

Is specialized palliative cancer care associated with use of antineoplastic treatment at the end of life? A population-based cohort study

Palliative Medicine

1–9

© The Author(s) 2018

Reprints and permissions:

sagepub.co.uk/journalsPermissions.nav

DOI: 10.1177/0269216318786393

journals.sagepub.com/home/pmj



Kirstine Skov Benthien^{1,2} , Mathilde Adersen³ ,
Morten Aagaard Petersen³, Eva Soelberg Vadstrup², Per Sjøgren²
and Mogens Groenvold^{3,4}

Abstract

Background: The use of chemotherapy in the last 14 days of life should be as low as possible.

Aim: To study the factors related to the use of chemotherapy in the last 14 days of life and the factors related to concurrent antineoplastic treatment and specialized palliative care.

Design: This was a population-based cohort study. The data were collected from the Danish Register of Causes of Death, the Danish National Patient Register, and the Danish Palliative Care Database. Analyses were descriptive and multivariate logistic regression.

Setting/participants: Cancer decedents between 2010 and 2013 in the Capital Region of Denmark.

Results: During the study period, 17,246 individuals died of cancer and 33% received specialized palliative care. In the last 14 days of life, 4.2% received chemotherapy. Younger patients and patients with hematological cancers were more likely to receive chemotherapy in the last 14 days of life. Receiving specialized palliative care was associated with a lower risk of receiving chemotherapy in the last 14 days of life—odds ratio 0.15 for hospices and 0.53 for palliative hospital units. A total of 8% of the population received concurrent antineoplastic treatment and specialized palliative care. Female gender, younger age, and breast and prostate cancer were significantly associated with this concurrent model.

Conclusion: Overall, the incidence of antineoplastic treatment in the last 14 days of life was low compared to other studies. Patients in specialized palliative care had a reduced risk of receiving chemotherapy at the end of life.

Keywords

Palliative care, palliative medicine, hospice care, registries, cohort studies, antineoplastic agents

What is already known about this topic?

- The use of chemotherapy in the last 14 days of life should be as low as possible.
- The association between specialized palliative care and use of chemotherapy is unclear.
- The use of concurrent antineoplastic treatment and specialized palliative care is unknown.

What this paper adds?

- This study demonstrates that specialized palliative care is associated with the reduced use of chemotherapy in the last 14 days of life.
- The proportion of patients in concurrent specialized palliative care and antineoplastic treatment is 8%.
- Type of specialized palliative care providers led to different outcomes.

¹Center for Clinical Research and Prevention, Frederiksberg Hospital, Copenhagen University Hospital, Copenhagen, Denmark

²Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

³The Research Unit, Department of Palliative Medicine, Bispebjerg Hospital, Copenhagen University Hospital, Copenhagen, Denmark

⁴Department of Public Health, University of Copenhagen, Copenhagen, Denmark

Corresponding author:

Kirstine Skov Benthien, Center for Clinical Research and Prevention, Frederiksberg Hospital, Copenhagen University Hospital, Nordre Fasanvej 57, 2000 Frederiksberg, Denmark.

Email: kirstine@skov-benthien.dk

Implications for practice, theory, or policy

- The association between specialized palliative care and reduced use of chemotherapy should be investigated in experimental studies.
- The low proportion of patients in concurrent antineoplastic treatment and specialized palliative care should lead to earlier referrals.

Introduction

Generally, chemotherapy for incurable cancer given with life-prolonging or palliative intent should be discontinued at the end of life if treatment burden exceeds treatment benefits. The American Society of Clinical Oncology has identified the lowest possible use of chemotherapy in the last 14 days of life as a quality indicator in the Quality Oncology Practice Initiative.^{1,2} The proportion of individuals who receive chemotherapy in the last 14 days of life has been reported ranging from 8.5% to 29%,^{3–6} but the current knowledge about the factors related to this use is mostly based on studies of small and selected samples and/or in single centers.

Use of chemotherapy at the end of life can impair quality of life and end-of-life care, as it may lead to later hospice referrals and more aggressive life-saving interventions without prolonging survival.^{7,8} Nevertheless, patients may perceive continued active treatment as the only acceptable option.⁹ In a prospective cohort of terminally ill patients with cancer ($n=386$), 31% preferred life-extending care rather than comfort care and as many as 77% preferred to receive chemotherapy even if it would extend their life by only one week.⁸ Further, healthcare professionals can find decisions and timely treatment cessation challenging.¹⁰

Palliative radiotherapy may relieve symptoms in a matter of days, weeks, or months depending on fraction and clinical circumstances, and thus the optimal overall use at the end of life is likely not discernable.¹¹ Also, the ideal time for cessation of the increasingly used biological agents at the end of life has yet to be determined.

