

Care at the end of life in Denmark

The role of underlying disease and socioeconomic position

PhD dissertation

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2022

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Acknowledgements

My sincere gratitude goes to everyone who supported and encouraged me throughout this PhD project, including the Department of Clinical Epidemiology and the undermentioned funding sources that made it possible to work on such an important health issue in an extremely inspiring working environment.

I would specifically like to express my gratitude to:

Søren Paaske Johnsen, for generously giving me the opportunity to perform my PhD studies under your great guidance. I have benefitted tremendously from your enthusiasm towards my research projects over the years and your extensive knowledge within the field of epidemiological research. You have provided thorough supervision with remarkable patience and engagement, greatly supporting the development of my research skills.

Christian Fynbo Christiansen, for your dedication towards the PhD project and my academic development and for always being available to provide advice and share your advanced epidemiological knowledge. Thank you for including me in your research group and for supporting my future plans for research.

Mette Asbjørn Neergaard, for thoughtful guidance and valuable insights into the clinical practice of palliative care – both by letting me experience the daily work in your department while I was still a medical student and for engaging in discussions of appropriate care at the end of life and challenges for the patients in this regard. Thank you also for consistently swift and encouraging feedback and for including me in your growing research network.

Jan Brink Valentin, for invaluable statistical support for the studies comprised by the PhD project.

Lars Holger Ehlers, co-author on *Study III*, for insightful advice and comments from the perspective of a healthcare economist.

Irene Petersen and Liz Sampson, for making my stay in London, working at the Research Department of Primary Care and Population Health, University College London, a memorable and rewarding experience and for being exceptionally welcoming to me and my family. Thank you for generously sharing your experience and knowledge while we were collaborating on general practice data from the United Kingdom.

Mette Nørgaard, for thoughtful advice on anything and everything at weekly iCure meetings and for much appreciated enthusiasm towards research, relentlessly adopting a positive mind set.

Bodil Hammer Bech, for meticulous supervision during my teaching activities at Aarhus University.

My kind and considerate colleagues and, particularly, my office mates over the years at the Department of Clinical Epidemiology for contributing to an inspiring and friendly environment.

My dear husband, Mads, for endless encouragement and support over the years and for always trusting that I will land on my feet, whatever I pursue.

Anne Høy Seemann Vestergaard, August 2022

Grants

The present PhD dissertation was made possible thanks to financial support from:

- The Independent Research Fund Denmark | Medical Sciences
- Fonden af 1870
- C.C. Klestrup & Hustru Henriette Klestrups Mindelegat
- Fabrikant Einar Willumsens Mindelegat
- Helga og Peter Kornings Fond

List of papers

The present PhD dissertation is based on the following three papers, which will be referred to by their Roman numerals (*Study I-III*):

Study I: Vestergaard AHS, Christiansen CF, Neergaard MA, Valentin JB, Johnsen SP.

Healthcare utilisation trajectories in patients dying from chronic obstructive pulmonary disease, heart failure or cancer: a nationwide register-based cohort study. *BMJ Open* 2021;11:e049661.

Study II: Vestergaard AHS, Christiansen CF, Neergaard MA, Valentin JB, Johnsen SP.

Socioeconomic disparity trends in end-of-life care for cancer and non-cancer patients: are we closing the gap? *Clin Epidemiol.* 2022;14:653-664.

Study III: Vestergaard AHS, Ehlers LH, Neergaard MA, Christiansen CF, Valentin JB,

Johnsen SP. Healthcare costs at the end of life for patients with non-cancer diseases and cancer in Denmark. *Submitted.*

Abbreviations

CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
DAGS	Danish Ambulatory Grouping System
DRG	Diagnosis-Related Group
EAPC	European Association for Palliative Care
ISCED	International Standard Classification of Education 2011
MeSH	Medical Subject Headings
PP	Prevalence proportion
PPR	Prevalence proportion ratio

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Introduction

A core political objective in most advanced healthcare systems is to ensure equity in health for all individuals.¹ Even so, considerable disparities exist in health status, access to healthcare and in quality of healthcare, even in healthcare systems with universal coverage.²⁻⁶ In addition, increasing life expectancy contributes to ageing populations and higher proportions of individuals suffering and dying from chronic diseases, requiring increased levels of care, which may potentially exacerbate disparities.⁷⁻¹⁰ Healthcare utilisation rates and healthcare costs are particularly high towards the end of life, as around 10% of healthcare budgets in high-income countries are spent in people's last year of life.¹¹⁻¹⁴ Thus, healthcare systems are challenged by rising resource demands and more efforts are, therefore, warranted to reduce the disparity gaps while ensuring financial sustainability.^{1,15}

Previous research has established that disparities in care at the end of life include disparities that are related to the underlying disease causing death.¹⁶⁻¹⁹ Hence, less predictable illness trajectories in patients suffering diseases other than cancer may lead to limited access to appropriate care at the end of life in these patients compared with patients suffering from cancer.^{20,21} In addition, disparities in care at the end of life according to socioeconomic position have been reported in somewhat older studies.^{18,22-25} Thus, patients with a high socioeconomic position receive care at the end of life that is superior to the care provided for patients with a low socioeconomic position.

On this basis, the present PhD dissertation intended to explore the following questions: Do illness trajectories ascertained in real-life data differ between patients dying from non-cancer diseases and patients dying from cancer? Has increasing political attention towards reducing socioeconomic disparities in health and in access to healthcare over the past years affected disparity trends in care at the end of life? Furthermore, the dissertation aimed to enhance our understanding of healthcare costs related to the end-of-life phase according to the underlying disease causing death.

The present PhD dissertation consists of ten chapters, mirroring the structure of a research paper. Thus, the first chapter provides the background for the dissertation, including a description of palliative care, inconsistencies in access to palliative care, various assessments of quality of care at the end of life and a review of the recent literature. The second and third chapters describe methods employed and results obtained in the three studies. The fourth chapter encompasses a discussion of relevant findings from the three studies in the context the existing literature and presents some methodological considerations. The fifth and sixth chapters present main conclusions and perspectives. The final chapters comprise summaries of the dissertation in English and Danish, references and appendices providing the full versions of the research papers reporting the three studies.

1. Background

1.2 Palliative care

Advancing medical technologies in the second half of the twentieth century increasingly produced new ways of prolonging life, which also extended the process of dying.²⁶ People suffering from life-threatening illness have a considerable need for patient-centred care. Thus, as a reaction against the life-prolonging medical advances, which perceived death as a medical failure, modern palliative care developed.²⁷ Subsequently, palliative care has grown through the hospice philosophy established in the United Kingdom in the 1960-1980 period, focusing on enhancing the quality of the remaining life through patient-centred holistic care.²⁸ Palliative care has gained growing acceptance, and in 1987 it became recognised as a medical subspecialty in the United Kingdom.²⁶ In Denmark, the first hospice was founded in 1992; this was followed by a steadily mounting number of hospices, specialised palliative care teams and specialised palliative care hospital in-bed units. However, palliative care has still to be recognised as a medical specialty in Denmark to this day.²⁹

Historically, the hospice movement and palliative care was developed focusing on symptom management for cancer patients; still, as far back as 1998, awareness was rising among specialists in palliative care that patients dying from non-cancer diseases also had considerable palliative care needs.³⁰ Accordingly, the World Health Organization's definition of palliative care was revised in 2002, emphasising that palliative care is pertinent for all life-threatening illnesses.

The definition now reads:

*"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."*²⁷

In Denmark, the Danish Health Authority published its first recommendations for palliative care in 1999, solely covering cancer patients who failed to respond to curatively intended treatment. These recommendations were in line with the World Health Organization's definition at the time (published in 1989).³¹ In 2011, the recommendations of palliative care in Denmark were revised in accordance with the World Health Organization's aforementioned definition from 2002, stating that palliative care should be provided for all patients suffering from life-threatening illness.³² Subsequently, in 2017, the Danish Health Authority published recommendations emphasising the need to broaden attention to cover all patients suffering from life-threatening illness.³³

1.2.1 End-of-life care versus palliative care

End-of-life care, including hospice care, is an important part of palliative care. It usually refers to the care provided for patients during their evident terminal phase of life, typically within the last few days, weeks or months of life.^{34 35} In contrast, palliative care may be applicable at any stage of a serious illness alongside life-prolonging curative treatment (Figure 1). Thus, palliative care can be provided across various healthcare settings.³⁵ Ideally, all health professionals should be capable of offering appropriate palliative care for patients with any advanced or terminal illness.^{33,36}

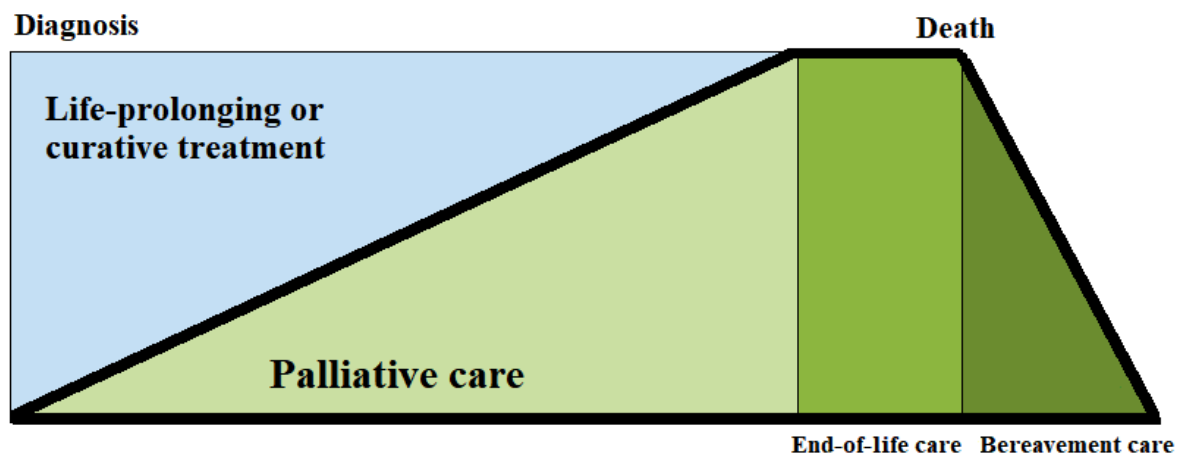


Figure 1 Palliative care from diagnosis to the end of life.

1.2.2 Levels of palliative care

Three levels of palliative care expertise were proposed by the European Association for Palliative Care (EAPC), an organisation, established in 1988, aiming to increase the awareness and development of palliative care and to promote education and research.³⁷ Thus, the three-tier framework of palliative care practice encompasses the following three levels, also presented in Figure 2: 1) Palliative care approach: integration of basic palliative care principles in general care settings by health professionals only occasionally treating patients suffering from terminal illness, including general practitioners, general hospital staff and homecare providers; 2) General palliative care: basic palliative care provision by health professionals treating patients with life-threatening illness who are often involved in palliative care but not as the main focus of their work, including primary care professionals and medical specialists, e.g. oncologists or geriatricians; 3) Specialist palliative care: specialised services in palliative care provided for patients with complex needs by multidisciplinary teams of highly qualified health professionals for whom palliative care is the main focus of their work, covering palliative care teams, palliative care hospital units and hospices.³⁶ The “palliative care approach” level and “general palliative care” level are often combined and simply described as “generalist palliative care”.

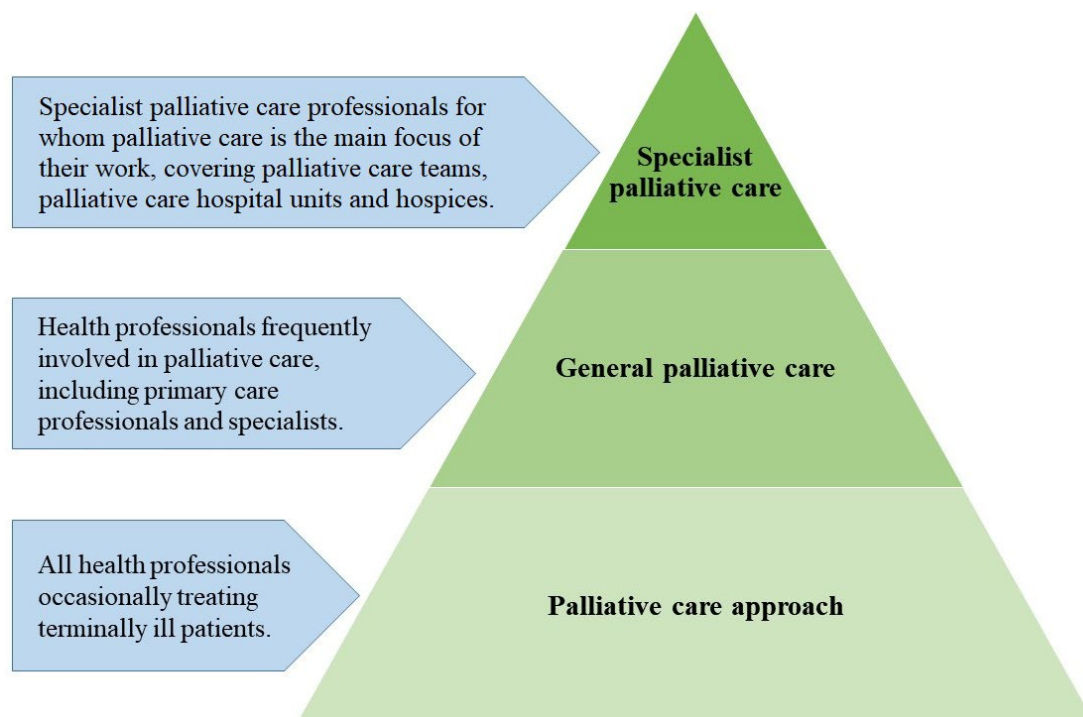


Figure 2 Levels of palliative care.

1.3 Access to palliative care

The EAPC recommends 80 to 100 specialist palliative care beds per million inhabitants, including beds in palliative care units and hospices.³⁸ However, substantial variability exists in the organisation and development of palliative care between countries as considerable structural and financial differences affect the implementation of palliative care.³⁹ Many high-income countries fail to comply with the level of service proposed by the EAPC. In Denmark, only a total of 347 specialist palliative care beds were available in 2019, corresponding to approximately 60 beds per million inhabitants.^{40,41} To comply with the level of service proposed by the EAPC, the number should be approximately 465-580 specialist palliative care beds in Denmark in 2019 population figures.⁴²

Worldwide, around 45% of the people who died in 2015 suffering from one of twenty selected health conditions experienced symptoms associated with serious health-related suffering, including physical (e.g. pain, fatigue, constipation and shortness of breath) and psychological suffering (e.g. anxiety, delirium and depression) and were presumably in need of palliative care late in life.¹⁶ However, it has been estimated that only approximately 14% of patients who are in need of palliative care receive it, and drivers of the need for palliative care are continuously growing due to population ageing.⁴³ Furthermore, extensive inconsistencies exist in access to palliative care, including inferior access for patients dying from non-cancer diseases and patients with a low socioeconomic position.^{16-19,22-25}

1.3.1 Different illness trajectories for different diseases

Although numerous studies have suggested an equivalent symptom burden in patients dying from non-cancer diseases and from cancer⁴⁴⁻⁴⁷ and increasing evidence of efficacious palliative care for patients with conditions other than cancer,⁴⁸⁻⁵⁵ palliative care is still predominantly offered to patients with advanced cancer.¹⁶⁻¹⁹ The reason for this inconsistency is probably multi-faceted but may, in part, be explained by reference to financial strains associated with extending palliative care to other patients than patients with cancer, shortage of palliative care health professionals with expertise in non-cancer diseases and weak evidence concerning appropriate models of care.⁵⁶ Difficulties in predicting decline in illness trajectories in patients with non-cancer diseases have also been suggested as a potential barrier to the extension of palliative care among patients suffering from other conditions than cancer.

