practice Guideline Update

Betty R. Ferrell, Jennifer S. Temel, Sarah Temin, Erin R. Alesi, Tracy A. Balboni, Ethan M. Basch, Janice I. Firn, Judith A. Paice, Jeffrey M. Peppercorn, Tanyanika Phillips, Ellen L. Stovall,† Camilla Zimmermann, and Thomas J. Smith

Author affiliations appear at the end of this article.

†Deceased.

Published at ascopubs.org/journal/jco on October 31, 2016

Clinical Practice Guideline Committee approved: August 15, 2016

A B S T R A C T

Purpose

To provide evidence-based recommendations to oncology clinicians, patients, family and friend caregivers, and palliative care specialists to update the 2012 American Society of Clinical Oncology (ASCO) provisional clinical opinion (PCO) on the integration of palliative care into standard oncology care for all patients diagnosed with cancer.

Recommendations

Inpatients and outpatients with advanced cancer should receive dedicated palliative care services, early in the disease course, concurrent with active treatment. Referral of patients to interdisciplinary palliative care teams is optimal, and services may complement existing programs. Providers may refer family and friend caregivers of patients with early or advanced cancer to palliative care services.

www.asco.org/guidelineswiki.

Reprint requests: 2318 Mill Rd, Suite 800, Alexandria, VA 22314; e-mail: guidelines@asco.org.

Corresponding author: American Society of Clinical Oncology, 2318 Mill Rd, Suite 800, Alexandria, VA 22314; e-mail: guidelines@asco.org.

0732-183X/17/3501w-96w/$20.00

quasiexperimental trial, and five secondary analyses from RCTs in the 2012 PCO on providing palliative care services to patients with cancer and/or their caregivers, including family caregivers, were found to inform the update.

Recommendations

Inpatients and outpatients with advanced cancer should receive dedicated palliative care services, early in the disease course, concurrent with active treatment. Referral of patients to interdisciplinary palliative care teams is optimal, and services may complement existing programs. Providers may refer family and friend caregivers of patients with early or advanced cancer to palliative care services.

J Clin Oncol 35:96-112. © 2016 by American Society of Clinical Oncology

ASCO Guideline Update 2017
Hvem skal yde den palliative indsats?

CLINICAL QUESTION 2

What are the most practical models of palliative care? Who should deliver palliative care (external consultation, internal consultations with palliative care practitioners in the oncology practice, or performed by the oncologist him- or herself)?

Recommendation 2

Palliative care for patients with advanced cancer should be delivered through interdisciplinary palliative care teams, with consultation available in both outpatient and inpatient settings (type: evidence based, benefits outweigh harms; evidence quality: intermediate; strength of recommendation: moderate).

Hvad er palliativ indsats?
ASCO (2017) anbefalinger

- Rapport and relationship building with patients and family caregivers
- Symptom, distress, and functional status management (eg, pain, dyspnea, fatigue, sleep disturbance, mood, nausea, or constipation)
- Exploration of understanding and education about illness and prognosis
- Clarification of treatment goals
- Assessment and support of coping needs (eg, provision of dignity therapy)
- Assistance with medical decision making
- Coordination with other care providers
- Provision of referrals to other care providers as indicated