Specialized palliative care aims to improve quality of life for patients with a life-threatening illness and complex symptoms.¹² The integration of specialized palliative care and oncology is widely recommended^{13–15} and may support end-of-life treatment decisions.¹² Specialized palliative care is increasingly implemented in the healthcare systems across many nations of Europe.¹⁶ In a randomized controlled trial of patients with lung cancer, Temel et al.¹⁷ demonstrated improved quality of life and survival following early specialized palliative care. This beneficial effect might have been related to differences in the use of chemotherapy since patients in the intervention group more often developed an accurate view of their own prognosis and were less likely to receive chemotherapy

near the end of life.^{18,19} The efficacy of early specialized palliative care on both survival and quality of life may have been mediated by influencing decision-making about chemotherapy. While there is growing evidence about the efficacy of specialized palliative care in quality of life,²⁰ knowledge about specialized palliative care and chemotherapy at the end of life is still uncertain and mostly confined to selected cancer types.^{19,21}

Therefore, specialized palliative care may be a promising way of supporting decision-making and thus diminishing futile use of antineoplastic treatment at the end of life. The aims of this study were to (1) study which factors were related to the use of chemotherapy in the last 14 days of life, (2) study which factors were related to concurrent antineoplastic treatment and specialized palliative care, and (3) assess the longitudinal use of specialized palliative care, chemotherapy, radiotherapy, and biological agents at the end of life.

Methods

This was a population-based study investigating a cohort of persons who died of cancer from 1 January 2010 to 31 December 2013 in the Capital Region of Denmark.

Setting

In Denmark, healthcare is free upon receipt and financed through taxes. The Capital Region offers specialized palliative care to its 1,750,000 inhabitants (January 2015) through nine specialized palliative care teams. Any physician can refer patients to specialized palliative care. There is no requirement of antineoplastic treatment to be discontinued, when specialized palliative care begins, which is mostly at home or in the outpatient setting. There are two cancer centers and one local hospital with an oncology department in the region.

Inclusion criteria

- Living in the Capital Region of Denmark;
- Adult (≥ 18 years);
- Died from cancer.

Data sources

- The cohort was extracted from the Danish Register of Causes of Death.²²
- The Danish Palliative Care Database provided information about all persons who received specialized palliative care.²³ The information in the database was entered upon the patients' death.
- The Danish National Patient Register provided information about antineoplastic treatment.²⁴ This Register contains information about treatments, but not indications. The information was recorded in the register upon contact with the healthcare system.

The registers were combined using the unique personal identity numbers. The data were analyzed using a remote access to Statistics Denmark that provided anonymized datasets.

Primary outcome

The primary outcome was the use of chemotherapy in the last 14 days of life (yes/no).

Secondary outcomes

Concurrent specialized palliative care and antineoplastic treatment may indicate the integration of or the collaboration between specialized palliative care and oncology. For this study, "the concurrent model" was defined as at least one dose of chemotherapy, radiotherapy, biological agents, or hormone therapy given after the initiation of specialized palliative care (yes/no). Additional secondary outcomes were the use (yes/no) of chemotherapy, external beam radiotherapy, and biological agents, respectively, during the last 3 months, 2 months, 1 month, and 2 weeks before death.

Primary independent variable of interest

The primary independent variable was specialized palliative care delivered by a hospice or a palliative hospital unit, both of which provide specialized palliative care in patients' homes as well as in inpatient setting. The hospices operate mainly as standalone organizations, whereas palliative hospital units have direct access to hospital diagnostics and treatments. In Denmark, specialized palliative care is provided to individuals with a life-threatening illness and complex care needs and their informal caregivers by a multi-professional team.¹²

Additional covariates

Covariates were age, gender, and ICD-10 cancer diagnoses.

Analysis

The association between specialized palliative care, the additional covariates, and chemotherapy in the last 14 days of life was analyzed using multiple logistic regression. Some patients changed provider of specialized palliative care or began specialized palliative care during the period studied (last 14 days of life). Since it was unclear whether they should be allocated to the first or the second specialized palliative care provider, only individuals who had started specialized palliative care at least 14 days before death were counted in the specialized palliative care groups for the analysis of the primary outcome. Factors related to the concurrent model were analyzed with multiple logistic regression.

The *p*-values were two-sided and a *p*-value < 0.05 was considered statistically significant. The statistical analyses were performed in SAS 9.4.

Results

During the study period 2010–2013, 17,246 people ≥ 18 years died from cancer in the Capital Region of Denmark and were included in the study. Three individuals had no record of previous hospital contact, 14,798 had hospital contacts with cancer as the main diagnosis, and 2448 (14%) had hospital contacts with main diagnoses other than cancer (Table 1).