In 1968, Glaser and Strauss described three distinct trajectories of dying, covering expected deaths, entry-re-entry deaths and surprise deaths.²¹ More recent studies have proposed a model with three different illness trajectories characterised by a different course of decline in physical health for people with progressive chronic diseases, including “terminal illness”, “organ failure” and “frailty” (Figure 3).^{20,57,58}

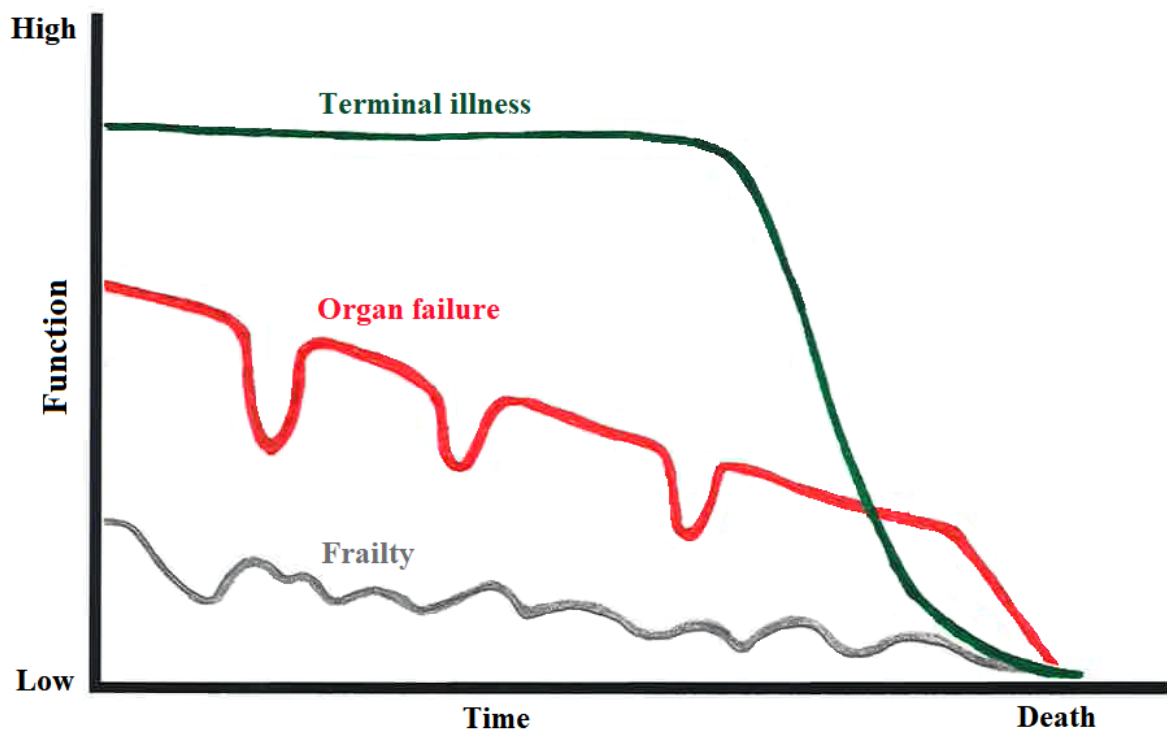


Figure 3 Model of illness trajectories for people suffering from progressive chronic illness. Adapted from Lynn and Adamson (2003)⁵⁸ and Murray et al.²⁰

For people with terminal illness, typically cancer, the illness trajectory is characterised by a fairly predictable and stable decline in physical health and evident decline in the terminal phase. In this manner, the illness trajectory of “terminal illness” matches the traditional palliative care approach, historically focusing on symptom management for cancer patients in the last weeks or months of life.^{20,21} The illness trajectory of “organ failure” represents the gradual decline in physical health in patients suffering from, e.g., chronic obstructive pulmonary disease (COPD) or heart failure. The slope of the “organ failure” illness trajectory is characterised by acute exacerbations in the underlying disease followed by incomplete recovery. As each exacerbation of the underlying disease may cause death, the prediction of death and planning of appropriate care is difficult. The third illness trajectory, coined “frailty”, is characterised by a progressively dwindling physical capability until death occurs in patients experiencing generalised frailty or dementia.^{20,21,57}

1.3.2 Socioeconomic position

Rooted in the concept of equity in health, it remains an essential health priority in tax-financed healthcare systems with universal coverage to ensure that individuals in equal need have equal opportunities to access healthcare services and to receive equal quality of healthcare.¹ However, in terminally ill patients, socioeconomic position has been reported to be associated with the type and intensity of care provided at the end of life.²²⁻²⁵ Thus, a low socioeconomic position is associated with inferior care, including an increased risk of dying in hospital, being acutely admitted to hospital in the terminal phase and not receiving specialist palliative care.²²⁻²⁵

A widely acknowledged understanding of socioeconomic position refers to an individual's position in society and in the social hierarchy as an aggregate measure of resources. Thus, people enter social hierarchies with different levels of control over resources, power and prestige which then contribute to the emergence of social disparities.^{59,60}

Socioeconomic position is often approximated by income and education. Income is the most direct measure of material resources and refers to any earnings received, e.g. salaries, social security, rents and dividend.⁶¹ Typically, income is measured as household income, which is useful since not all individuals in a household have the same flow of earnings. Using this measure, however, assumes that all individuals of the family have an even distribution of income according to their needs.⁶¹ Education is another frequently used indicator of socioeconomic position, reflecting cognitive functioning. Thus, education may also, to some extent, affect people's ability to navigate the healthcare system. Level of education is either measured as years of completed education or as the highest attained educational level; and it is a fairly constant indicator in adulthood, to some extent predicting future employment and income.⁶¹

However, socioeconomic position is a multi-faceted concept which cannot be completely captured by measures of, e.g., income and education. Thus, additional non-medical factors, all potentially affected by socioeconomic position, may play a role in the explanation of social disparities in health status, access to healthcare services and in quality of healthcare. Non-medical factors encompass, e.g., individual behaviour, environmental factors and psychological factors.⁶⁰ In sum, the least well-off people may be in a less favourable position to navigate the healthcare system, to obtain good quality of care and to ensure that their needs are met. At the end of life, in particular, receiving high-quality care may improve the quality of the remaining life by treatment of pain, symptoms and emotional stress of the life-threatening illness, and by provision of emotional and social support to patients and their families (Figure 4).

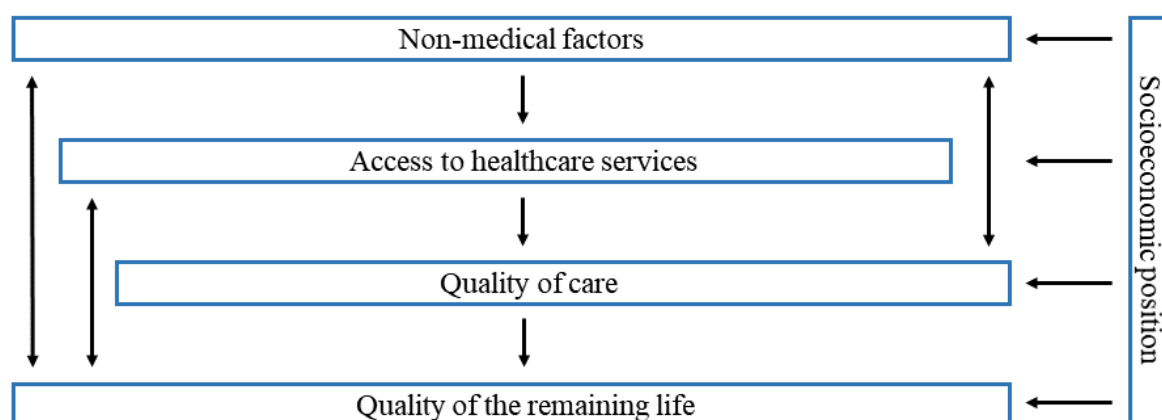


Figure 4 Associations between socioeconomic position and care at the end of life.

1.4 Quality of care at the end of life

Measuring quality of care at the end of life remains essential to improve clinical care initiatives for patients with advanced or terminal illness and also to drive research and health policy decisions.⁶²⁻⁶⁵

The Danish Palliative Care Database was established in 2010 to monitor and evaluate the clinical quality of specialist palliative care in Denmark. The database has published annual reports on various quality indicators since its inception.⁶⁶ The database encompasses information on all patients referred to and/or admitted to specialist palliative care in Denmark, including hospital-based specialist palliative care teams and units as well as hospices. The quality indicators measured in the database are: 1) Proportion of relevant patients referred to specialist palliative care who receive it (82% in 2020); 2) Proportion of referred patients with ten or fewer days between referral and admission (76% in 2020); 3) Proportion of decedents who died from cancer and received specialist palliative care, including hospice care (49% in 2020); 4) Proportion of patients answering the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-

Core-15-Palliative Care (61% in 2020);⁶⁷ 5) Proportion of patients receiving specialist palliative care who were discussed at a multidisciplinary conference (69% in 2020).⁶⁶

During 2020, only 8% of patients registered in the Danish Palliative Care Database and receiving specialist palliative care were dying from diseases other than cancer.⁶⁸ Thus, in order to explore quality of care at the end of life from administrative data across underlying diseases, various measures, corresponding to the indicators evaluated in the Danish Palliative Care Database, have previously been developed and reported.⁶⁹⁻⁷¹ These measures assess metrics of high-intensity care intended to prolong life rather than improve quality of life. The measures include hospital admissions, emergency room visits and intensive care unit admissions at the end of life, among others.⁶⁹⁻⁷¹ Accordingly, death during a hospital admission is regarded as a proxy for inferior quality of care at the end of life since home death is considered more appreciable.⁷² Thus, high-intensity care is regarded inappropriate towards the end of life, and information on high-intensity care utilisation is, therefore, valuable when examining quality of care at the end of life across underlying diseases from administrative data, regardless of the palliative care received.

1.5 Literature review

Three separate literature reviews were conducted to review the literature describing illness trajectories at the end of life (*Study I*), temporal trends in socioeconomic disparities in care at the end of life (*Study II*) and healthcare costs at the end of life according to the underlying disease causing death (*Study III*). In May-June 2022, MEDLINE (PubMed) was used to search for recently published papers by completing a Medical Subject Headings (MeSH) search and a free-text search (MEDLINE search queries are provided in Tables 1-3). The searches were restricted to observational studies, clinical studies, clinical trials, systematic reviews and meta-analyses published in English, Danish, Swedish or Norwegian from 1995 onwards.

The same procedure was followed in all three literature reviews. First, databases were searched followed by an initial screening of titles and abstracts and any relevant full-text papers were retrieved. Next, the retrieved full-text papers were evaluated for eligibility, including assessment of data extraction and risk of bias. Subsequently, the reference lists of the retrieved full-text papers were inspected to identify additional relevant papers. The identified literature included in the present PhD dissertation is summarised in Tables 1-3.

1.5.1 End-of-life illness trajectories

Previous studies, presented in Table 1, have reported varying results when charting different end-of-life illness trajectories. Comparing various non-cancer diseases with cancer, the studies explored

illness trajectories associated with decline in physical health as reflected in various metrics, including activities of daily living, disability, performance status and healthcare costs (Table 1).

Assessing functional impairment, covering activities of daily living, disability and performance status, as measures of physical health in patients approaching death, Teno et al. (2001),⁷³ Lunney et al. (2003),⁷⁴ Chen et al. (2007)⁷⁵ and Stolz et al. (2021)⁷⁶ studied patterns of illness trajectories in different regions of the United States. They all found that the patterns proposed in the concept of illness trajectories originally put forward by Glaser and Strauss were consistent with the illness trajectories of patients dying from cancer and organ failure, and in the study by Lunney et al. (2003)⁷⁴ also sudden death and frailty.²¹ In contrast, in a large Australian dataset, Morgan et al. (2019)⁷⁷ compared functional impairment measured by performance status in patients receiving specialist palliative care and found comparable patterns of gradual functional decline before death with a rapidly declining terminal phase in patients dying from cancer, organ failure or cardiovascular diseases. Correspondingly, Barnes-Harris et al. (2021)⁷⁸ found similarly shaped trajectories of functional decline when restricting analyses to patients dying from lung cancer and non-malignant respiratory diseases in specialist palliative care in Australia with a rapidly declining performance status being observed in the last month of life.

Some previous studies have attempted to chart illness trajectories by assessing the pattern of healthcare costs in the months preceding death according to the underlying disease causing death.^{79,80} Thus, Sullivan et al. (2017)⁷⁹ studied monthly healthcare costs within the last 24 months of life in the United States among patients dying from chronic diseases, system failure or cancer. Similarly, Luta et al. (2020)⁸⁰ studied monthly inpatient healthcare costs within the last 12 months of life in the United Kingdom among patients dying from cancer, respiratory diseases, circulatory diseases and other diseases. Both studies found increasing healthcare cost trajectories and a steep increase in the last months of life, following almost identical shapes for all of the diseases studied.

Various factors may have contributed to the conflicting results reported in previous studies. Hence, most studies are rather small, ranging from 553 to 4,190 included decedents, and are, therefore, susceptible to random variation. It should be noted that the three larger studies by Luta et al. (2020),⁸⁰ Morgan et al. (2019)⁷⁷ and Barnes-Harris et al. (2021),⁷⁸ showing similar patterns for patients dying from non-cancer diseases and from cancer, are all relatively recent. The consistency of the findings in these studies may, therefore, both reflect a higher statistical precision and recent years' developments in disease-modifying therapies that may have changed the trajectories. However, the study by Luta et al. (2019)⁸⁰ was not specifically aiming to chart illness trajectories, which hampers the interpretation to some extent. Furthermore, Barnes-Harris et al. (2021)⁷⁸ focused on lung cancer and non-malignant respiratory diseases that may have a more similar course of disease and symptom burden than the overall cancer versus non-cancer comparison made in other studies. Moreover, Barnes-Harris et al. (2021)⁷⁸ and Morgan et al. (2019)⁷⁷ only included patients

receiving specialist palliative care, and their findings may, therefore, not be fully representative of all terminally ill patients.

Therefore, insights are needed from large nationwide studies specifically exploring the illness trajectories of all patients dying from various types of non-cancer diseases and comparing these trajectories with those of patients dying from cancer in the years leading up to death in a contemporary setting.

1.5.2 Socioeconomic disparity trends in end-of-life care

Socioeconomic disparities in care at the end of life have been reported across underlying diseases, favouring patients with a high socioeconomic position.²²⁻²⁵ However, extant knowledge on potential changes over time is sparse. Table 2 presents the few previous studies exploring temporal trends in socioeconomic disparities in care at the end of life, particularly regarding place of death and receipt of palliative care by various socioeconomic measures.

In unadjusted analyses, Higginson et al. (1999) examined the proportion of patients suffering from cancer who died at home in England according to an underprivileged area score, a composite measure of socioeconomic position including, e.g., employment, car ownership and overcrowding.⁸¹ They established that marked socioeconomic disparities existed. These disparities remained largely stable during the 1985-1994 period.⁸¹ Specifically, patients residing in the least deprived areas were more likely to die at home than were patients residing in the most deprived areas.⁸¹ Adjusting for the effects of various confounders, Gao et al. (2013) further explored cancer decedents in England from 1993 through 2010. They found that the least deprived cancer patients were only slightly more likely to die at home or in hospice than the most deprived cancer patients. Furthermore, the authors found that this minor socioeconomic disparity gap remained constant during the 1993-2010 period.⁸² In 2014, using an area deprivation score in England in the 1984-2010 period, Gao et al. reported similar results regarding place of death when separately examining decedents dying from cancer and non-cancer diseases.⁸³ In contrast, while solely examining hospice deaths in England in 1993-2012, Sleeman et al. (2017)⁸⁴ found more pronounced socioeconomic disparities in hospice deaths, favouring patients with a high socioeconomic position, and that socioeconomic disparities have increased in recent years despite an overall increase in hospice deaths.⁸⁴

In recent years, evident socioeconomic disparities in place of death were also found by Barret et al. in England (2017).⁸⁵ Including decedents of all ages and underlying diseases in England from 2001 through 2012, Barret et al. (2017) established from unadjusted analyses that patients from the most deprived areas had a greater risk of dying in hospital.⁸⁵ Moreover, the authors suggested that the socioeconomic disparity gap remained constant throughout the 2001-2012 period despite an overall reduction in hospital deaths.⁸⁵ In line with these findings, Mondor et al. (2020) studied adult

decedents of all causes in Canada and found persisting socioeconomic disparities in place of death and receipt of palliative care from 2009 through 2016.⁸⁶ Hence, results from unadjusted analyses showed that patients with a low neighbourhood-level socioeconomic position remained less likely to die at home and to receive palliative care before death.⁸⁶

Similarly, in the United States, Khan et al. (2022) found persisting socioeconomic disparities when exploring specialist palliative care utilisation during hospital admission by income level from unadjusted analyses of patients diagnosed with acute ischaemic stroke from 2002 through 2017.⁸⁷

Thus, varying levels of socioeconomic disparities in care at the end of life have been suggested in a number of studies conducted in healthcare systems that differ with respect to organisation and financing but also in regard to the structure and development of palliative care. Thus, remaining seemingly constant over the recent years, the trend is that patients with a low socioeconomic position tend to receive care at the end of life that is inferior to care received by those with a high socioeconomic position, particularly regarding place of death and receipt of palliative care. However, the presented knowledge base consists predominantly of studies reaching back several decades.⁷⁻⁹ Hence, it remains unclear whether health policy attention directed at reducing socioeconomic disparities in health and in access to healthcare services may have affected disparities in recent years.¹ It also remains unclear whether socioeconomic disparities have been exacerbated by ageing populations and increasing care demands, especially within a healthcare system with universal coverage.⁷⁻⁹ Furthermore, a remarkable paucity exists regarding information on socioeconomic disparity trends in care at the end of life with inclusion of a broader spectrum of healthcare services and consideration of potential confounding factors. Moreover, as it is well-established that patients dying from non-cancer diseases receive poorer palliative care at the end of life than patients dying from cancer, knowledge is also needed to establish whether socioeconomic disparities may be linked to the underlying disease.^{19,20}

1.5.3 Healthcare costs at the end of life

The escalating resource demands caused by ageing populations are challenging existing health policies aiming to control healthcare-related costs and ensure prioritisation of limited resources.^{1,7-9} Furthermore, healthcare costs at the end of life may vary by the chronic disease causing death. Hence, although conducted for different purposes, the previous studies presented in Table 3 have rather consistently suggested that patients dying from various non-cancer diseases incur considerably lower healthcare costs at the end of life than patients dying from cancer.^{79,80,88-93} Yet, most studies adopted mixed economic perspectives when examining costs related to care at the end of life, covering costs from a healthcare sector perspective (e.g. costs of hospital, general practice and medicine), while also including some, but not all, public sector costs (e.g. homecare

costs).^{79,90,92-95} Furthermore, only few studies can be identified that have explored the patterns of various healthcare costs by the disease causing death.^{80,88,89}

From the same cohort of decedents in Australia, Langton et al. (2016)⁸⁸ and Reeve et al. (2018)⁸⁹ examined costs of care at the end of life from a healthcare sector perspective in the six months leading up to death. Both studies found that total healthcare costs at the end of life were lower in patients who were dying from non-cancer diseases than in patients dying from cancer and that costs of hospital contacts primarily drove up costs.^{88,89} Furthermore, the unadjusted relative difference in mean monthly costs between patients diagnosed with non-cancer diseases and patients diagnosed with cancer diminished in the last month of life. Accordingly, Luta et al. (2020) found similar results when examining healthcare costs from a healthcare sector perspective in patients dying from non-cancer diseases and patients dying from cancer in England in the year leading up to death.⁸⁰

Still, knowledge is warranted that identifies the patterns of costs of care as death approaches within a healthcare system with universal coverage, comparing patients dying from non-cancer diseases and patients dying from cancer, while also considering potential confounding factors. By applying a cost-of-illness methodology and adopting a healthcare sector perspective, the economic burden of end-of-life healthcare services may be quantified, and any variation in the allocation of resources by the underlying disease causing death may be illustrated. This may provide information to be considered when developing more efficient healthcare planning in healthcare systems specifically aiming to facilitate equity in healthcare utilisation.^{96,97} Thus, as part of the efforts aiming to increase financial sustainability in healthcare, it is crucial to enhance our understanding of the patterns of healthcare costs related to care at the end of life according to the underlying disease causing death.

