UNIVERSITY OF COPENHAGEN
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# PhD Thesis

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# Child mortality and parents' perspectives on losing a child with a life-limiting diagnosis: Population-based studies

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Rigshospitalet

børne | cancer | fonden

# *PhD Thesis*
## *Camilla Lykke*

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# Child mortality and parents' perspectives on losing a child with a life-limiting diagnosis: Population-based studies

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**PhD thesis**

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# Acknowledgement

The last three years has been a challenging academic and personal journey. It has been strenuous, but truly rewarding. This thesis was originally designed to provide a basis for the future planning and organization of specialized paediatric palliative care and to contribute to improving the care of children with life-limiting diagnoses and their parents. I certainly hope that some of these intensions will be fulfilled.

Although my name appears on the cover of this thesis, I could not have got so far without the many who believed in the project and in me. First and foremost a very special and heartfelt thanks to my primary supervisor Professor **Per Sjøgren** for believing in me and granting me the opportunity, for your availability, enthusiasm and your always meticulous feedback. A special thanks to my co-supervisor **Ola Ekholm,** who has always been ready to help when I was statistically challenged or needed some good advice. Your qualified input has been an invaluable help and support. Many thanks also to my co-supervisor Professor **Kjeld Schmiegelow.** Your dedication has been contagious and instructive and your professional insight and knowledge invaluable. Thanks to **Marianne Olsen** for your contribution at my supervisory meetings.

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**To Emilie and Niclas**

# Summary

In recent years specialized paediatric palliative care (SPPC) has received increasing attention both from healthcare professionals (HCPs) as well as from the public in Denmark. There is a consensus that SPPC should be strengthened; however, there is some disagreement regarding the organization, structure, content and scope of it. This disagreement may be due to the lack of knowledge and insight regarding the children's diagnoses, place of care, death and the needs of the families, which have not formerly been investigated in a Danish context. To support and initiate sound decision-making regarding the development and the organization of SPPC in Denmark, the purposes of the present thesis were: 1) to examine causes and places of death in children below 18 years of age who died in the period 1994-2014 ***(study I)***, 2) to investigate anxiety and depression in bereaved parents after losing a child due to life-limiting diagnoses ***(Study II)***, and 3) to investigate bereaved parents' perception of end-of-life communication with healthcare professionals during their child's life-limiting disease and imminent death ***(Study III)***.
***Study I*** was a national register-based epidemiological study identifying diagnoses and places of death in children between the ages of 0-17 years, who died between 1994-2014. ***Study II and III*** was a national cross-sectional questionnaire survey, where a modified version of the self-administered questionnaire "To lose a child" was used. The survey included a selected population of bereaved parents, who lost a child under the age of 18 years due to life-limiting diagnoses in the period 2012-2014.
***Study I*** showed that during the observation period the all-cause mortality rate decreased more than 50% and infants under the age of one accounted for around 60% of all deaths. Regarding place of death, the relative proportion of hospital deaths increased, whereas home deaths decreased. These results may reflect more aggressive, but likely also more effective treatments to save lives; however, in some cases children may be deprived of the option of dying at home.
***Study II*** assessed anxiety and depression in bereaved parents 3-5 years after the loss of a child. The bereaved parents reported high levels of anxiety and depression during the child's disease. However, 3-5 years after the loss anxiety had decreased markedly in both parents, but the level of depression was unchanged. Parents who were unmarried or had lower education were associated with severe depression. Although bereaved parents' reporting of depression may be difficult to distinguish from grief, the results indicated that there may be a need for interventions to treat and support parents during their child's disease and after the loss. ***Study III*** found that bereaved parents want timely and accurate information regarding their child's life-limiting

disease and imminent death. HCPs communicated late about end-of-life care issues and some of the parents felt that they were deprived of taking leave with their child in the way they wished. This may indicate that the parents' needs for information were not sufficiently met, which may raise awareness of the necessity for specific communication training and education of HCPs working in this field. In ***study II and III*** non-response surveys identified reasons for a lack of response.

This project has provided new knowledge that can be used in future development and organization of SPPC in Denmark as well as enrich the international endeavours in this field.