The mean age of the population was 76 years and the most prevalent cancer causes of death were lung and gastrointestinal cancers. One third of the population received specialized palliative care.

Use of specialized palliative care and antineoplastic treatment at the end of life

Figure 1 demonstrates the use of antineoplastic treatment, which declined continuously during the last 3 months of life. A total of 9% of the population received at least one dose of chemotherapy; another 9% received at least one fraction of radiotherapy within 1 month before death; 1% received biological agents; and 4% of the population received chemotherapy in the last 14 days of life.

There were 6389 specialized palliative care trajectories allocated to 5735 persons. The main reason for more than one specialized palliative care trajectory was that some individuals in palliative hospital units were referred to hospice close to death.

Figure 2 demonstrates the proportion of patients in specialized palliative care approaching death. The mean duration of specialized palliative care was 48 (standard deviation (SD): 76) days for the 3009 persons in the hospice group and 84 (SD: 129) days for the 2726 persons in the palliative hospital group (*p* < 0.0001).

Likelihood of receiving chemotherapy in the last 14 days of life

One third of the persons in specialized palliative care were enrolled during the last 14 days of life ($n=1786$). Because this group changed group affiliation in the period of

Table 1. Sample characteristics.

	$n=17,246$
Gender, female n (%)	8507 (49)
Age, mean (SD)	76 (12)
Underlying cancer cause of death, n (%)	
Breast	1365 (8)
Central nervous system	495 (3)
Gynecological	782 (5)
Upper gastrointestinal	2798 (16)
Lower gastrointestinal	2161 (13)
Leukemia or lymphoma	1159 (7)
Lung	4056 (24)
Prostate	1246 (7)
Head/neck	559 (3)
Malignant melanoma	292 (2)
Urinary	965 (6)
Other	468 (3)
Unknown	900 (5)
In SPC, n (%)	5735 (33)
Hospice	3009 (17)
SPC unit	2726 (16)

SD: standard deviation; SPC: specialized palliative care.

outcome, it was exempt from further analysis. At 14 days before death, 1897 individuals received specialized palliative care by a hospice, 2052 by a palliative hospital unit, and 11,511 had never received specialized palliative care. These three groups (total $n=15,460$) were included in the following analyses of antineoplastic treatments in the last 14 days of life.

Table 2 presents the results of the logistic regression analysis. There was an inverse relationship between age and use of chemotherapy. The likelihood of receiving chemotherapy in the last 14 days of life was the highest for hematological malignancies and the lowest for urinary and prostate cancer. There was a significantly lower likelihood of receiving chemotherapy when the patient had been in contact with specialized palliative care at least 14 days before death. The risk was lower for individuals in the hospice group compared to the palliative hospital group.

Due to the longer duration of specialized palliative care by palliative hospital units, a secondary analysis was performed to investigate whether the difference between the specialized palliative care providers could be attributed to the duration of contact. The logistic regression analysis was controlled for the duration of specialized palliative care, age, gender, and cancer cause of death. The difference in risk of chemotherapy in the last 14 days of life by provider of specialized palliative care remained significant: hospice versus palliative hospital unit odds ratio (OR) was 0.33 (95% confidence interval (CI): 0.23–0.48).