Table 1 Summary of the existing literature describing illness trajectories at the end of life.

Illness trajectories at the end of life			
Author, journal, year	Design, setting, data sources, period	Population, main outcome measures of interest	Results
Teno <i>et al.</i> , ⁷³ Journal of Palliative Medicine, 2001	<ul style="list-style-type: none"> - Cohort study - United States - Death certificates and National Followback Survey - 1993 	<ul style="list-style-type: none"> - Decedents of all ages dying from cancer (n=1,655), congestive heart failure (n=291), diabetes (n=157), cerebral vascular accident (n=452) and COPD (n=1,059). - Information on activities of daily living and mobility for the year leading up to death obtained from interviews with bereaved next of kin. 	<ul style="list-style-type: none"> - Age-adjusted activities of daily living score and proportion of patients with trouble transferring out of bed or chair by month before death showed a steep functional decline in the last months of life in cancer patients but slower gradual functional decline in non-cancer populations.
Lunney <i>et al.</i> , ⁷⁴ Journal of the American Medical Association (JAMA), 2003	<ul style="list-style-type: none"> - Cohort study - Four United States regions - Data from the Established Populations for Epidemiologic Studies of the Elderly - 1981-1987 	<ul style="list-style-type: none"> - Decedents aged ≥ 65 years with a diagnosis of sudden death (n=649), cancer (n=897), organ failure (n=817) and frailty (n=837), who provided baseline interviews for the year leading up to death. - Self- and proxy-reported information on activities of daily living for the year leading up to death. 	<ul style="list-style-type: none"> - Patterns of monthly activities of daily living scores in the year leading up to death showed a stable functional status for patients with cancer and a clear decline in the last three months of life. - Both the organ failure and frailty populations recorded gradual decline in functional status during the final year of life.
Chen <i>et al.</i> , ⁷⁵ Journal of Gerontology, 2007	<ul style="list-style-type: none"> - Cohort study - Boston, Massachusetts, United States - Hebrew Senior Life medical records - 1994-2004 	<ul style="list-style-type: none"> - Decedents aged ≥ 65 years who lived in long-term care for \geqone year and died from cancer (n=63), organ failure (n=370) (congestive heart failure, COPD) or dementia (n=314). - Quarterly scores of activities of daily living score for the year leading up to death. 	<ul style="list-style-type: none"> - Age- and sex-adjusted activities of daily living score for patients with cancer and organ failure showed a gradually declining functional status and a sharp decline in the three months leading up to death; sharpest for patients with cancer. - Functional status of patients with dementia declined gradually during the last year of life.

Stolz <i>et al.</i> , ⁷⁶ Journals of Gerontology: Medical Sciences, 2021	<ul style="list-style-type: none"> - Cohort study - Greater New Haven, Connecticut, United States - The Yale Precipitating Events Project (PEP Study) - 2013-2018 	<ul style="list-style-type: none"> - Respondents in the PEP Study aged ≥ 70 dying from cancer (n=105), organ failure (n=135), frailty (n=178), dementia (n=131), sudden death (n=14) or other conditions (n=74). - Monthly disability assessments based on the need for personal assistance for activities of daily living for the five years leading up to death. 	<ul style="list-style-type: none"> - Patients with cancer had gradually increasing disability and a steep terminal increase at six months before death. - Patients with organ failure, frailty and dementia also experienced increasing disability but no clear terminal phase during the five-year period leading up to death.
Sullivan <i>et al.</i> , ⁷⁹ Journal of Nursing Administration, 2017	<ul style="list-style-type: none"> - Cohort study - United States - Medicaid data (Centers for Medicare & Medicaid Services) - 2008 	<ul style="list-style-type: none"> - Medicare beneficiaries dying from chronic disease (n=900) (chronic lung disease, diabetes, coronary artery disease, atherosclerosis and other neurology and behavioural disorders), system failure (n=687) (cirrhosis, multiple sclerosis, kidney failure, heart failure, cardiopulmonary disease) or cancer (n=243). - Monthly Medicare expenditures for the 24 months leading up to death, based on, e.g., claims for inpatient, outpatient, homecare and hospice claims. 	<ul style="list-style-type: none"> - Trajectories of Medicare expenditures remained relatively stable until precipitously increasing, regardless of underlying disease category during the last three months of life.
Luta <i>et al.</i> , ⁸⁰ British Medical Journal Supportive & Palliative Care, 2020	<ul style="list-style-type: none"> - Cohort study - England - Clinical Practice Research Datalink, Hospital Episode Statistics and Office for National Statistics death registration data - 2010-2017 	<ul style="list-style-type: none"> - Decedents aged ≥ 60 dying from cancer (n=25,406), respiratory diseases (n=16,304), circulatory diseases (n=29,378) and other diseases (n=37,422). - Total costs of in- and outpatient hospital care, primary care contacts (general practice consultations) and dispensed prescription medicine in the year leading up to death. 	<ul style="list-style-type: none"> - Gradually increasing trajectories of hospital costs with almost identical shapes for the four patient populations in the year leading up to death.

Morgan <i>et al.</i> , ⁷⁷ Palliative Medicine, 2019	<ul style="list-style-type: none"> - Cohort study - Australia - The Australian National Palliative Care Outcomes Collaboration - 2013-2015 	<ul style="list-style-type: none"> - Decedents of all ages dying in specialist palliative care from cancer (n=39,783), solid organ failure (n=4,038), neurological conditions (n=2,500), cardiovascular disease (n=2,369) or dementia (n=1,336) with one or more recorded Australia-modified Karnofsky Performance Status scores. - Functional status measured by the Australia-modified Karnofsky Performance Status Scale at each clinical contact within the four months preceding death. 	<ul style="list-style-type: none"> - The shape of trajectories of functional decline at the end of life were similar for patients dying from cancer, organ failure or cardiovascular diseases and were characterised by a rapid decline in the last month of life. - Trajectories of functional decline in patients dying from neurological conditions or dementia remained stable until the last two weeks of life in which they decreased.
Barnes-Harris <i>et al.</i> , ⁷⁸ Thorax (British Medical Journal), 2021	<ul style="list-style-type: none"> - Cohort study - Australia - The Australian National Palliative Care Outcomes Collaboration - 2013-2018 	<ul style="list-style-type: none"> - Decedents of all ages dying in specialist palliative care from lung cancer (n=18,586) and chronic respiratory disease (n=4,279) with one or more recorded Australia-modified Karnofsky Performance Status scores. - Functional status measured by the Australia-modified Karnofsky Performance Status Scale at each clinical contact within the four months preceding death. 	<ul style="list-style-type: none"> - Trajectories of functional decline were similar in the two patient populations, climbing rapidly in the last month of life.

MEDLINE search query (Study I):

((("Death"[Mesh]) OR ("Terminally Ill"[Mesh]) OR ("Palliative Care"[Mesh]) OR ("Terminal Care"[Mesh]) OR ("Mortality"[Mesh])) AND "trajector*" AND "cancer" AND (Danish[Filter] OR English[Filter] OR Norwegian[Filter] OR Swedish[Filter]) AND (1995:2022[pdat]))

Table 2 Summary of the existing literature describing temporal trends in socioeconomic disparities in care at the end of life.

Temporal trends in socioeconomic disparities in care at the end of life			
Author, journal, year	Design, setting, data sources, period	Population, socioeconomic measures, main outcome measures of interest	Results
Higginson <i>et al.</i> , ⁸¹ Journal of Public Medicine, 1999	- Cohort study - England - Office for National Statistics - 1985-1994	- Cancer decedents of all ages (n=1.3 million). - Underprivileged area score, including, e.g., employment, car ownership and overcrowding. - Temporal trends in home deaths.	- The least deprived were more likely to die at home than were the most deprived and this remained constant during 1985-1994 (unadjusted analyses).
Gao <i>et al.</i> , ⁸² PLOS Medicine, 2013	- Cohort study - England - Office for National Statistics - 1993-2010	- Cancer decedents aged ≥ 25 years (n=2,281,223). - Index of multiple deprivation (area-specific deprivation measure, including, e.g., income, employment and education). - Temporal trends in place of death.	- The least deprived were somewhat more likely to die in hospice or at home than were the most deprived, and this stayed relatively stable during 1993-2010 (adjusted analyses).
Gao <i>et al.</i> , ⁸³ Health Services and Delivery Research, 2014	- Cohort study - England - Office for National Statistics - 1984-2010	- Decedents aged ≥ 25 years dying from cancer (n=3,468,284) or non-cancer diseases (n=9,679,266). - Index of multiple deprivation (area-specific deprivation measure, including, e.g., income, employment and education). - Temporal trends in place of death.	- In 1984-1992, the least deprived patients with cancer and non-cancer diseases were more likely to die at home than were the most deprived, but in 2001-2010 no socioeconomic gradient was observed.
Sleeman <i>et al.</i> , ⁸⁴ Palliative Medicine, 2016	- Cohort study - England - Office for National Statistics - 1993-2012	- Decedents of all causes aged ≥ 25 years (n=446,615) dying in inpatient hospice units. - Index of multiple deprivation (area-specific deprivation measure, including, e.g., income, employment and education). - Temporal trends in inpatient hospice death.	- Socioeconomic disparities in hospice death increased over time since the least deprived patients were increasingly more likely to die in hospice compared with the most deprived. - Annual number of hospice deaths increased over time.

Barratt <i>et al.</i> , ⁸⁵ Journal of Health Services Research & Policy, 2017	<ul style="list-style-type: none"> - Cohort study - England - Office for National Statistics - 2001-2012 	<ul style="list-style-type: none"> - Decedents of all causes and ages (n=5,260,871). - Index of multiple deprivation (area-specific deprivation measure, including, e.g., income, employment and education). - Temporal trends in hospital deaths. 	<ul style="list-style-type: none"> - The most deprived were more likely to die in hospital and this remained constant during 2001-2012 (unadjusted analyses). - The proportion of patients dying in hospital decreased during the study period (from 50% to 44%).
Mondor <i>et al.</i> , ⁸⁶ Palliative Medicine, 2020	<ul style="list-style-type: none"> - Cohort study - Ontario, Canada - Office of the Registrar General vital statistics database - 2009-2016 	<ul style="list-style-type: none"> - Decedents of all causes aged ≥ 18 years (n=729,290). - Neighbourhood-level socioeconomic position. - Temporal trends in place of death and receipt of physician-based palliative care, including both generalist and specialist care. 	<ul style="list-style-type: none"> - Patients with a low neighbourhood-level socioeconomic position remained less likely to die in the community and receive palliative care before death during 2009-2016 (unadjusted analyses). - The socioeconomic disparity gap declined slightly for community deaths. - The proportion of patients dying in the community and of patients receiving palliative care before death increased during the study period.
Khan <i>et al.</i> , ⁸⁷ Cardiovascular Revascularization Medicine, 2022	<ul style="list-style-type: none"> - Cohort study - United States - The National Inpatient Sample - 2002-2017 	<ul style="list-style-type: none"> - Hospitalised patients aged ≥ 18 years with any diagnosis code of acute ischaemic stroke (n=9,542,169 hospitalisations). - Median income of patients' address by zip code. - Temporal trends in specialist palliative care utilisation during hospitalisation. 	<ul style="list-style-type: none"> - Patients with the highest income level were more likely to receive specialist palliative care than were patients with low income level, and this remained relatively stable during 2002-2017 (unadjusted analyses). - Specialist palliative care encounters increased from 0.5% of the patients in 2002 to 8.3% in 2017.

MEDLINE search query (Study II):

((("Death"[Mesh]) OR ("Terminal Care"[Mesh]) OR ("Palliative Care"[Mesh])) AND (("Socioeconomic Factors"[Mesh]) OR "depriv*" OR "socioeconomic") AND ("trend*") AND (Danish[Filter] OR English[Filter] OR Norwegian[Filter] OR Swedish[Filter])) AND (1995:2022[pdat]))

Table 3 Summary of the existing literature describing healthcare costs at the end of life by cause of death

Healthcare costs at the end of life by cause of death			
Author, journal, year	Design, setting, data sources, period	Population, main outcome measures of interest	Results
Langton <i>et al.</i> , ⁸⁸ British Journal of Cancer, 2016	<ul style="list-style-type: none"> - Cohort study - New South Wales, Australia - Australian Government Department of Veterans' Affairs clients and New South Wales Central Cancer Registry - 2005-2008 	<ul style="list-style-type: none"> - Decedents aged ≥ 65 dying from cancer (n=4,271) and non-cancer diseases (n=3,072). - Costs of hospital admissions, emergency room visits, dispensed prescription medicine and clinician visits and procedures within the last six months of life. 	<ul style="list-style-type: none"> - Mean total costs in the six months leading up to death were AUD\$ 30,001 per patient with cancer and AUD\$ 26,131 per patient with non-cancer disease, mainly driven by hospital costs (80%). - Adjusted incidence rate ratio: 1.06 (95% confidence interval: 1.02; 1.11). - The unadjusted relative difference between patient populations diminished in the last month of life.
Reeve <i>et al.</i> , ⁸⁹ BioMed Central Palliative Care, 2018	<ul style="list-style-type: none"> - Cohort study - New South Wales, Australia - Australian Government Department of Veterans' Affairs clients; New South Wales Central Cancer Registry - 2005-2009 	<ul style="list-style-type: none"> - Decedents aged ≥ 65 dying from cancer (n=9,862) and non-cancer diseases (n=15,483). - Costs of hospital admissions, emergency room visits, dispensed prescription medicine and clinician visits and procedures within six months before death. 	<ul style="list-style-type: none"> - Mean total costs in the six months leading up to death were AUD\$ 28,091 per patient with cancer and AUD\$ 19,696 per patient with non-cancer disease, mainly driven by hospital costs (80%). - Adjusted incidence rate ratio: 1.27 (95% confidence interval: 1.24; 1.30). - The unadjusted relative difference between patient populations diminished in the last month of life.
Luta <i>et al.</i> , ⁸⁰ British Medical Journal Supportive & Palliative Care, 2020	<ul style="list-style-type: none"> - Cohort study - England - Clinical Practice Research Datalink, Hospital Episode Statistics and Office for National Statistics death registration data - 2010-2017 	<ul style="list-style-type: none"> - Decedents aged ≥ 60 dying from cancer (n=25,406) and non-cancer diseases (n=83,104). - Total monthly costs of in- and outpatient hospital care, primary care contacts (general practice consultations) and dispensed prescription medicine in the year leading up to death. 	<ul style="list-style-type: none"> - Mean total costs in the year leading up to death were highest for patients dying from cancer (£8,994) and patients dying from COPD (£9,373). - Hospital costs accounted for over 60% of total costs, regardless of the underlying disease. - The unadjusted relative difference in hospital costs between patients with non-cancer diseases and cancer was diminished during the last month of life due to more rapid increase of costs in patients dying from non-cancer diseases.

Tangka <i>et al.</i> , ⁹⁰ Health Services Research, 2015	<ul style="list-style-type: none"> - Cohort study - Georgia and Illinois, United States - Medicaid data (Centers for Medicare & Medicaid Services) and cancer registry data - 2000-2003 	<ul style="list-style-type: none"> - Medicaid beneficiaries aged 21-64 dying after a cancer diagnosis (n=3,512), matched to a cohort of beneficiaries without cancer (n=7,024), also dying in the 2000-2003 period. - Total Medicaid payments within four months before death, including costs of hospital admissions, ambulatory care services, prescription medicine and long-term care. 	<ul style="list-style-type: none"> - Mean total costs in the four months leading up to death were US\$ 34,749 per patient with cancer and US\$ 24,109 per patient without cancer, mainly driven by hospital costs.
Gielen <i>et al.</i> , ⁹¹ Health Policy, 2010	<ul style="list-style-type: none"> - Cohort study - Belgium - The Belgian Cancer Registry and reimbursed healthcare data from the Christian Mutuality - 2005-2006 	<ul style="list-style-type: none"> - Decedents aged >40 dying with (n=11,216) or without (n=29,575) a diagnosis of cancer. - Total costs of hospital admissions, care home, homecare services, consultations, medicine and diagnostic/therapeutic interventions in the six months leading up to death. 	<ul style="list-style-type: none"> - Mean total costs in the six months leading up to death were €17,976 per patient with cancer and €12,806 per patient without cancer, mainly driven by hospital costs.
Polder <i>et al.</i> , ⁹² Social Science & Medicine, 2006	<ul style="list-style-type: none"> - Cohort study - Netherlands - Health insurance data, long-term care and nursing home registries, and mortality figures from Statistics Netherlands - 1998-1999 	<ul style="list-style-type: none"> - Decedents of all ages dying from various causes of death (n=3,091). - Total costs of physician services, hospitals, medicine and related services as well as costs of nursing homes and homecare in the year leading up to death. 	<ul style="list-style-type: none"> - Mean total costs in the year leading up to death were higher for cancer compared with other major causes of death, mainly driven by hospital costs (54%).
Hung <i>et al.</i> , ⁹³ Value in Health, 2020	<ul style="list-style-type: none"> - Cohort study - United States, Surveillance, Epidemiology, and End Results database and Medicare claims database - 2001-2013 	<ul style="list-style-type: none"> - Medicare beneficiaries dying after a diagnosis of cancer (n=186,343), heart failure (n=18,652), COPD (n=25,015) or dementia (n=10,216) more than 360 days before death. - Monthly Medicare expenditures in the 24 months leading up to death, based on, e.g., inpatient, outpatient, homecare and hospice claims. 	<ul style="list-style-type: none"> - Mean total costs in the year leading up to death were US\$ 67,781 per patient with cancer, US\$ 51,768 per patient with heart failure, US\$ 47,577 per patient with COPD and US\$ 27,651 per patient with dementia.

Kelley <i>et al.</i> , ⁹⁴ Annals of Internal Medicine, 2015	<ul style="list-style-type: none"> - Cohort study - United States, Medicare claims database and data from interviews in the Health and Retirement Study - 2005-2010 	<ul style="list-style-type: none"> - Medicare beneficiaries aged ≥ 70 dying with high probability of dementia (n=555) or dying from cancer (n=279), heart disease (n=431) or other causes (n=437). - Total societal costs in the five years leading up to death, including out-of-pocket spending, informal care costs, Medicaid payments, private insurance and Medicare expenditures (all claims for inpatient, outpatient, skilled-nursing facility, homecare, hospice and durable medical equipment). 	<ul style="list-style-type: none"> - Mean total costs of all types in the five-year period leading up to death were US\$ 287,038 per individual with dementia, US\$ 173,383 per patient with cancer and US\$ 175,136 per patient with heart disease. - Medicare expenditures were rather similar across patient populations, but mean out-of-pocket spending was 81% higher for people with dementia than for decedents without dementia.
Sullivan <i>et al.</i> , ⁷⁹ The Journal of Nursing Administration, 2017	<ul style="list-style-type: none"> - Cohort study - United States - Medicaid data (Centers for Medicare & Medicaid Services) - 2008 	<ul style="list-style-type: none"> - Medicare beneficiaries dying from chronic disease (n=900) (chronic lung disease, diabetes, coronary artery disease, atherosclerosis and other neurology and behavioural disorders), system failure (n=687) (cirrhosis, multiple sclerosis, kidney failure, heart failure, cardiopulmonary disease) or cancer (n=243). - Monthly Medicare expenditures in the 24 months leading up to death, based on, e.g., inpatient, outpatient, homecare and hospice claims. 	<ul style="list-style-type: none"> - Mean monthly costs were higher for cancer patients compared than for patients without cancer (e.g. US\$ 10,450 versus US\$ 7,384-5,927 each month in the three months leading up to death). - The unadjusted relative difference was diminished during the last month of life caused by a relatively slower increase in costs of cancer patients.
Kaur <i>et al.</i> , ⁹⁸ Age and Ageing, 2022	<ul style="list-style-type: none"> - Cohort study - Tan Tock Seng Hospital, Singapore - Regional Health Systems administrative database - 2015-2017. 	<ul style="list-style-type: none"> - Decedents of all ages diagnosed with advanced cancer (n=3,095) and various non-cancer diseases (n=3,503). - Hospital costs in the year leading up to death, covering costs of hospital admissions, surgery, emergency room visits and outpatient clinics. 	<ul style="list-style-type: none"> - Compared with patients with cancer, patients with non-cancer diseases incurred 1.6 times more hospital costs in the year leading up to death. - In patients whether dying from cancer or non-cancer diseases, costs were mainly driven by costs of inpatient admissions (80%).

Kendzerska <i>et al.</i> , ⁹⁹ International Journal of Chronic Obstructive Pulmonary Disease, 2019	<ul style="list-style-type: none"> - Cohort study - Ontario, Canada - Datasets held at Institute for Clinical Evaluative Sciences - 2010-2015 	<ul style="list-style-type: none"> - Decedents aged ≥ 35 diagnosed with COPD without lung cancer (n=150,999), lung cancer without COPD (n=15,638), both COPD and lung cancer (n=24,082) or neither COPD nor lung cancer (n=254,769). - Total costs of in- and outpatient hospital care, complex continuing care, long-term care, physician services, homecare, prescription medicine and equipment in the 90 days leading up to death. 	<ul style="list-style-type: none"> - Mean total costs within 90 days leading up to death were CA\$ 29,176 for patients with COPD only, CA\$ 30,255 for patients with lung cancer only, CA\$ 30,742 for patients with COPD and lung cancer and CA\$ 26,047 for patients with neither COPD nor lung cancer.
Spilsbury <i>et al.</i> , ¹⁰⁰ BioMed Central Palliative Care, 2017	<ul style="list-style-type: none"> - Cohort study - Western Australia - Data Linkage Branch at the Western Australian Department of Health, Australian Redefined-Diagnostic Related Groups (AR-DRG) system and National Hospital Cost Data - 2009-2010 	<ul style="list-style-type: none"> - Decedents of all ages dying from cancer (n=7392), heart failure (n=2017), renal failure (n=1138), COPD (n=1089), Alzheimer's (n=605), liver failure (n=206), motor neurone disease (n=136) and Parkinson's (n=181). - Daily inpatient hospital costs in the year leading up to death. 	<ul style="list-style-type: none"> - Daily mean hospital costs in the year leading up to death were highest for decedents dying from renal failure (AUD\$ 133), liver failure (AUD\$ 131) and cancer (AUD\$ 112).
Yi <i>et al.</i> , ⁹⁵ Palliative Medicine, 2020	<ul style="list-style-type: none"> - Cohort study - England, Ireland, United States - Self-report questionnaire by informal carers, health and societal data from the Client Service Receipt Inventory 	<ul style="list-style-type: none"> - Decedents aged ≥ 65 dying from cancer (n=375) and non-cancer diseases (n=392) and receiving palliative care 4-10 months prior to death in England, Ireland and in the United States. - Total costs of hospital services, homecare, care homes and palliative care in the three months leading up to death. 	<ul style="list-style-type: none"> - Variation in total costs within the three months leading up to death were limited when comparing patients with cancer and patients with non-cancer diseases, but it differed among the three countries. - Hospital costs accounted for around 80% of total healthcare costs at the end of life regardless of diagnosis and country.

MEDLINE search query (Study III):

((("Health Care Costs"[Mesh]) OR ("Costs and Cost Analysis"[Mesh]) OR ("Cost of Illness"[Mesh])) AND (("Terminal Care"[Mesh]) OR ("Palliative Care"[MeSH Terms]) OR ("Terminally Ill"[Mesh])) OR (("Palliative care/economics"[MeSH Terms]) OR ("Terminal care/economics"[MeSH Terms]))) AND (Danish[Filter] OR English[Filter] OR Norwegian[Filter] OR Swedish[Filter]) AND (1995:2022[pdat]) AND "cancer*"

1.6 Aims of the dissertation

The overall aim of the present PhD dissertation was to examine the association of underlying disease and socioeconomic position with the utilisation and costs of healthcare services at the end of life in large-scale nationwide studies within a tax-supported healthcare system with equal access healthcare.

In **Study I**, illness trajectories reflected by healthcare utilisation in people dying from COPD, heart failure and cancer were explored, estimating the prevalence proportion of place of care on any given day in their last years of life, including all-cause hospital admissions and consultations in general practice in the five years leading up to death and intensive care unit admissions and non-medical homecare provision in the six months leading up to death.

In **Study II**, socioeconomic disparity trends from 2006 through 2016 were examined, covering the association between socioeconomic position and the use of healthcare services in the three months leading up to death in patients dying from non-cancer diseases and patients dying from cancer. Healthcare services included hospital contacts (hospital admissions, intensive care unit admissions, emergency room visits and hospital-based specialist palliative care admissions), hospice admissions, general practice contacts and non-medical homecare provision.

In **Study III**, the costs of providing healthcare services in the year leading up to death in patients dying from non-cancer diseases and patients dying from cancer were estimated. Adopting a healthcare sector perspective, the study aimed to include all costs to the public healthcare sector, encompassing costs of primary care, prescription medicine, somatic hospitals, including hospital-based specialist palliative care, and hospice care.

2. Methods

The following sections describe the materials and methods used in the three studies comprised by the present PhD dissertation, including an overview provided in Table 4.

2.1 Setting

The present PhD dissertation includes three nationwide studies conducted in Denmark. Denmark is a welfare society that provides equal and free access to tax-financed healthcare services for all Danish residents, including primary care, hospitals and hospices.¹⁰¹

All hospital medicines are provided free of charge to all patients in Denmark. However, for all prescription medicines sold in Danish pharmacies, a fixed co-payment scheme is in place with an annual maximum of DKK 4,320 per patient (2022 level).¹⁰² Even so, terminally ill patients with a life-expectancy of weeks to months may be granted drug reimbursement to receive all prescription medicine dispensed at Danish pharmacies free of charge.¹⁰³

On a national level, health financing and legislation, covering all healthcare-related responsibilities in Denmark, are administered by the Danish state through the Danish Ministry of Health.^{101,104} Furthermore, the administration of the Danish healthcare system is handled by regional and local authorities. Regional authorities are represented by the five Danish regions responsible for the healthcare services provided in primary care by private health professionals (e.g. general practitioners and dentists), at hospitals and in hospices. Furthermore, representing the local authority, the 98 Danish municipalities administer public healthcare services, homecare, social security and rehabilitation services.^{101,104}

2.2 Data sources

The studies comprised by the present PhD dissertation were based on individual-level data from population-based national medical and administrative registries that are recorded routinely for each Danish resident using their unique civil registration number. The civil registration number is a personal identification number assigned to all Danish residents at birth or emigration, which enables linkage across the various registries.¹⁰⁴ Hence, the data for the three studies were retrieved from seven population-based data sources covering cause of death, healthcare utilisation, healthcare costs and demographic factors, including data on socioeconomic position.

The Civil Registration System, established in 1968, assigns civil registration numbers to all Danish residents and records individual-level administrative data, including date of birth and death, emigration and address.¹⁰⁵

The Danish Registry of Causes of Death is a nationwide registry, which has collected data from death certificates for all Danish decedents as from 1970. The registry is virtually complete and

encompasses information on date and place of death, cause of death, including a chain of one to four events that led to death and other diseases that may have contributed, manner of death and whether an autopsy was performed.¹⁰⁶

The Danish National Patient Registry is a nationwide registry, which has contained records on all discharges from Danish hospitals since 1977. All Danish hospitals have a duty to submit information to the Danish National Patient Registry continuously, at least monthly, regarding hospital admissions, outpatient specialist clinic visits and emergency room visits. Data from the Danish National Patient Registry cover dates of all admissions and discharges, discharge diagnoses, surgical procedures and patients' place of residence.¹⁰⁷

The Diagnosis-Related Group (DRG) grouped Danish National Patient Registry covers DRG and Danish Ambulatory Grouping System (DAGS) tariffs. Since 2002, the registry has served as the basis for the payment of public and private hospitals via the DRG and DAGS tariffs.¹⁰⁸ The DRG and DAGS tariffs are determined at the national administrative level and reflect the average costs of treatment of patients across Danish hospitals, covering all hospital costs.¹⁰⁸

Statistics Denmark is the central authority of Danish statistics and provides a collection of individual-level administrative registry data for each Danish resident in the Danish society. Since 2006, municipal data have been transferred directly from the municipalities' electronic care systems into the databases of Statistics Denmark.¹⁰¹ Indicators from municipal data of homecare nursing and homecare provision have been collected from 2011 onwards. However, the data collection by the municipalities has, not been entirely complete.^{109,110}

Education and income registries are also provided by Statistics Denmark.^{111,112} Information on education includes data on individuals who have attended educational programmes authorised by the Danish Ministry of Education.¹¹¹ Education data have a completeness of approximately 97% among the ethnic Danish population and 85-90% among the immigrant population.¹¹¹ Data on income include information on annual income, individual income and household income.¹¹²

The National Health Service Registry has been operational since 1990 and contains data on private practice services performed by private practicing health professionals, including general practitioners, practicing medical specialists, physiotherapists, chiropractors, psychologists, dentists and chiropodists. The registry encompasses data on the date and type of services provided, the type and specialty of the provider and the gross fee charged for the services.¹¹³ Since registration of services in the National Health Service Registry is based on payments reimbursed by the National Health Insurance, the completeness is assumed to be good.¹¹³

The Danish National Prescription Registry holds individual-level information on all prescriptions redeemed at Danish pharmacies since 1995.¹¹⁴ The registry covers various dispensing details, including pharmacy selling price, dispensing fee and patient co-payment.¹¹⁴

2.3 Study populations

For the three studies comprised by the present PhD dissertation, the Danish Registry of Causes of Death was used to identify patient populations of adult decedents who had been residents in Denmark for at least five years prior to their death.

In *Study I*, patients registered with COPD, heart failure or cancer as the disease causing their death between 1 January 2006 and 31 December 2016 were included for investigation of illness trajectories reflected in hospital admissions and general practice consultations. For the analyses of intensive care unit admissions, only patients dying from COPD, heart failure or cancer between 1 June 2011 and 31 December 2016 were included, since the completeness of recordings of date and time of intensive care unit discharge had a completeness below 78.7% before 2011 but one of 95.1% in 2015.¹¹⁵ Accordingly, for the analyses of non-medical homecare provision, only decedents dying between 1 June 2011 and 31 December 2016 were included if the recordings of non-medical homecare provision data in the municipality they resided in had been stated as valid by Statistics Denmark in the six months leading up to death.¹¹⁰

In *Study II* and *Study III*, patients registered with one of seven selected non-cancer diseases or cancer as the cause of their death were identified. In accordance with the Dartmouth Atlas Project of end-of-life care, non-cancer diseases causing death included dementia, diabetes, heart failure, ischaemic heart disease, stroke, chronic liver disease and COPD.¹¹⁶

In *Study II*, patients dying from one of the selected non-cancer diseases or cancer between 1 January 2006 and 31 December 2016 were included for analyses of potential time trends in the use of hospital, emergency room and general practice according to socioeconomic position. Because of the aforementioned availability of data, only decedents dying between 1 April 2011 and 31 December 2016 were included in the analyses of intensive care unit admissions, homecare nurse visits and non-medical homecare provision. Correspondingly, data on hospice admissions have not been registered before 2009; therefore, only decedents dying between 1 April 2009 and 31 December 2016 were included in analyses of hospice admissions.

In *Study III*, patients who died from one of the selected non-cancer diseases or from cancer between 1 January 2010 and 31 December 2016 were included for the main analyses. In subgroup analyses, the study population was restricted to include patients dying only from COPD and lung cancer.

2.4 Outcomes

2.4.1 Healthcare utilisation (Study I and II)

In *Study I*, the outcomes of healthcare utilisation encompassed the prevalence proportion of place of care on any given day in the years leading up to death. Information on place of care included data on all-cause hospital admissions and consultations in general practice in the five years leading up to

death as well as intensive care unit admissions and non-medical homecare provision in the six months leading up to death.

Information on all hospital admissions in the five years leading up to death and intensive care unit admissions in the six months leading up to death was retrieved from the Danish National Registry of Patients. Accordingly, data on all in-office consultations and home visits provided by a general practitioner in the five years leading up to death were obtained from the National Health Service Registry, whereas the homecare documentation from Statistics Denmark was used to include data on non-medical homecare provision in the six months leading up to death.

In *Study II*, potential trends over time in the use of healthcare services in the three months leading up to death or dying in hospital served as the outcome. Data included hospital admissions, intensive care unit admissions, emergency room visits, use of hospital-based specialist palliative care, hospice admissions and death during hospital admission retrieved from the Danish National Registry of Patients. Furthermore, data on all in-office consultations and home visits provided by a general practitioner were obtained from the National Health Service Registry. Information on the number of homecare nurse visits and number of days with non-medical homecare provision was retrieved from the homecare documentation provided by Statistics Denmark.

2.4.2 Healthcare costs (Study III)

In *Study III*, a cost-of-illness methodology was applied to estimate the value of the resources used for providing healthcare services related to care at the end of life in Denmark.^{117,118} Thus, a healthcare sector perspective was adopted and costs to the public healthcare sector in the year leading up to death were the outcome of interest. Relevant costs included costs of primary care, prescription medicine, somatic hospitals, including hospital-based specialist palliative care, and hospice care.

Data on primary care costs included a weekly gross fee for practice services from private practicing health professionals reimbursed by the National Health Insurance, retrieved from the Danish National Health Service Registry. Hence, primary care costs included costs of all services in private practice, covering contacts with general practitioners, practicing medical specialists, physiotherapists, chiropractors, psychologists, dentists and chiropractists.

From the Danish National Prescription Registry, data on the costs of out-of-hospital prescription medicine dispensed from all Danish pharmacies were obtained, including the pharmacy selling price and dispensing fee from which patient co-payment was deducted.

The direct costs of somatic hospital care were computed from the DRG and DAGS tariffs from the Danish National Patient Registry, encompassing costs of inpatient hospital admissions, including medicine given during hospital admissions and medicine handed out by the hospital,

during outpatient specialist clinic visits, emergency room visits and when receiving hospital-based specialist palliative care.

Though the five Danish regions are the administrative bodies responsible for the costs of hospice care, the costs are not included in the DRG/DAGS system. Thus, hospice care costs were computed according to a daily bed charge determined by the regions, used to reimburse the hospices' care costs directly from the regions.

2.5 Covariates

Various covariates were included in the three studies comprised by the present PhD dissertation, enabling characterisation of the study populations, confounder adjustment, identification of potential effect modification by stratification and, in *Study II*, measuring the exposure of socioeconomic position.