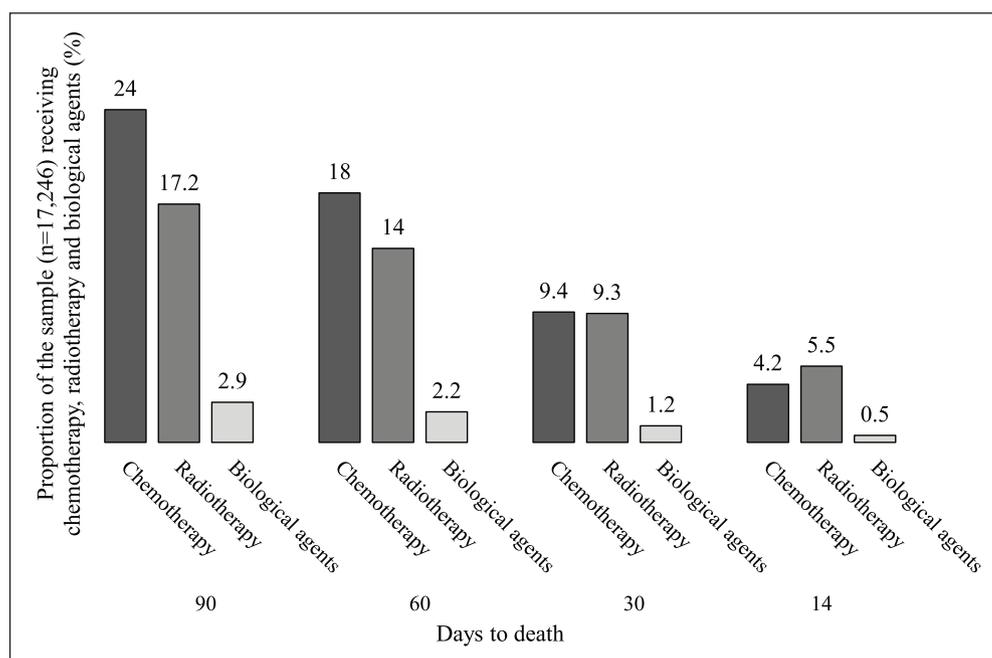


Figure 1. Proportion of the population receiving chemotherapy, radiotherapy, and biological agents at 90, 60, 30, and 14 days before death.

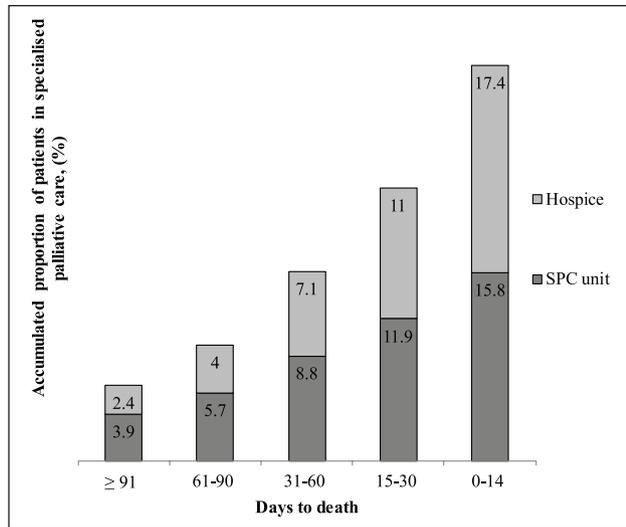


Figure 2. Accumulated proportion of the population in specialized palliative care at ≥91, 61–90, 31–60, 15–30, and 0–14 days before death by hospice and palliative hospital unit.

Likelihood of receiving concurrent antineoplastic treatment and specialized palliative care

A total of 8% (n=1388) of the population received concurrent antineoplastic treatment after initiation of specialized palliative care: the concurrent model (Table 3).

Younger patients and females were more likely to receive concurrent antineoplastic treatment and specialized palliative care. Individuals with cancer in the central nervous system or hematological malignancies were least likely, while individuals with breast or prostate cancer were most likely to receive concurrent antineoplastic treatment. The palliative hospital group was more likely to receive chemotherapy after initiation of specialized palliative care compared to the hospice group, even when controlling for the duration of specialized palliative care. Individuals in the concurrent model received specialized palliative care for a mean of 143 days (SD: 161), while those who received specialized palliative care without

Table 2. Factors associated with receipt of chemotherapy in the last 14 days of life.

n = 15,460	Crude OR (95% CI)	Adjusted* OR (95% CI)	p-value
Gender			0.4489
Male	1	1	
Female	1.12 (0.96–1.31)	1.07 (0.90–1.28)	
Age			<0.0001
<60 years	1	1	
60–69 years	0.94 (0.73–1.20)	0.91 (0.71–1.18)	
70–79 years	0.66 (0.52–0.85)	0.59 (0.45–0.75)	
80–89 years	0.36 (0.27–0.47)	0.29 (0.22–0.39)	
≥90 years	0.09 (0.05–0.16)	0.07 (0.04–0.13)	
Underlying cancer cause of death			<0.0001
Lung	1	1	
Breast	1.06 (0.78–1.43)	1.19 (0.86–1.63)	
Central nervous system	0.62 (0.35–1.10)	0.57 (0.32–1.01)	
Gynecological	1.22 (0.85–1.75)	1.46 (1.00–2.12)	
Head/neck	0.61 (0.36–1.05)	0.52 (0.30–0.90)	
Leukemia or lymphoma	3.34 (2.65–4.21)	3.64 (2.87–4.61)	
Lower gastrointestinal	0.59 (0.43–0.80)	0.73 (0.53–1.00)	
Prostate	0.12 (0.06–0.26)	0.19 (0.09–0.40)	
Malignant melanoma	0.97 (0.52–1.81)	1.08 (0.57–2.02)	
Upper gastrointestinal	0.81 (0.62–1.05)	0.84 (0.65–1.10)	
Urinary	0.29 (0.16–0.52)	0.33 (0.18–0.60)	
Other	0.62 (0.34–1.12)	0.68 (0.37–1.24)	
Unknown	0.59 (0.38–0.93)	0.68 (0.44–1.07)	
SPC			<0.0001
No SPC	1	1	
Hospice ≥ 14 days	0.18 (0.12–0.30)	0.15 (0.09–0.24)	
SPC unit ≥ 14 days	0.69 (0.54–0.89)	0.53 (0.41–0.69)	

OR: odds ratio; CI: confidence interval; SPC: specialized palliative care.