Data on the decedents' sex, age at death, residential region at time of death and marital/cohabitation status at the time of death were obtained from the Danish Civil Registration System. Furthermore, a comorbidity score was calculated from weights of 19 selected diagnoses in relation to hospitalisation and outpatient visits during the last ten years before death, excluding the disease causing death.^{119,120} Data on patients' discharge diagnoses from hospitalisations and outpatient visits were obtained from the Danish National Registry of Patients.

In *Study II*, the exposure of socioeconomic position among patients dying from non-cancer diseases and cancer was measured based on individual-level information on patients' educational and household income level, obtained from Statistics Denmark.^{111,112}

Levels of education were defined using the framework provided by the International Standard Classification of Education (ISCED 2011) as: low (ISCED levels 0-2: primary and lower secondary education), middle (ISCED levels 3-5: upper secondary education up to bachelor's or equivalent level) and high educational level (ISCED levels 6-8: equivalent to bachelor's level or more).¹¹¹

Household income levels were defined by the mean annual household income during the five years leading up to the year of death, that is, excluding the year of death. Household income were grouped into three levels according the national medians of household income in the year of death, obtained from Statistics Denmark: low (less than 50% of the national median), middle (50-100% of the national median) and high household income level (above the national median).^{112,121}

Study I and *Study III* solely included information on the decedents' household income level obtained from Statistics Denmark.

2.6 Statistical analyses

A summary of the statistical analyses used for each of the three studies comprised by the present PhD dissertation is provided in Table 4, and a more thorough description is included in Appendices I-III.

In all three studies, contingency tables were prepared to describe demographic characteristics of the cohorts of patients dying from non-cancer diseases and patients dying from cancer.

In *Study I*, daily prevalence proportions (PPs) of being admitted to hospital, consulting a general practitioner, being admitted to intensive care units or receiving non-medical homecare were computed for patients dying from COPD, heart failure and cancer. Thus, the PPs were the daily number of patients admitted to hospital or consulting a general practitioner divided by the number of patients in the study population on that specific day in the five years leading up to death. Accordingly, the daily PPs of patients admitted to an intensive care unit or receiving non-medical homecare were computed in the six months leading up to death. All daily PPs were plotted by day before death according to the diseases causing the death. Furthermore, daily PPs were calculated and plotted by date before death according to major types of cancer (breast cancer, prostate cancer, lung cancer, colon cancer, pancreatic cancer and haematological cancer).¹²²

In the comparison of patients dying from COPD or from heart failure with patients dying from cancer, daily prevalence proportion ratios (PPRs) of patients being admitted to hospital, consulting a general practitioner, being admitted to intensive care or receiving non-medical homecare were estimated and plotted. The daily PPRs were adjusted for age at death, sex, comorbidity, marital/cohabitation status, residential municipality and income level using a Poisson regression model with a robust variance estimator.

In *Study II*, the proportion of patients with non-cancer diseases and the proportion of patients with cancer who used one of the included healthcare services in the three months leading up to death were computed (hospital admissions, including intensive care unit admissions, emergency room visits, general practice contacts, homecare nurse visits, non-medical homecare provision, hospital-based specialist palliative care and hospice) as well as the proportion of patients who died in hospital. The estimates were plotted by socioeconomic position and calendar year of death.

The adjusted differences in mean use of the included healthcare services were computed and plotted by calendar year of death for patients with a middle and patients with a high educational level, compared with patients with a low educational level as well as for patients with a middle and patients with a high income level, compared with patients with a low income level; this was done separately for patients with non-cancer diseases and for patients with cancer. A linear regression model with a robust variance estimator was used to calculate differences mean use of the included healthcare services adjusted for age at death, sex, comorbidity, marital/cohabitation status and residential municipality. However, for the analyses of differences in mean number of homecare

nurse visits, a robust regression was used since several outliers were observed, probably caused by registration error. Furthermore, cohabitation was not included as a covariate in analyses of income level because of its correlation with household income.

In *Study III*, mean monthly and annual costs per patient with a non-cancer disease and per patient with cancer were computed. The costs covered costs of primary care, prescription medicine, somatic hospitals, including hospital-based specialist palliative care, and hospice care. Additionally, the mean total costs of all the included healthcare services by month and as a total within the last year of life were estimated. The mean monthly costs per patient were plotted by the underlying disease causing death in the year leading up to death. Furthermore, the mean monthly costs of hospital-based specialist palliative care and hospice care were plotted by the underlying disease in the three months leading up to death.

Relative monthly costs of patients with non-cancer diseases compared with patients with cancer were computed and adjusted for age at death, sex, comorbidity, marital/cohabitation status, residential region and income level using the Poisson regression with robust variance estimator. The adjusted relative monthly costs were plotted by month before death in the year leading up to death. However, the adjusted relative monthly costs of hospital-based specialist palliative care and hospice care were plotted by months before death for the three months leading up to death.

Subsequently, all analyses were repeated for a subpopulation only including patients dying from COPD and for patients dying from lung cancer as recent data suggest comparable levels of symptom burden and palliative care needs in these two patient populations.^{123,124}

All statistical analyses were conducted on a secure remote server at Statistics Denmark using Stata 17 software (StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC).

2.7 Ethical considerations

For the studies comprised by the present PhD dissertation, an approval was obtained for use of the included data sources from the Danish Data Protection Agency (record number 2015-57-0002) by registration at Aarhus University (Aarhus University record number 2016-051-000001/977).

Under Danish law, approvals from ethics committees and consent from patients are not required when conducting observational studies.

Table 4 Overview of materials and methods.

	Study I	Study II	Study III
Objectives	To investigate illness trajectories reflected in healthcare utilisation before death comparing patients with COPD, heart failure and cancer.	To examine time trends in use of healthcare services at the end of life by SEP in patients with non-cancer diseases and patients with cancer.	To examine costs of care from a healthcare sector perspective in patients with non-cancer diseases and patients with cancer in the year leading up to their death.
Setting	Denmark 2001-2016.	Denmark 2006-2016.	Denmark 2009-2016.
Data sources	Danish Registry of Causes of Death, CRS, DNPR, National Health Service Registry, Statistics Denmark.	Danish Registry of Causes of Death, CRS, DNPR, National Health Service Registry, Statistics Denmark.	Danish Registry of Causes of Death, CRS, DNPR, National Health Service Registry, Statistics Denmark, Danish National Prescription Registry, DRG grouped DNPR.
Study population	Patients dying from COPD, heart failure and cancer in the 2006-2016 period (analyses of hospital admissions and GP consultations) and in the 2011-2016 period (analyses of ICU admissions and non-medical homecare provision).	Dementia, diabetes, heart failure, ischaemic heart disease, stroke, chronic liver disease, COPD and cancer decedents dying in 2006-2016 (analyses of hospital admissions, emergency room visits and GP consultations), in 2011-2016 (analyses of ICU admissions, homecare nurse and non-medical homecare provision) and in 2009-2016 (analyses of hospice admissions).	Dementia, diabetes, heart failure, ischaemic heart disease, stroke, chronic liver disease, COPD and cancer decedents dying in the 2010-2016 period.
Exposures	Underlying COPD, heart failure or cancer causing death.	SEP reflected by educational level and income level.	Underlying non-cancer disease or cancer causing death.
Outcomes	Hospital admissions and GP consultations in the five years leading up to death. ICU admissions and non-medical homecare provision in the six months leading up to death.	Hospital admissions, ICU admissions, emergency room visits, hospital-based specialist palliative care, hospice admissions, GP consultations, homecare nurse visits, non-medical homecare provision in the three months leading up to death and death in hospital.	Direct healthcare costs in the year leading up to death, covering costs of primary care, prescription medicine, somatic hospitals, including hospital-based specialist palliative care, and hospice care.
Covariates	Age, sex, comorbidity, marital/cohabitation status, residential municipality and income level.	Age, sex, comorbidity, marital/cohabitation status and residential municipality.	Age, sex, comorbidity, marital/cohabitation status, residential region and income level.
Statistical analyses	Daily prevalence proportions of patients receiving the included healthcare services were calculated and plotted according to underlying disease. Adjusted daily prevalence proportion ratios were computed and plotted using the Poisson regression model with robust variance estimator.	Analyses were conducted separately for patients with non-cancer diseases and patients with cancer (computed and plotted): - Proportions of patients receiving the included healthcare services or dying in hospital according to SEP by calendar year of death. - Adjusted differences in mean use of the included healthcare services using a linear regression model with robust variance estimator. - Adjusted difference in mean number of homecare nurse visits using robust regression.	Mean monthly healthcare costs in the year leading up to death were estimated and plotted by underlying disease. Adjusted relative monthly costs were computed and plotted using the Poisson regression with robust variance estimator. All analyses were repeated for a subpopulation of patients with COPD and lung cancer.

Abbreviations: COPD=chronic obstructive pulmonary disease; SEP=socioeconomic position; GP=general practitioner; CRS=Danish Civil Registration System; DNPR=Danish National Registry of Patients; DRG=Diagnosis Related Group; ICU=intensive care unit.

3. Results

The main findings from the three studies comprised by the present PhD dissertation are presented in the following sections. A more detailed description is presented in the full versions of the research papers provided in Appendices I-III.

3.1 Healthcare utilisation trajectories at the end of life (Study I)

In *Study I*, regarding healthcare utilisation trajectories at the end of life, a sample of 174,086 patients dying from COPD, heart failure or cancer in 2006-2016 were identified for analyses of hospital admissions and consultations in general practice. Furthermore, analyses of intensive care included 87,273 patients dying in 2011-2016, whereas analyses of non-medical homecare provision included 61,286 patients dying from COPD, heart failure or cancer in 2011-2016.

In Figure 5, the graph curve representing the daily PPs of patients admitted to hospital followed a gradually increasing trend for each of the three patient populations until the year leading up to death in which it ascended steeply. The graph curve representing the daily PPs of patients consulting a general practitioner progressed slowly until it increased precipitously for each of the three patient populations in the last months of their life (Figure 5). Correspondingly, the daily PPs of patients admitted to intensive care showed some progress during the last six months of life but climbed within the last month of life in patients with COPD, heart failure and cancer alike (Figure 5). Throughout the six-month period leading up to death, the graph curve representing daily PPs of patients with COPD and heart failure receiving non-medical homecare remained stable with a slight decrease in the final month leading up to death (Figure 5). Even so, the graph curve representing daily PPs of cancer patients receiving non-medical homecare increased during the last six months of life and decreased slightly during the final month of life; similarly to the curve for patients with COPD and heart failure (Figure 5).

Compared with patients with cancer, the adjusted daily PPR of patients with either COPD or heart failure admitted to hospital or consulting a general practitioner declined gradually during the five years leading up to death. The adjusted daily PPR of patients admitted to intensive care stayed stable for patients with COPD and patients with heart failure compared with patients with cancer throughout the six months leading up to death, whereas the adjusted daily PPR of patients receiving non-medical homecare declined during the six months leading up to death.

When stratifying on major cancer types, no differences were found in the course of daily PPs of patients being admitted to hospital, including daily PPs of patients who received intensive care, and daily PPs of patients who consulted a general practitioner. For the provision of non-medical homecare, the trajectories of breast cancer and prostate cancer mirrored the trajectories of the non-cancer diseases closely with a slower increase in the level of non-medical homecare provision.

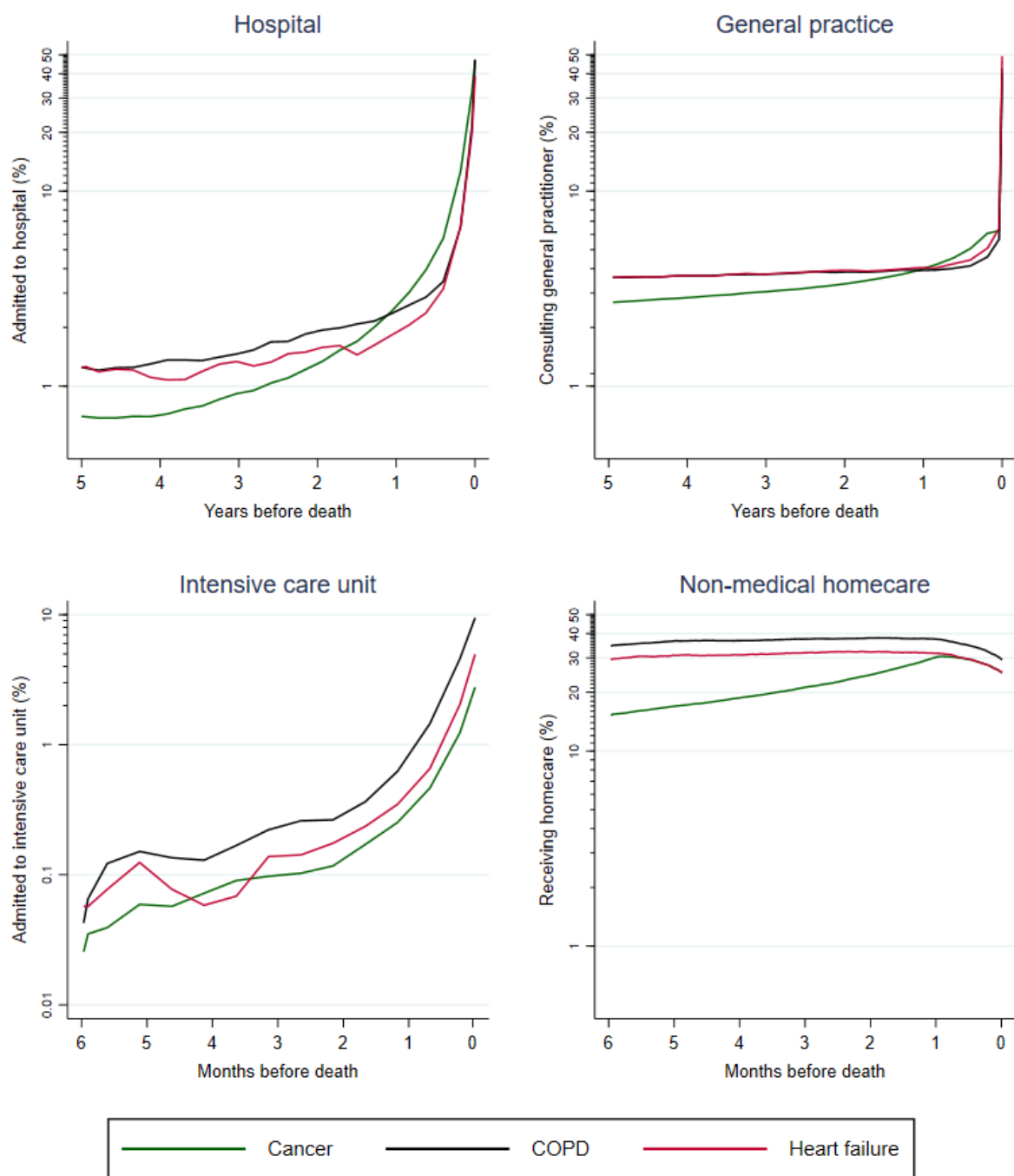


Figure 5 Daily prevalence proportions of patients admitted to hospital, admitted to intensive care, consulting a general practitioner or receiving non-medical homecare by underlying disease causing death.

3.2 Socioeconomic disparity trends in care at the end of life (Study II)

Study II explored socioeconomic disparity trends in care at the end of life. The study included 180,223 patients dying from one of the seven selected non-cancer diseases and 169,694 patients dying from cancer in the 2006-2016 period. The analyses of intensive care included 178,179 decedents dying in 2011-2016. From this population of decedents, a sample of 121,376 decedents was identified for the analyses of homecare nursing and 123,981 decedents for the analyses of non-medical homecare provision. Correspondingly, the analyses of hospice care included 241,997 decedents dying in 2009-2016.

In patients dying from non-cancer diseases and patients dying from cancer alike, limited socioeconomic disparities and changes over time were discovered for the use of hospital, intensive care, emergency room, general practice, homecare nurse and hospice during the study period (Figure 6, Figure 7).

For patients dying from non-cancer diseases, a high income level was associated with a higher risk of dying in hospital than was a low income level (Figure 6). Furthermore, compared with patients with a low income level, seven percentage points more patients dying from non-cancer diseases with a middle income level died while being admitted to hospital in 2006/2007 (adjusted mean difference: 0.07 (95% CI: 0.05; 0.08)). In 2016, this difference decreased to two percentage points more patients with a middle income level dying in hospital compared with patients with a low income level (adjusted mean difference: 0.02 (95% CI: 0.01; 0.04)) (Figure 6).

Socioeconomic position, based on educational level and income level, was associated with use of hospital-based specialist palliative care for patients with cancer. Specifically, patients with cancer with a high socioeconomic position received more hospital-based specialist palliative care at the end of life than those with low a socioeconomic position (Figure 7).

The socioeconomic disparity gap based on income level increased during the 2006-2016 period, although the proportion of patients with cancer receiving hospital-based specialist palliative care generally increased considerably. Hence, compared with patients dying from cancer with a low income, one percentage point more patients dying from cancer with a high income level received hospital-based specialist palliative care in 2006/2007 (adjusted mean difference: 0.01 (95% CI: 0.01; 0.02)). In 2016, this difference increased to 12 percentage points more patients with a high income level receiving hospital-based specialist palliative care compared with patients with a low income level (adjusted mean difference: 0.12 (95%CI: 0.09; 0.14)) (Figure 7).

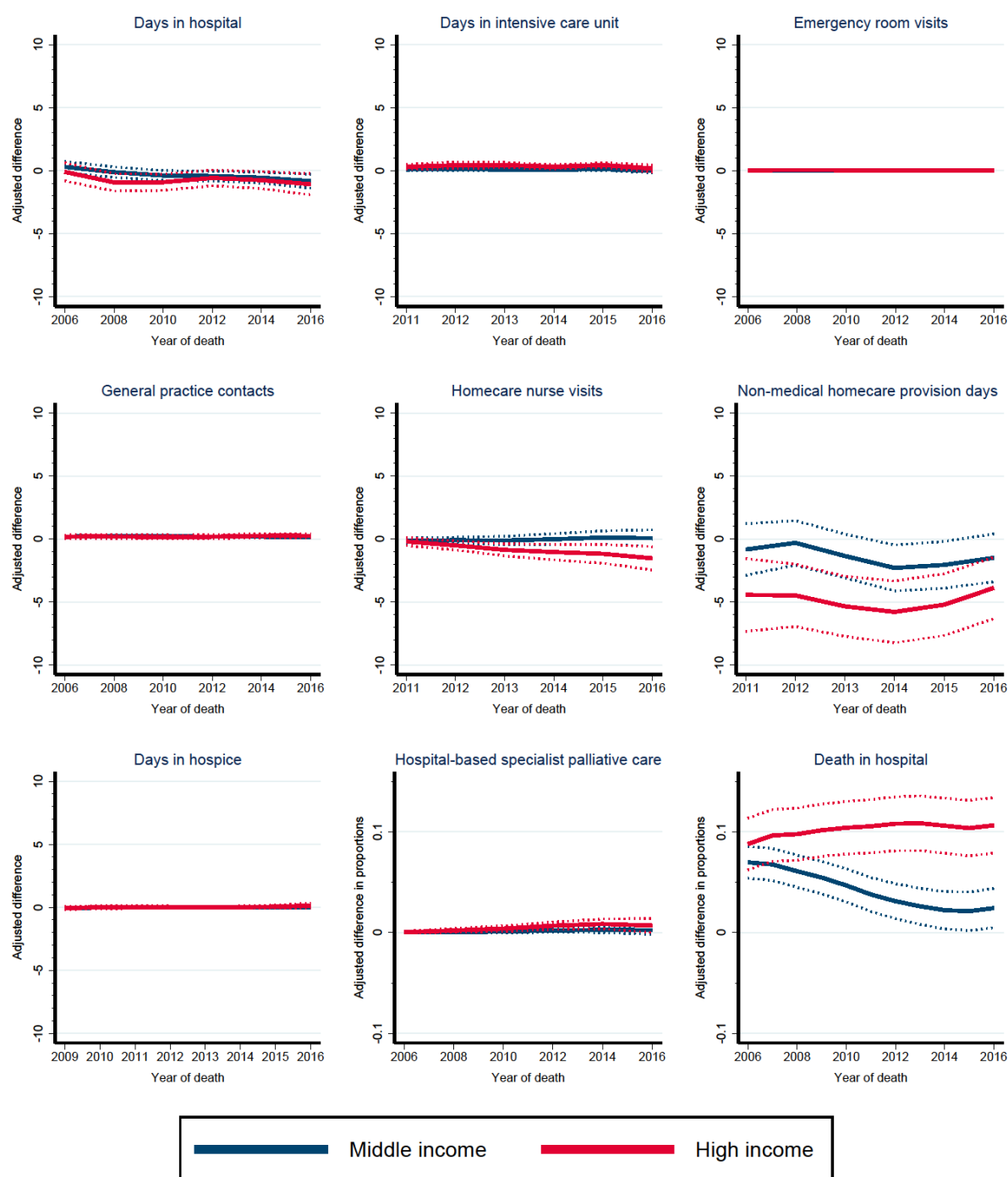


Figure 6 Adjusted mean difference in use of healthcare services for **patients dying from non-cancer diseases** by calendar year of death and a middle and high income level compared with patients with a low income level.

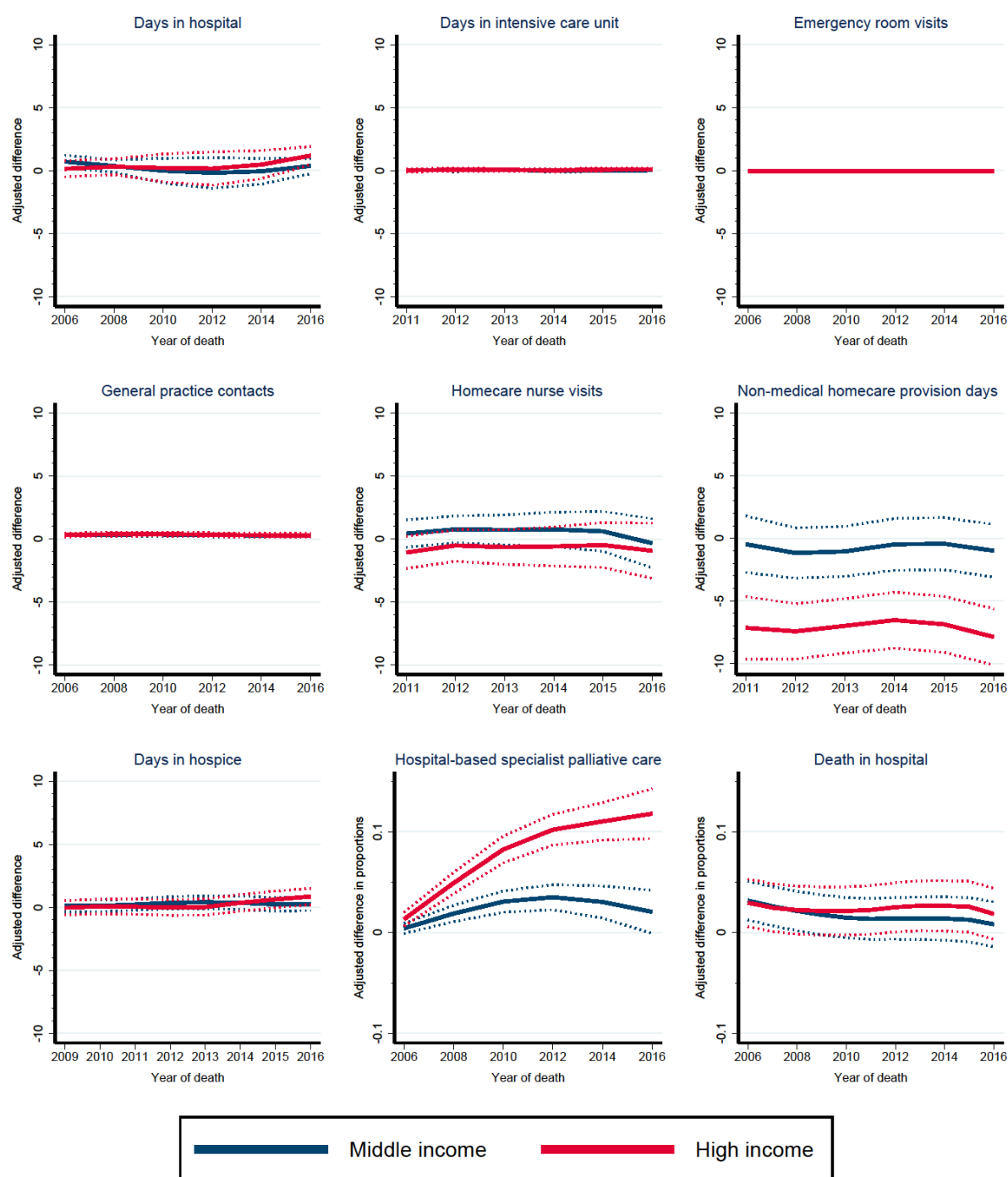


Figure 7 Adjusted mean difference in use of healthcare services for **patients dying from cancer** by calendar year of death and a middle and high income level compared with patients with a low income level.

3.3 Healthcare costs at the end of life (Study III)

In *Study III*, estimating healthcare costs at the end of life, 109,723 patients dying from one of the selected non-cancer diseases and 108,889 patients dying from cancer in 2010-2016 were identified.

The mean total costs of the included healthcare services in the year leading up to death were considerably lower for patients with non-cancer diseases than for patients with cancer. Thus, the mean total costs of the included healthcare services were €24,353 (95% CI: 24,159; 24,546) per patient with non-cancer disease and €45,997 (95% CI: 45,773; 46,221) per patient with cancer. In both patient populations, hospital costs were the primary driver of total healthcare costs within the last year of life (Figure 8).

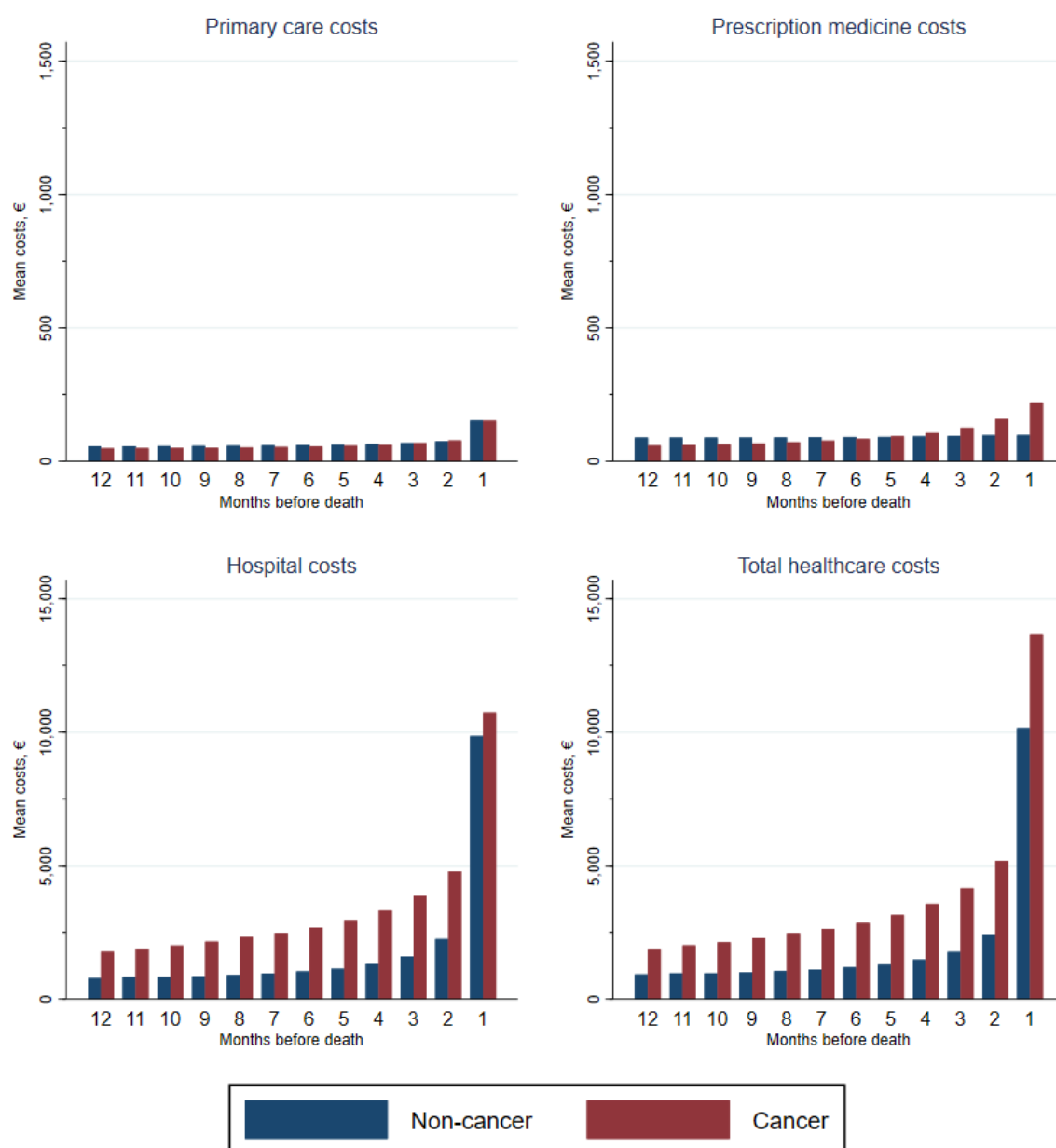


Figure 8 Mean monthly costs per patient for primary care, prescription medicine, somatic hospitals and total healthcare costs in the year leading up to death for patients dying from non-cancer diseases and patients dying from cancer.

In the final months before death, differences in total healthcare costs among patients dying from non-cancer diseases and patients dying from cancer were reduced (Figure 9). Hence, when compared with patients with cancer, the adjusted relative total healthcare costs of patients with non-cancer diseases was 0.64 (95% CI: 0.63; 0.66) at 12 months before death and 0.53 (95% CI: 0.52; 0.55) at four months before death, but this difference was reduced to 0.91 (95% CI: 0.90; 0.92) within 30 days before death (Figure 9).

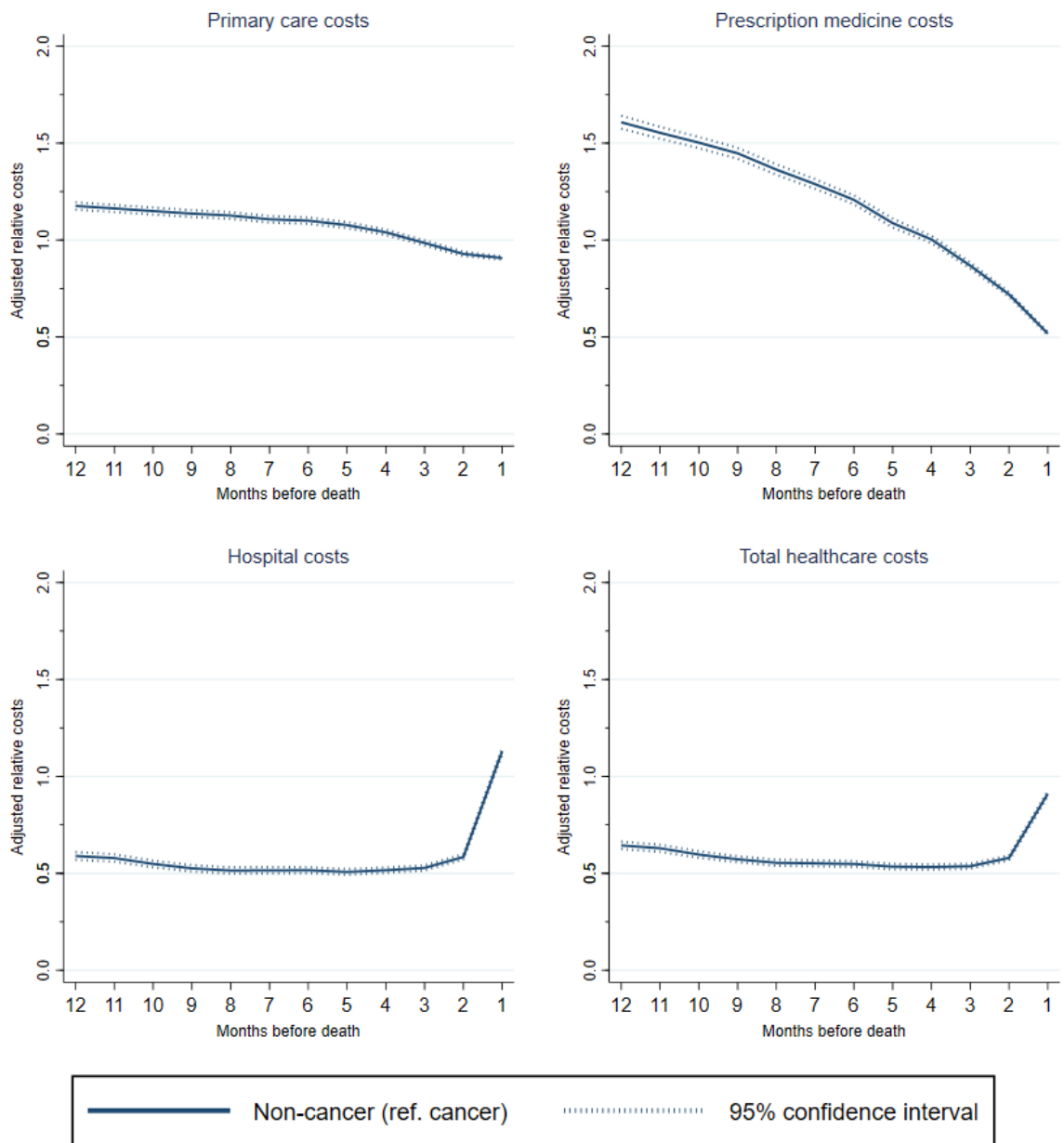


Figure 9 Adjusted relative costs of primary care, prescription medicine, somatic hospitals and total healthcare costs in the year leading up to death for patients dying from non-cancer diseases compared with patients dying from cancer.

Hospital-based specialist palliative care and hospice care were predominantly provided for patients with cancer, and these services were mainly utilised in the last month of life. Thus, in the last 30 days leading up to death, the mean costs of hospital-based specialist palliative care were €8 (95% CI: 6; 10) per patient with non-cancer disease and €691 (95% CI: 672; 709) per patient with cancer (Figure 10). Accordingly, the mean costs of hospice care were €51 (95% CI: 42; 59) per non-cancer patient and €2,569 (95% CI: 2,515; 2,623) per patient with cancer (Figure 10).

In analyses restricted to patients dying from COPD and patients dying from lung cancer, similar cost patterns were found in the months preceding death. However, differences were slightly less pronounced in total healthcare costs but virtually identical for hospital-based specialist palliative care costs and hospice care costs.