Results of multiple logistic regression.

*Adjusted for SPC, age, gender, and cancer cause of death. Statistically significant values are bold.

Table 3. Variables associated with the concurrent model.

<i>n</i> = 17,246	Crude OR (95% CI)	Adjusted* OR (95% CI)	<i>p</i> -value
Gender			0.0069
Male	1	1	
Female	1.19 (1.07–1.33)	1.20 (1.05–1.38)	
Age			<0.0001
<60 years	1	1	
60–69 years	0.53 (0.46–0.62)	0.54 (0.47–0.64)	
70–79 years	0.29 (0.25–0.34)	0.28 (0.24–0.33)	
80–89 years	0.12 (0.10–0.15)	0.11 (0.09–0.14)	
≥90 years	0.03 (0.02–0.04)	0.02 (0.01–0.04)	
Underlying cancer cause of death			<0.0001
Lung	1	1	
Breast	2.05 (1.69–2.48)	1.97 (1.60–2.43)	
Central nervous system	0.80 (0.54–1.17)	0.57 (0.38–0.84)	
Gynecological	1.53 (1.19–1.96)	1.39 (1.06–1.82)	
Head/neck	0.93 (0.66–1.31)	0.76 (0.53–1.08)	
Leukemia or lymphoma	0.58 (0.43–0.78)	0.69 (0.51–0.94)	
Lower gastrointestinal	0.93 (0.76–1.14)	1.16 (0.95–1.43)	
Prostate	1.32 (1.05–1.64)	2.75 (2.15–3.51)	
Malignant melanoma	1.41 (0.95–2.10)	1.28 (0.85–1.93)	
Upper gastrointestinal	1.08 (0.91–1.30)	1.06 (0.88–1.27)	
Urinary	0.88 (0.66–1.16)	1.10 (0.83–1.47)	
Other	1.44 (1.05–1.98)	1.42 (1.02–1.98)	
Unknown	0.62 (0.45–0.86)	0.80 (0.57–1.11)	

OR: odds ratio; CI: confidence interval.

Result of multiple logistic regression. Higher OR indicates higher likelihood of being in the concurrent model. Concurrent model—any dose of chemotherapy, radiotherapy, biological agents, or hormone therapy after the initiation of specialized palliative care.

*Adjusted for age, gender, and cancer cause of death. Statistically significant values are bold.

subsequent antineoplastic treatment alone did so for a mean of 41 days (SD: 65; $p < 0.0001$). Individuals provided with specialized palliative care by a palliative hospital unit were more likely to be in the concurrent model compared to those provided with specialized palliative care by a hospice: OR 2.74 (95% CI: 2.36–3.18, controlled for age, gender, cancer cause of death, and days in specialized palliative care; data not shown).

Discussion

Main results

This population-based study demonstrated a declining use of antineoplastic treatment at the end of life. The Capital Region of Denmark is representative of the whole country in terms of life expectancy (80.8 vs 80.9 years)²⁵ and would also be comparable to countries with similar life expectancy and healthcare systems, mainly in Western Europe. The most robust findings regarding the use of chemotherapy at the end of life were presented by Bekelman et al.²⁶ in a study of healthcare utilization for patients dying with cancer in seven developed nations—Belgium, Canada, England, Germany, The Netherlands, Norway, and the United States. The

prevalence of the use of chemotherapy in the last month of life ranged from 4.8% to 12.7%, placing our results of 9.4% within this range. Published results on the use of chemotherapy in the last 14 days are few and mostly documented in selected samples. This study population consisted of cancer decedents, some of which may not have been eligible to cancer treatment due to comorbidity. This could be the case for the 14% who did not have hospital contacts with cancer as a main diagnosis. Rates of use of chemotherapy in the last 14 days may be higher when study samples are identified in departments of oncology. Patients dying in cancer centers represent a selected subset of the population, whose use of chemotherapy at the end of life is undoubtedly higher, which would explain the relatively low use of chemotherapy in the last 14 days of 4.2% found in this population-based study compared to other studies.^{3–5} We are not aware of other population studies describing the use of biological agents at the end of life. Future studies may find higher proportions, since the use is increasing and the data in this cohort are from 2010–2013. Few studies have described radiotherapy at the end of life; 14% of a Medicare-insured sample of 39,619 from 2004–2011 received radiotherapy in the last 14 days of life²⁷ compared to the 5.5% in our region.