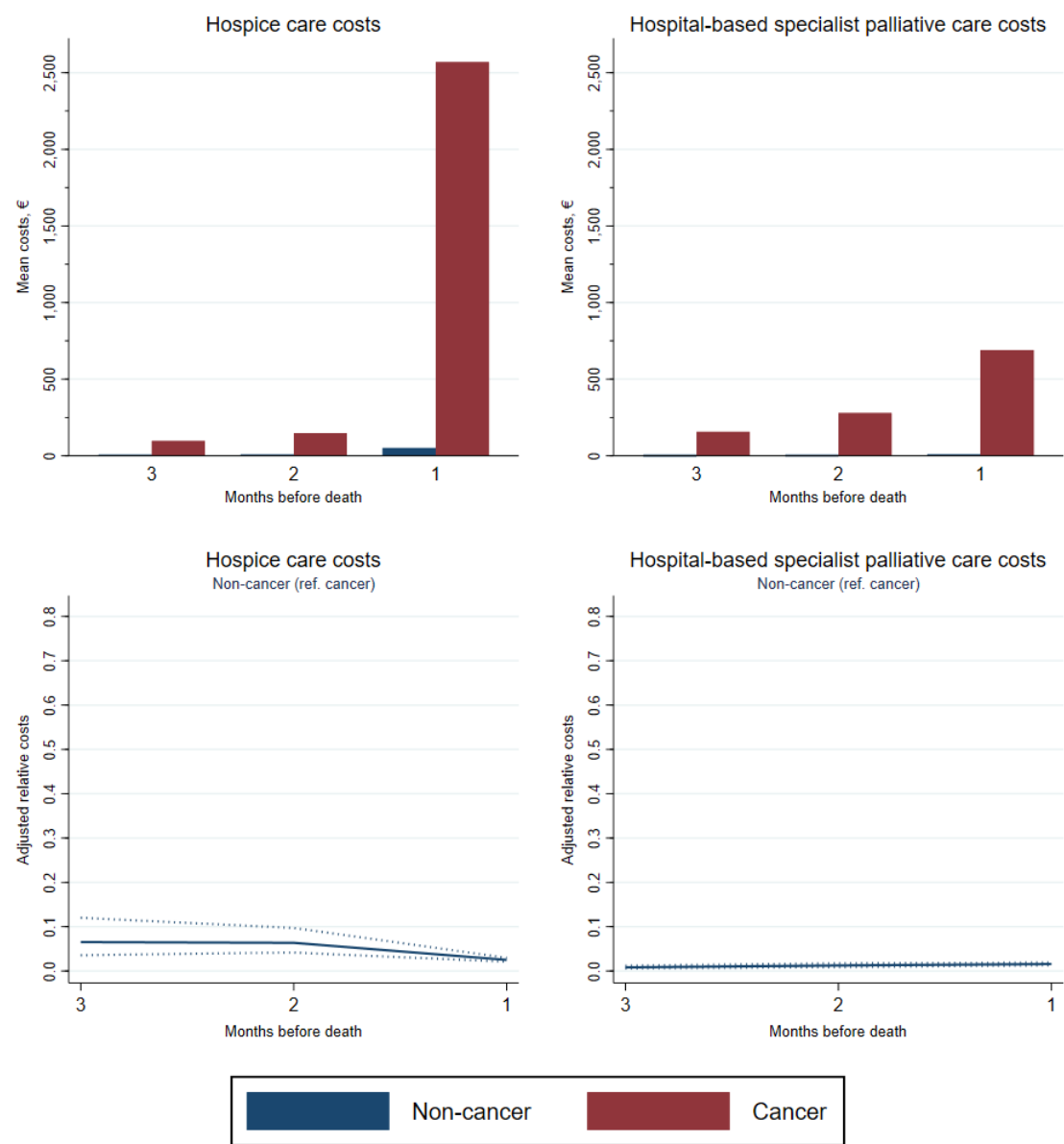


Figure 10 Mean monthly costs per patient and adjusted relative costs of hospital-based specialist palliative care and hospice care in patients dying from non-cancer diseases and from cancer.

4. Discussion

4.1 Main findings

Healthcare resource utilisation trajectories at the end of life for patients dying from COPD or heart failure varied little from those of patients dying from cancer. Thus, illness trajectories as death approaches were found to be equivalent for the three patient populations estimated by the use of hospital services, including intensive care and general practitioner. However, in the months preceding death, trajectories of non-medical homecare provision were at a high but constant level for patients dying from non-cancer diseases, whereas patients dying from cancer were increasingly cared for.

Even though an increasing proportion of patients dying from cancer received hospital-based specialist palliative care during the 2006-2016 period, a widening socioeconomic disparity gap was discovered regarding the use of hospital-based specialist palliative care in patients dying from cancer, favouring patients with high a socioeconomic position. In patients dying from non-cancer diseases, a low socioeconomic position was found to be associated with an increased risk of dying at home, but this socioeconomic disparity gap narrowed during the 2006-2016 period, though differences were modest. However, in both patient populations, socioeconomic position was inversely associated with provision of non-medical homecare but without clear temporal trends. Thus, the higher socioeconomic position, the fewer days of homecare provision. Furthermore, limited socioeconomic disparities were recorded in the use of other included healthcare services, and no clear temporal trends were found for either patients dying from non-cancer diseases or for patients dying from cancer.

During the year leading up to death, the total healthcare costs, mainly driven by hospital costs, increased regardless of the disease causing the death, but costs were considerably lower for patients dying from non-cancer diseases than for patients dying from cancer. Even so, the relative differences were reduced, although persisting, in the last months of life. In the year leading up to death, substantially lower costs of hospital-based specialist palliative care and hospice care were found for patients with non-cancer diseases than for patients with cancer.

4.2 Findings contextualised by existing literature

The following sections include discussions of the findings from each of the three studies comprised by present PhD dissertation in the context of existing literature.

4.2.1 Healthcare utilisation trajectories at the end of life (Study I)

The overall findings of comparable illness trajectories in non-cancer and cancer populations as reflected in healthcare resource utilisation challenge current efforts in the planning and delivery of

palliative care interventions based on previously established models from smaller data sources.⁷³⁻⁷⁶ Thus, previous smaller studies confirmed that illness trajectories of patients dying from cancer and organ failure follow the patterns originally presented by Glaser and Strauss.²¹ Yet, there were also some resemblances with these models for the trajectories of non-medical homecare provision as cancer was associated with a more steeply increasing level of terminal non-medical homecare provision than COPD and heart failure.

Several other studies have also aimed to chart the course of different end-of-life illness trajectories from large real-life data sources to ensure that appropriate palliative care is provided for patients and their families at the end of life. Hence, while comparing functional impairment in patients dying from cancer, organ failure or cardiovascular diseases in a large Australian dataset, Morgan et al. (2019)⁷⁷ found comparable patterns of gradual decline in physical health and a clear terminal phase for the three patient populations. This was consistent with the findings made in *Study I* and corresponded to the findings from another large Australian study exploring functional decline among patients dying from lung cancer and patients dying from non-malignant respiratory disease.⁷⁸

In line with the methods examining illness trajectories by describing healthcare resource utilisation, recent studies have charted illness trajectories by assessing the pattern of healthcare costs at the end of life according to the underlying disease causing death.^{79,80} Hence, similar to the findings in *Study I*, healthcare costs trajectories at the end of life showed a precipitous increase in the last months of life with virtually identical healthcare utilisation curves for the various diseases causing death.

Over the past decade, developments in disease-modifying therapies for several cancer types (e.g. breast cancer and prostate cancer) may have changed the course of illness trajectories that can be observed in contemporary data.⁷⁷⁻⁸⁰ Hence, treatment improvements in some cancer types may have changed the course of illness trajectories, making them mimic those of some non-cancer diseases with a more gradual decline in physical health and episodes of acute deterioration in the period leading up to death.^{125,126} To some extent this may explain the conflicting findings in other, predominantly older, studies compared with the findings in *Study I*.⁷³⁻⁷⁶

Receiving palliative care improves the quality of the remaining life in patients, whether they have non-cancer diseases or cancer, while reducing costly and potentially stressful hospital admissions at the end of life.⁴⁸ Furthermore, several studies have suggested an equivalent symptom burden at the end of life in patients suffering from non-cancer diseases and patients suffering from cancer.^{44-48,78} This warrants consideration, particularly in the light of the findings from *Study I* describing virtually parallel healthcare resource utilisation trajectories at the end of life, suggesting a similar progression in illness severity and functional impairment in patients with non-cancer diseases versus patients with cancer. Thus, development of palliative care service for patients suffering from non-cancer diseases needs to remain a priority, including ensuring more proactive

referrals to specialist palliative care. Furthermore, in patients dying from non-cancer diseases and from cancer alike, offering palliative care triggered by patients' needs rather than by prognosis and treatment intention may mitigate prognostication difficulties.^{127,128}

4.2.2 Socioeconomic disparity trends in care at the end of life (Study II)

Although health policies aim to reduce socioeconomic disparities in health and access to healthcare services in developed countries, a widening socioeconomic disparity gap was found in *Study II* when examining hospital-based specialist palliative care utilisation among patients dying from cancer.¹

Corresponding to the growing specialist palliative care capacity observed in Denmark during the study period,²⁹ increasing proportions of cancer patients receiving hospital-based specialist palliative care were discovered. However, the increasing socioeconomic disparities, favouring patients with a high socioeconomic position, may indicate that specialist palliative care utilisation is improving more rapidly in these patients than in patients with a low socioeconomic position. This may be explained by the latter group's poorer ability to navigate the healthcare system and a lack of knowledge of the possibility of specialist palliative care.¹²⁹ However, it may also reflect reluctance towards specialist palliative care services which may be perceived as an inadequate substitute for curative treatment.¹³⁰ However, patients with a low socioeconomic position tend to be facing more extensive psychosocial challenges and may receive less support from their family and from informal caregivers. This may be reflected in the findings of greater use of non-medical homecare in these patients, which may reflect a greater need for care. Therefore, it warrants serious consideration that these patients, potentially the more vulnerable patient group, are less likely to receive hospital-based specialist palliative care than patients with a high socioeconomic position. Thus, this shewed allocation of specialist palliative care interventions may reflect poor quality of care in patients with a low socioeconomic position and unmet palliative needs in this patient population at the end of life.

No previous studies were identified that explored temporal trends in socioeconomic disparities in care at the end of life approximated by individual-level indicators and including various healthcare services stratified according to the underlying disease causing death with consideration of potential confounding factors. Furthermore, only few studies demonstrated socioeconomic disparities when examining temporal trends in place of death as a measure of quality of care at the end of life.⁸¹⁻⁸⁶ Thus, patients with a high socioeconomic position were more likely to die at home or in hospice, but the gradients remained relatively constant over time.^{81-83,85,86} Only a single study, by Gao et al. (2014), analysed decedents with non-cancer diseases and cancer separately in the analyses but reported similar results.⁸³ In contrast to other studies, the results obtained in *Study II* suggested that a high income level was associated with hospital deaths in patients dying from non-cancer diseases despite an overall decrease in deaths during hospital admission. However, previous studies, barring Gao et al. (2014), either included only cancer decedents or all decedents regardless of

underlying disease, which hampers the comparison with the findings of *Study II*. Most notably, however, previous studies were conducted within healthcare systems with a far higher specialist palliative care capacity than that of the Danish healthcare system.³⁹

The findings of a tendency towards increasing socioeconomic disparities in the use of hospital-based specialist palliative care in cancer patients is in line with prior studies.^{86,87} Thus, including decedents of all underlying diseases, Mondor et al. (2020) found a constant socioeconomic gradient during 2009 through 2014 as patients with a low socioeconomic position were less likely to receive palliative care before their death.⁸⁶ Khan et al. (2022) studied patients dying from acute ischaemic stroke and reported similar findings.⁸⁷

The results from *Study II* did not confirm previous reports indicating an inferior care at the end of life for terminally ill patients with a low socioeconomic position across various healthcare services according to underlying disease, including dying in hospital, being acutely admitted to hospital in the terminal phase and not receiving specialist palliative care.²²⁻²⁵ This may suggest that the Danish healthcare system with universal coverage provides more equality in access to healthcare services as death approaches than other healthcare systems do. However, substantial differences exist in the organisation and financing of healthcare systems between countries. Thus, it cannot be established from the present data whether the findings of limited socioeconomic disparities in care at the end of life reflect equity in care that is appreciable for patients at the end of life and in accordance with their needs.

Even so, increasing socioeconomic disparities in the provision of hospital-based specialist palliative care at the end of life is a concern because it demonstrates the shortfall of current political strategies aiming to diminish the socioeconomic gradients in health and healthcare throughout the study period.

4.2.3 Healthcare costs at the end of life (Study III)

The results from *Study III* are consistent with findings from few previous studies by Langton et al. (2016),⁸⁸ Reeve et al. (2018)⁸⁹ and Luta et al. (2020),⁸⁰ which also adopted a healthcare sector perspective when examining healthcare costs at the end of life. Thus, these previous studies also suggested that patients with non-cancer diseases incurred considerably lower total healthcare costs at the end of life than patients with cancer, and that hospital contacts were the primary driver of costs.^{80,88,89} Conversely, previous research, from the research group, exploring healthcare service utilisation at the end of life in Denmark found that the number of hospital admissions and length of stay in patients dying from non-cancer diseases do not vary considerably from those of patients dying from cancer.¹³¹ Still, 75-82% of patients with non-cancer diseases and 93% of patients with cancer were admitted to hospital during the six months leading up to death.¹³¹ This may be explained by a more active treatment approach among patients with cancer, often involving

expensive medicine administered during hospital admission.¹³² Even so, consistent with Langton et al. (2016),⁸⁸ Reeve et al. (2018)⁸⁹ and Luta et al. (2020),⁸⁰ the findings from *Study III* showed that the relative difference in total healthcare costs when comparing patients dying from non-cancer diseases with patients dying from cancer was reduced during the last months of life, although it did persist.^{80,88,89} One possible explanation of this may relate to a relatively faster rise in the use of high-intensity treatments and potentially costly medical interventions especially in the last month of life in patients with non-cancer diseases rather than in patients with cancer. This is in accordance with findings from our previous research showing that in the six months leading up to death, patients dying from non-cancer diseases were twice as frequently admitted to intensive care units and had a greater risk of dying there than patients dying from cancer.¹³³

A mounting body of evidence describes that palliative care improves quality of life^{48,50,134-136} and reduces healthcare costs at the end of life,^{100,137-141} regardless of the disease causing death. Moreover, some cost-effective palliative care interventions have even been presented.^{137,142} This, however, has not noticeably affected practice for patients with non-cancer diseases as palliative care is still received mainly by patients with cancer.¹⁶⁻¹⁹ This is in accordance with the findings in *Study III* of extremely low average costs of hospital-based specialist palliative care and hospice care in patients with non-cancer diseases. Considered in conjunction with the beneficial effects of palliative care provision, this may indicate that cancer patients receiving specialist palliative care, including hospice care, may have been spared some costly, potentially futile, high-intensity interventions at the end of life, which may have improved the quality of life for these patients and their families. Furthermore, it cannot be excluded that patients suffering from non-cancer diseases have, to some extent, had their palliative needs met in other healthcare settings, e.g. at home by private or municipal homecare providers.

The findings of differences in terms of costs of hospital-based specialist palliative care and hospice care for patients with non-cancer diseases and patients with cancer were similar to the observed difference in the analyses of patients with COPD and patients with lung cancer only. Thus, substantially lower costs were observed among patients with COPD. This difference between patients with COPD and patients with lung cancer is remarkable since both patient populations experience fairly equivalent symptoms and needs of care at the end of life^{123,124} and would most likely benefit somewhat equally from palliative care interventions.¹⁴³

Overall, the findings within a healthcare system with universal coverage, focusing on the comparison between patients dying from non-cancer diseases and patients dying from cancer while considering potential confounding factors, provide information valuable to health professionals and policy makers engaged in healthcare planning.

4.3 Methodological considerations

The epidemiological research conducted in the studies comprised by the present PhD dissertation aimed to establish accurate measures of the relationship between exposures and outcomes.

However, the accuracy of epidemiological measures may be impaired by random and systematic error.¹⁴⁴ Random error relates to statistical imprecision resulting from chance or random variation, which can be quantified by the width of the confidence intervals as done in the studies included in the present PhD dissertation. Given the size of the present studies, the role of random error in the estimates was relatively small. Even so, systematic error, described as biases, persists even in large sample sizes, and the major types include selection bias, information bias and confounding. These potential threats to internal validity, detracting from accuracy, should be appraised critically in any study.

4.3.1 Selection of decedents

In all three studies comprised by the present PhD dissertation, a sample of decedents with non-cancer diseases and cancer were identified using the nationwide Danish Registry of Causes of Death to enable inclusion of terminally ill patients approaching death. This method artificially eliminates the uncertainty of prognostication in patients with advanced diseases. However, a traditional cohort study would have been difficult to conduct as it remains a major clinical challenge to determine the life expectancy in patients with advanced illness and to establish when they enter the terminal phase of life.

Selection bias may arise if the association between exposure and outcome among individuals included in a study differs systematically from that of the source population of interest.¹⁴⁴ This may lead to a systematic error of varying effect, and the extent and direction of the impact of this error is usually difficult to determine.¹⁴⁵ The virtually complete nationwide data registered for several decades in the Danish Registry of Causes of Death render selection bias unlikely.¹⁰⁶ Thus, it is improbable that decedents from the source population not registered in the registry should have a markedly different association between the exposures and outcomes than the included decedents.

Incompleteness of data on intensive care unit admissions, non-medical homecare in *Study I* and *Study II* and data on homecare nursing in *Study II* prompted restriction of study populations to only include patients dying in periods for which data collection on these outcomes had been stated complete.^{109,110,115} This was done after ensuring comparability of covariates for included and excluded decedents. Since incompleteness of data was caused by registration practice and not patient-related factors, comparability was also expected. Hence, the probability that the association between outcomes and exposures varied between included and excluded decedents, causing selection bias, is likely to be low.

4.3.2 Misclassification of underlying disease

Systematic, inaccurate measurement or classification of the key exposure or outcome variables is referred to as information bias, resulting in a distortion in the measure of association.¹⁴⁴ Such misclassification of study variables may be classified as either non-differential or differential. Non-differential misclassification arises by equal misclassification of exposure, independently of whether individuals experience the outcome, or by equal misclassification of outcome, independently of exposure status. Conversely, differential misclassification occurs when misclassification of the exposure is dependent on whether individuals experience the outcome or when misclassification of the outcome varies with exposure status.¹⁴⁵

Correct classification of the diseases causing death depends on the quality of the disease diagnosis and on quality of reporting to the Danish Registry of Causes of Death. The registry is virtually complete, but it warrants consideration that validation of the registration of death causes is sparse.¹⁰⁶ Although cause of death is coded by a physician at the time of death, it remains challenging to determine and differentiate between the underlying and immediate conditions causing death. We sought to reduce this uncertainty about classification by including only well-defined chronic conditions. Despite the reporting to the Danish Register of Causes of Death after registration of healthcare utilisation and costs, the risk of differential misclassification is believed to be low. Thus, due to the routinely collected death registry data, potential misclassification of the diseases is presumably unaffected by end-of-life healthcare service utilisation and costs and evenly distributed among the non-cancer and cancer populations.

Even so, it is of concern in the present studies that patients with one of the included causes of death may have been overlooked due to misclassification. Still, it is considered to be unlikely that patients dying from non-cancer diseases and cancer included in the study would differ in terms of the association between exposures and outcomes of the three studies from the ones misclassified and therefore potentially left out of the study populations. Thus, the risk of bias caused by misclassification of the disease causing death is assumed to be low.

4.3.3 Misclassification of socioeconomic position

In *Study II*, Statistics Denmark provided information regarding the exposure of socioeconomic position based on patients' educational level and household income level among patients dying from non-cancer diseases and cancer.^{111,112} Although data on education in general enjoy a high (97%) completeness in the Danish population born in 1945-1990, data on education were missing for approximately 14% of the decedents included in the study. Since the data were missing due to incomplete registration, the missing data were presumably equally distributed between the groups being compared with respect to educational level and independent of healthcare utilisation at the end of life. Therefore, the risk of differential misclassification is considered to be low.

Accordingly, the data on education and income are of high validity, and the results are, therefore, not expected to be influenced by misclassification to any noticeable extent.

4.3.4 Misclassification of outcomes

Misclassification of the outcome measures in the three studies comprised by the present PhD dissertation is most likely non-differential and dependent on factors related to the quality of information on healthcare service utilisation and costs as well as reporting to the registries. The prospective collection of outcome data in the studies counteracts the risk of differential misclassification introduced when the outcome measure is affected by exposure status.

The Danish National Patient Registry is generally believed to have high validity and completeness of its administrative data on hospital admissions, reducing the risk of misclassification.^{115,146} Data from the Danish National Health Service Registry cover all Danish residents and serve as basis for payment; therefore, the coverage is assumed to be good, indicating a low risk of misclassification of primary care utilisation and costs.¹¹³

Indicators from municipal data on non-medical homecare provision and homecare nursing may be misclassified but are presumably evenly distributed on the groups compared. Yet, the extent and direction of this impact is difficult to determine due to the non-dichotomous nature of the outcome measures.

To estimate hospital costs in *Study III*, DRG and DAGS tariffs were used, which are measures of average service costs rather than a fee-for-service approach. Thus, it cannot be ascertained whether costs of terminally ill patients are actually reflected by the DRG and DAGS tariffs. Hence, if terminally ill patients incur more costs than accounted for by the DRG and DAGS tariffs, the actual costs of hospital contacts are most likely underestimated. Correspondingly, hospice care costs are measured by a daily bed charge that fails to take into account variation in costs. Yet, this uncertainty of outcome measures is assumed to be equally distributed between patients with non-cancer diseases and patients with cancer, wherefore this is unlikely to have introduced substantial information bias.

As data on prescription medicine costs from the Danish National Prescription Registry were considered complete and valid, the risk of misclassification related to these data was low.¹¹⁴

4.3.5 Confounding

Confounding may be referred to as a mixing of effects, which occurs when an additional factor is a common cause of both the exposure and the outcome of interest.¹⁴⁴ Confounding may result in a distortion of the true association between the exposure and outcome, potentially leading to masking of an actual association or falsely revealing an association between the exposure and outcome. Therefore, it remains challenging to establish a causal association between an exposure and an

outcome of interest unless confounders are appropriately controlled for by design (restriction, matching or randomisation) or by analysis (stratification, standardisation or adjustment).

In all three studies comprised by the present PhD dissertation, control for various confounding factors was endeavoured by adjusting for relevant factors using regression analyses. Nonetheless, estimates adjusted for several potential confounding factors may still be influenced by residual confounding caused by misclassification of the included covariates. Furthermore, the estimates from the present studies may be confounded by unmeasured factors on which information was unavailable in the current study or by unknown confounding factors.

In *Study I*, the main objective was merely to describe the patterns of healthcare utilisation by days before death according to the underlying disease causing death. Even so, adjusted analyses were made trying to assess the extent to which the healthcare utilisation pattern was driven by the diagnosis at the end of life. Thus, we compared the amount of healthcare services utilised for patients dying from COPD or heart failure with the amount utilised by patients dying from cancer by days before death while adjusting for potential confounding factors. Unmeasured confounding factors in these analyses may include, e.g., lifestyle factors (e.g. smoking, alcohol and Body Mass Index) associated with both the underlying disease and healthcare utilisation.

In *Study II*, exploring socioeconomic disparity trends in healthcare utilisation based on educational level and income level, it was impossible to adjust for potential confounding factors such as severity of illness and lifestyle factors. Confounding from these factors may have explained, among others, some of the socioeconomic disparities that were found regarding hospital-based specialist palliative care utilisation. However, as the conditions presumably have not changed considerably during the 2006-2016 period, these unmeasured confounding factors are unlikely to explain the temporal trends established in socioeconomic disparities in care at the end of life.

In *Study III*, estimating costs of healthcare services at the end of life, potential confounding from unmeasured factors that may vary by underlying disease and influence healthcare costs included lifestyle factors. Yet, it is hardly probable that these confounding factors could explain the entire, extensive difference in end-of-life healthcare costs between patients with non-cancer diseases and patients with cancer.

4.3.6 Generalisability

In the Danish healthcare setting, patients dying from non-cancer diseases and from cancer are presumably not that different from patients dying from these causes in similar developed countries, and the three studies comprised by the present PhD dissertation are generally considered to possess a high internal validity. However, the study setting within a tax-financed healthcare system is fundamentally different from that of other healthcare systems with respect to financing and structure, even other Western countries. Accordingly, palliative care also varies tremendously in

terms of organisation, development and capacity. Therefore, the results may not be fully generalisable to other settings embedded in fundamentally different healthcare systems.

However, the results are likely of relevance in other healthcare settings facing similar capacity strains and challenges in extending palliative care to patients suffering from diseases other than cancer.

5. Conclusions

In the present PhD dissertation, trajectories of illness in patients with non-cancer diseases approaching death were found to differ little from those of patients with cancer when ascertained in real-life data, particularly when reflected in the use of hospital, including intensive care and general practitioners.

In patients suffering from non-cancer diseases or from cancer, socioeconomic disparities in healthcare service utilisation at the end of life were generally limited, and no clear temporal trends were established. Even so, for patients dying from cancer, socioeconomic position has been increasingly associated with the reception of hospital-based specialist palliative care over the years, favouring patients with a high socioeconomic position. In contrast, regardless of the underlying disease causing death, non-medical homecare was less frequently provided to patients with a high socioeconomic position and this difference persisted over the years.

Considerable healthcare costs were related to care at the end of life according to the disease causing death. Moreover, healthcare costs were found to increase in the year leading up to death, regardless of underlying disease, but were markedly lower for patients with non-cancer diseases than for patients with cancer. Furthermore, the costs of hospital-based specialist palliative care and hospice care were extremely limited in patients suffering from non-cancer diseases.

In conclusion, the PhD dissertation highlighted that timely access to palliative care must remain a priority both in patients who are dying from non-cancer diseases and in those who are dying from cancer. Furthermore, palliative care should be provided based on palliative needs rather than diagnosis and treatment intention. Additionally, a focus may be needed on political strategies and considerations aiming to secure appreciable palliative care interventions regardless of the underlying disease and the patient's socioeconomic position to reduce disparities in care at the end of life and to better balance and prioritise healthcare resources.

6. Perspectives

Palliative care utilisation throughout the illness trajectory is not assigned high priority compared with curatively intended treatments for seriously ill patients, and it is predominantly offered once life-prolonging treatment has failed. Moreover, although patients with non-cancer diseases and patients with cancer are reported to face an equivalent symptom burden at the end of life, palliative care is offered mainly to patients with cancer.^{44-48,78} Furthermore, the present PhD dissertation described virtually parallel healthcare resource utilisation patterns, indicating comparable illness trajectories, in patients with non-cancer diseases and patients with cancer approaching death and revealed extremely limited costs of hospital-based specialist palliative care in patients with non-cancer diseases. Therefore, efforts should be made to further strengthen palliative care services, particularly for patients suffering from conditions other than cancer. As reflected by the increasing socioeconomic disparities in hospital-based specialist palliative care presented in the dissertation, the practice and policies behind palliative care interventions need to be reassessed to secure appreciable palliative care interventions regardless of underlying disease and socioeconomic position. Yet, simply expanding the specialist palliative care capacity by increasing the number of specialist palliative care teams and hospices may not be sufficient to solve the problem of unmet palliative care needs as the majority of patients facing serious illness may still be overlooked. Hence, generalist palliative care provision also needs to be improved and initiated alongside standard medical treatment across patient populations with serious illness. Such a shift in care provision calls for an increase in health professionals' awareness and a change in political strategies behind palliative care, reducing disparities in care at the end of life. Prompting this, evidence from interventional studies seems needed to define the most effective palliative care approaches across various healthcare settings and underlying diseases. Furthermore, future research is warranted to elucidate barriers to palliative care, including exploration of factors potentially affecting palliative care utilisation in seriously ill patients. Additionally, for specific patient populations, a paucity of carefully conducted evidence exists regarding the effect of various palliative care components on high-intensity healthcare interventions and patient-reported outcomes at the end of life (e.g. by assessment of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core-15-Palliative Care).

In addition, thorough systematic evaluation of initiatives at local and regional levels aiming to improve end-of-life care is warranted to ensure that these initiatives are efficiently expanded to all Danish residents if they provided improved care at the end of life for the patients.

Further evidence on the economic aspects of palliative care interventions is also required to balance and prioritise limited resources in the face of the growing concern over escalating resource demands in healthcare systems. Thus, future research should aim to explore whether receiving palliative care may also reduce total costs at the end of life by estimating the potential economic

benefit of palliative care in non-cancer and cancer populations alike, preferably by applying a cost-effectiveness methodology.

In order to improve palliative care, utilised throughout the illness trajectory, all health professionals caring for seriously ill patients must be capable of practicing basic palliative care regardless of where they work in the healthcare sector. Achieving this capacity will require better training of health professionals in palliative care. Better training may in turn affect the attitude towards and confidence in this area of medicine, which health professionals tend to give low priority. Integrating palliative care throughout the illness trajectory may call for implementation science to inform educational programmes for all health professionals.

Overall, knowledge that seriously ill patients receiving palliative care, regardless of their diagnosis or prognosis, have better clinical outcomes and experience a higher quality of their remaining life at lower total healthcare costs would compellingly advocate for a coordinated development of palliative care services.

Summary

Reducing disparities in health remains a core political objective in advanced healthcare systems, but ageing populations requiring increased levels of care, particularly at the end of life, may exacerbate existing disparities. On this basis, the present PhD dissertation explored the role of underlying disease and socioeconomic position for disparities in care at the end of life. Using individual-level data from population-based national registries, the studies examined end-of-life illness trajectories as reflected by healthcare utilisation (*Study I*), socioeconomic disparity trends over time in use healthcare services at the end of life (*Study II*) and healthcare costs at the end of life (*Study III*).

Study I included 174,086 patients dying from chronic obstructive pulmonary disease, heart failure and cancer in 2006-2016. Limited differences in healthcare resource utilisation patterns among the patient populations indicated comparable illness trajectories. Thus, for all patient populations, daily prevalence proportions of patients admitted to hospital, intensive care units and consulting a general practitioner progressed gradually and accelerated in the last months of life.

Study II included 350,044 patients dying from non-cancer diseases and cancer in 2006-2016. Socioeconomic disparities in use of hospital-based specialist palliative care tended to increase over time among patients dying from cancer. Thus, compared with cancer patients with a low income level, one percentage point more patients with a high income level received hospital-based specialist palliative care in 2006/2007 (adjusted mean difference: 0.01 (95% confidence interval (CI): 0.01; 0.02)) and 12 percentage points more patients in 2016 (adjusted mean difference: 0.12 (95% CI: 0.09; 0.14)). In both patients with non-cancer diseases and cancer, socioeconomic disparities were limited and without clear temporal trends in use of other healthcare services at the end of life.

Study III included 218,612 patients dying from non-cancer diseases and cancer in 2010-2016. Applying a cost-of-illness methodology and adopting a healthcare sector perspective, the study estimated total healthcare costs to be considerably lower for patients with non-cancer diseases than for patients with cancer in the year leading up to death. Thus, the mean total healthcare costs were €24,353 (95% CI: 24,159; 24,546) per patient with non-cancer disease and €45,997 (95% CI: 45,773; 46,221) per patient with cancer. Within the last months of life, differences persisted although they were reduced. Furthermore, the mean costs of hospital-based specialist palliative care and hospice care were extremely limited for patients with non-cancer diseases.

In conclusion, the studies comprised by the present PhD dissertation suggested that although illness trajectories as reflected in healthcare utilisation patterns seemed comparable, substantial disparities were observed in care at the end of life according to the disease causing death. Even within a tax-financed healthcare system, patients dying from non-cancer diseases incurred considerably lower healthcare costs at the end of life than patients with cancer, including limited costs and utilisation of specialist palliative care which was also increasingly provided to patients with a high socioeconomic position.

Dansk resumé

Det er et centralt politisk mål i avancerede sundhedssystemer at reducere uligheden i sundhed, men aldrende populationer, som kræver ekstra ressourcer særligt i slutningen af livet, kan potentielt medføre, at eksisterende uligheder eskalerer. På denne baggrund beskriver denne ph.d.-afhandling betydningen af underliggende sygdom og socioøkonomisk position for uligheder i forbindelse med pleje og behandling i slutningen af livet. Baseret på individdata fra populationsbaserede, nationale registre undersøgtes sygdomsforløb ud fra forbrug af sundhedsydelser frem mod døden (*Studie I*), socioøkonomiske uligheder og udviklingen over tid i brugen af sundhedsydelser (*Studie II*) og omkostningerne forbundet med pleje og behandling i den sidste tid (*Studie III*).

Studie I inkluderede 174.086 patienter, som døde af kronisk obstruktiv lungesygdom, hjertesvigt eller kræft i 2006-2016. Sygdomsforløbene fremstod sammenlignelige, idet den daglige prævalensproportion af indlagte patienter og patienter, der konsulterede almen praktiserende læger, var gradvist stigende og steg stejlt i de sidste måneder af livet i de tre patientpopulationer.

Studie II inkluderede 350.044 patienter, som døde af ikkemaligne sygdomme og kræft i 2006-2016. Socioøkonomisk ulighed i adgangen til specialiseret palliativ behandling var stigende over tid for patienter, der døde af kræft. Sammenlignet med kræftpatienter med lav indkomst var der ét procentpoint flere patienter med høj indkomst, der modtog hospitalsbaseret specialiseret palliativ behandling i 2006/2007 (justeret gennemsnitlig difference: 0,01 (95% sikkerhedsinterval (SI): 0,01; 0,02)), men tolv procentpoint flere patienter i 2016 (justeret gennemsnitlig difference: 0,12 (95% SI: 0,09; 0,14)). De socioøkonomiske uligheder var begrænsede, og der var ingen udvikling over tid i forbrug af øvrige sundhedsydelser hverken for patienter med ikkemaligne sygdomme eller for patienter med kræft.

Studie III inkluderede 218.612 patienter, som døde af ikkemaligne sygdomme og kræft i 2010-2016. Estimeret ved sygdomsbyrdeestimer ud fra et sundhedssektorperspektiv var de totale omkostninger betragteligt lavere for patienter med ikkemaligne sygdomme end for patienter med kræft i det sidste år af livet. De gennemsnitlige totale omkostninger var €24.353 (95% SI: 24.159; 24.546) per patient med ikkemalign sygdom og €45.997 (95% SI: 45.773; 46.221) per patient med kræft. Forskellene var lidt mindre i de sidste måneder af livet, men var fortsat til stede. De gennemsnitlige omkostninger til hospitalsbaseret specialiseret palliativ behandling og hospice var meget lave for patienter med ikkemaligne sygdomme.

Selvom sygdomsforløbene for patienter med ikkemaligne sygdomme og patienter med kræft var sammenlignelige, var der substantielle forskelle i pleje og behandling frem mod døden. Selv i et skattefinansieret sundhedssystem som det danske var omkostningerne til patienter med ikkemaligne sygdomme langt lavere end omkostningerne til patienter med kræft – herunder omkostningerne og forbruget af specialiseret palliativ behandling, som også i stigende grad blev tilbudt patienter med høj socioøkonomisk position.

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Appendices

Full versions of Paper I-III are provided in the Appendices I-III:

Appendix I

Paper I

Appendix II

Paper II

Appendix III

Paper III

The papers have been removed from the file due to copyright issues