As demonstrated in Figure 2, specialized palliative care is mostly initiated in the last month of life. The limited capacity for specialized palliative care in Denmark requires prioritized patient uptake and patients with the most heavy symptom burden and complex needs are first in line, thereby leaving sparse resources for the prevention of symptoms in patients earlier in the disease trajectory.

To our knowledge, this is the first study of a population with all cancer types of the association between receiving chemotherapy at the end of life and the provision of specialized palliative care. We demonstrated that the use of chemotherapy in the last 14 days of life was associated with younger age, hematological malignancies, and not receiving specialized palliative care. In a multi-center study of 279,846 patients, who died from cancer in hospitals, Rochigneux et al.³ similarly demonstrated that older patients were less likely to receive chemotherapy in the last month of life, but also that women were, which we could not replicate. The selection of participants precluded generalizability and the use of specialized palliative care was not determined. They did find that hospitals without palliative care units presented with higher administration rates of chemotherapy near the end of life. Diagnosis differences in the use of chemotherapy in the last 14 days of life may reflect differences in disease trajectories, in healthcare organization, or in availability of treatment lines. Specifically, patients with hematological cancers were most likely to receive chemotherapy in the last 14 days of life. This observation is known and may reflect the fluctuating course of disease, which makes timely treatment cessation and referral to specialized palliative care difficult.^{28,29}

The association between age and chemotherapy in the last 14 days of life could indicate a shift in elderly patients' priorities or that elderly patients may be less likely to complete palliative chemotherapy.³⁰ Older age is also associated with an increasing prevalence of comorbidities, which reduce patients' treatment eligibility, and finally older patients are underrepresented in clinical trials which may lead to uncertainty about chemotherapy efficacy and reluctance toward prescription.^{31–33}

The association between specialized palliative care and a reduced use of chemotherapy in the last 14 days of life was observed in a setting with no formal barrier for specialized palliative care and antineoplastic treatment to take place concurrently. The key hypotheses of the interaction between specialized palliative care and the reduced use of antineoplastic treatment in the last 14 days of life are as follows:

- Patients identified as being at the end of life would be less likely to receive chemotherapy and more likely to receive specialized palliative care. Thus, the association might be two consequences of the same condition.

- Patients may associate antineoplastic treatment directly with hope and a singular interest in pursuing anticancer treatments can impact on the delivery of palliative care.³⁴
- Specialized palliative care may influence decisions about antineoplastic treatment directly or indirectly by advising the patient about prognosis implications and priorities.¹²
- The lower risk of chemotherapy found in the hospice group might stem from the organization of hospices as culturally and physically separate from hospitals. Palliative hospital units may be closer to oncology departments, which may be associated with the higher likelihood of the concurrent model.

To our knowledge, this is also the first study to investigate the use of the concurrent model (defined as antineoplastic treatment after first contact with specialized palliative care). Simultaneous care is one among the 38 indicators of integration of specialized palliative care and oncology identified by Hui and Bruera.³⁵ This one indicator does not attest to the attainment of related indicators such as communication and coordination between oncology and specialized palliative care. Our result of 8% indicates that it is still rare in Denmark. Several barriers prevent optimal integration for the benefit of patients. For example, the limited capacity of specialized palliative care³⁶ can preclude early referrals, objective referral criteria are not routinely applied, and traditions for care and treatment in oncology and specialized palliative care might not easily adapt to recommendations or each other. Breast, gynecological, and prostate cancers had increased likelihood of being in the concurrent model, which may be explained by longer disease trajectories and multiple available antineoplastic treatment options.

Strengths and limitations

The registers and clinical database that provide the data for this study ensure a highly representative study population consisting of one third of the Danish population. There is close to 0% loss of follow-up or missing data. Simultaneously, the data in the registers represent a limitation of this study, as information about performance status and treatment indication was not available. The decision-making process about chemotherapy is outside the scope of this study and any interventions to lower the use of chemotherapy in the last 14 days of life should be based on further interviews and observation studies.

Information about dose of radiotherapy was not available, which makes it difficult to distinguish between futile treatments and those that may provide almost immediate relief and thus are appropriate in the last weeks of life.

Information about level of income, education, and ethnicity is not available in the Danish health registers.

Immigrants and descendants from non-Western countries make out 8.6% of the Danish population.³⁷

The concurrent model appeared rarely and included cases of concurrent treatment without any kind of coordination of collaboration and cases with only one day of overlap. Therefore, the concurrent model may indicate rather than equate integration of specialized palliative care and oncology.

What this study adds?

This study demonstrated a reduced use of antineoplastic treatment at the end of life when in specialized palliative care, and although the mechanisms of this association cannot be determined from this study, it adds to the growing evidence base^{20,38} that supports the increased use of specialized palliative care in cancer trajectories.

Knowledge about the content and outcome of specialized palliative care by different providers is essential for organizational planning. Only 8% of the population received concurrent antineoplastic treatment and specialized palliative care. In integrated specialized palliative care and oncology, specialized palliative care can support decision-making and oncology treatment by improving patients' eligibility to receive palliative antineoplastic treatment through symptom relief early in the trajectory and later in the trajectory by supporting the timely cessation of palliative antineoplastic treatment. While the latter seems to occur, the former requires an effort to ensure earlier and integrated specialized palliative care and oncology.³⁹

The European Association for Palliative Care recommends 1 team per 100,000 inhabitants,¹² but currently the regional specialized palliative care capacity is approximately half the recommended number. Palliative care is still a new discipline in many countries and further development of clinical, organizational, and academic structures is required to achieve sufficient integration.

Acknowledgements

All authors made substantial contributions to the concept, design, planning of analysis, interpretation of data, and critical revision and approved the publication.

Data management and sharing

The corresponding author may be contacted with requests.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

This study was based only on data from registers and a clinical database and had no impact on any individuals' care and

treatment. It did not require person participation or analyses of biological tissue and therefore did not require Ethics Committee approval according to Danish law. The study was approved by and stored according to the requirements of the Data Protection Agency (RH-2015-72). In analysis, the dataset was anonymous with no possibility of individual person identification.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Kirstine Skov Benthien  <https://orcid.org/0000-0002-5439-0492>
Mathilde Adersen  <https://orcid.org/0000-0001-6260-8896>

References

1. American Society of Clinical Oncology. Quality oncology practice initiative, <http://www.instituteforquality.org/qopi/measures>
2. Earle CC, Park ER, Lai B, et al. Identifying potential indicators of the quality of end-of-life cancer care from administrative data. *J Clin Oncol* 2003; 21: 1133–1138.
3. Rochigneux P, Raoul JL, Beaussant Y, et al. Use of chemotherapy near the end of life: what factors matter? *Ann Oncol* 2017; 28: 809–817.
4. Colombet I, Montheil V, Durand JP, et al. Effect of integrated palliative care on the quality of end-of-life care: retrospective analysis of 521 cancer patients. *BMJ Support Palliat Care* 2012; 2: 239–247.
5. Saito AM, Landrum MB, Neville BA, et al. The effect on survival of continuing chemotherapy to near death. *BMC Palliat Care* 2011; 10: 14.
6. Monem EA, Mehdi I, Al Bahrani BJ, et al. Utilization of systemic palliative chemotherapy at the end of life: a local experience. *J Pak Med Assoc* 2014; 64: 863–868.
7. Prigerson HG, Bao Y, Shah MA, et al. Chemotherapy use, performance status, and quality of life at the end of life. *JAMA Oncol* 2015; 1: 778–784.
8. Wright AA, Zhang B, Keating NL, et al. Associations between palliative chemotherapy and adult cancer patients' end of life care and place of death: prospective cohort study. *BMJ* 2014; 348: g1219.
9. Brom L, Onwuteaka-Philipsen BD, Widdershoven GA, et al. Mechanisms that contribute to the tendency to continue chemotherapy in patients with advanced cancer. Qualitative observations in the clinical setting. *Support Care Cancer* 2016; 24: 1317–1325.
10. Clarke G, Johnston S, Corrie P, et al. Withdrawal of anti-cancer therapy in advanced disease: a systematic literature review. *BMC Cancer* 2015; 15: 892.
11. Jones JA, Lutz ST, Chow E, et al. Palliative radiotherapy at the end of life: a critical review. *CA Cancer J Clin* 2014; 64: 296–310.
12. European Association of Palliative Care. White paper on standards and norms for hospice and palliative care in Europe: part 1. *Eur J Palliative Care* 2009; 16(6): 278–289.
13. Kaasa S, Payne S and Sjogren P. Challenges related to palliative care. *Lancet Oncol* 2011; 12: 925–927.

14. Ferrell BR, Temel JS, Temin S, et al. Integration of palliative care into standard oncology care: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2017; 35: 96–112.
15. Cherny N, Catane R, Schrijvers D, et al. European Society for Medical Oncology (ESMO) program for the integration of oncology and palliative care: a 5-year review of the designated centers' incentive program. *Ann Oncol* 2010; 21: 362–369.
16. Centeno C, Lynch T, Garralda E, et al. Coverage and development of specialist palliative care services across the World Health Organization European Region (2005–2012): results from a European Association for Palliative Care Task Force survey of 53 countries. *Palliat Med* 2016; 30: 351–362.
17. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 2010; 363: 733–742.
18. Temel JS, Greer JA, Admane S, et al. Longitudinal perceptions of prognosis and goals of therapy in patients with metastatic non-small-cell lung cancer: results of a randomized study of early palliative care. *J Clin Oncol* 2011; 29: 2319–2326.
19. Greer JA, Pirl WF, Jackson VA, et al. Effect of early palliative care on chemotherapy use and end-of-life care in patients with metastatic non-small-cell lung cancer. *J Clin Oncol* 2012; 30: 394–400.
20. Kavalieratos D, Corbelli J, Zhang D, et al. Association between palliative care and patient and caregiver outcomes: a systematic review and meta-analysis. *JAMA* 2016; 316: 2104–2114.
21. Maltoni M, Scarpi E, Dall'Agata M, et al. Systematic versus on-demand early palliative care: a randomised clinical trial assessing quality of care and treatment aggressiveness near the end of life. *Eur J Cancer* 2016; 69: 110–118.
22. Helweg-Larsen K. The Danish Register of Causes of Death. *Scand J Public Health* 2011; 39: 26–29.
23. Groenvold M, Adersen M and Hansen MB. Danish Palliative Care Database. *Clin Epidemiol* 2016; 8: 637–643.
24. Lyng E, Sandegaard JL and Rebolj M. The Danish National Patient Register. *Scand J Public Health* 2011; 39: 30–33.
25. Statistics Denmark, 2017, <http://www.statistikbanken.dk/10015>
26. Bekelman JE, Halpern SD, Blankart CR, et al. Comparison of site of death, health care utilization, and hospital expenditures for patients dying with cancer in 7 developed countries. *JAMA* 2016; 315: 272–283.
27. Kress MA, Jensen RE, Tsai HT, et al. Radiation therapy at the end of life: a population-based study examining palliative treatment intensity. *Radiat Oncol* 2015; 10: 15.
28. Button E, Chan R, Chambers S, et al. Lack of palliative mortality prediction tools for people with a hematological malignancy: call for action. *J Palliat Med* 2017; 20: 802–803.
29. Grendarova P, Sinnarajah A, Trotter T, et al. Variations in intensity of end-of-life cancer therapy by cancer type at a Canadian tertiary cancer centre between 2003 and 2010. *Support Care Cancer* 2015; 23: 3059–3067.
30. Groene O, Crosby T, Hardwick RH, et al. A population-based observational study on the factors associated with the completion of palliative chemotherapy among patients with oesophagogastric cancer. *BMJ Open* 2015; 5: e006724.
31. McCleary NJ, Dotan E and Browner I. Refining the chemotherapy approach for older patients with colon cancer. *J Clin Oncol* 2014; 32: 2570–2580.
32. Santos FN, de Castria TB, Cruz MR, et al. Chemotherapy for advanced non-small cell lung cancer in the elderly population. *Cochrane Database Syst Rev* 2015; 10: CD010463.
33. Fang P, He W, Gomez DR, et al. Influence of age on guideline-concordant cancer care for elderly patients in the United States. *Int J Radiat Oncol Biol Phys* 2017; 98: 748–757.
34. Pfeil TA, Laryionava K, Reiter-Theil S, et al. What keeps oncologists from addressing palliative care early on with incurable cancer patients? An active stance seems key. *Oncologist* 2015; 20: 56–61.
35. Hui D and Bruera E. Integrating palliative care into the trajectory of cancer care. *Nat Rev Clin Oncol* 2016; 13: 159–171.
36. Adersen M, Thygesen LC, Neergaard MA, et al. Admittance to specialized palliative care (SPC) of patients with an assessed need: a study from the Danish Palliative Care Database (DPD). *Acta Oncol* 2017; 56: 1210–1217.
37. Statistics Denmark, 2018, <https://www.dst.dk/da/Statistik/emner/befolkning-og-valg/indvandrerere-og-efterkommere/indvandrerere-og-efterkommere>
38. Gaertner J, Siemens W, Meerpohl JJ, et al. Effect of specialist palliative care services on quality of life in adults with advanced incurable illness in hospital, hospice, or community settings: systematic review and meta-analysis. *BMJ* 2017; 357: j2925.
39. Jordan K, Aapro M, Kaasa S, et al. European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. *Ann Oncol* 2018; 29: 36–43.