# **Dansk Resumé** (Danish summary)

Det seneste år har specialiseret pædiatrisk palliation haft stigende fokus både i faglige kredse og i offentligheden i Danmark. Der hersker enighed om, at indsatsen skal styrkes, men der eksisterer uenighed om tilbuddets udformning, omfang og kvalitet. Denne uenighed kan skyldes den manglende viden og indsigt i børn med livsbegrænsende diagnoser og behov hos deres familier, hvilket ikke tidligere er blevet udforsket i en dansk kontekst. For at støtte planlægningen og tilrettelæggelsen af specialiseret pædiatrisk palliation var formålet med denne afhandling følgende: 1) at undersøge dødsårsager og dødssteder hos børn under 18 år som døde i perioden 1994-2014 ***(studie I)***, 2) at undersøge angst og depression hos efterladte forældre, der har mistet et barn med en livsbegrænsende diagnose ***(Studie II)***, og 3) at undersøge de efterladte forældres opfattelse af kommunikation med sundhedspersonale under deres barns sygdom og nært forestående død ***(Studie III)***.

***Studie I*** var et nationalt registerbaseret epidemiologisk studie, der identificerede dødsårsager og dødssteder hos børn (0-17 år), der døde i perioden 1994-2014. ***Studie II og studie III*** er baseret på en national tværsnitsundersøgelse, hvor en modificeret udgave af det selv-rapporterede spørgeskema ”At miste et barn” blev anvendt. Undersøgelsen omfatter en selekteret population af efterladte forældre, der i perioden 2012-2014 mistede et barn under 18 år på grund af livsbegrænsende sygdomsdiagnoser.

***Studie I*** fandt at dødeligheden faldt i observationsperioden med mere end 50%, og at børn under 1 år udgjorde ca. 60% af dødsfaldene. Angående dødssted viste studiet, at den relative andel af dødsfald på hospital steg, mens hjemmedød faldt. Disse resultater kan afspejle en mere aggressiv, men også effektiv behandling for at redde børnenes liv, hvilket i nogle tilfælde kan fratage børn og forældre muligheden for, at barnet kan dø i eget hjem. ***Studie II*** vurderede angst og depression hos de efterladte forældre 3-5 år efter barnets død og fandt, et højt niveau af angst og depression under barnets sygdom. Imidlertid faldt begge forældres oplevelse af angst signifikant 3-5 år efter, at de havde mistet deres barn, mens niveauet af depression forblev uændret i samme periode. Yderligere blev der fundet en sammenhæng mellem forældre, der var ugifte eller havde en lavere uddannelse og svær depression. De efterladte forældres oplevelse af depression 3-5 år efter at de har mistet af deres barn, kan dog imidlertid være vanskelig at skelne fra deres sorg, men studiets resultaterne indikerer, at der synes at være et øget behov for behandling og/eller støtte til forældrene både under barnets sygdom og efter barnets død. ***Studie III*** fandt, at efterladte forældre ønsker rettidig og præcis information om deres barns

livsbegrænsende sygdom og forestående død. Sundhedspersonalet kommunikerede sent om emner relateret til palliativ indsats, og en betydelig del af forældrene følte, at de blev frataget muligheden for at tage afsked med deres barn på den måde, de ønskede. Dette indikerer, at forældrenes behov for information ikke er tilstrækkeligt opfyldt, hvilket bør øge fokus på kommunikationstræning og uddannelse af sundhedsprofessionelle.

***Studie II og III*** indeholdt non-response undersøgelser for at identificere årsager til den manglende respons blandt forældrene.

Projektet har således tilført ny og vigtig viden, som kan være med til at udvikle og organisere den fremtidige specialiserede palliative indsats til børn og deres forældre i Danmark samt berige den internationale indsats på området.

# Abbreviations

**SPPC:** Specialized paediatric palliative care
**HCPs**: Healthcare professionals
**PPC**: Paediatric palliative care
**WHO**: The World Health Organization
**ACT**: The Association for Children´s Palliative Care
**RCPCH**: Royal College of Paediatrics and Child Health
**EAPC**: European Association for Palliative Care
**SPC**: Specialized palliative care
**ICPCN**: The International Children’s Palliative Care Network
**ICD-10**: International Statistical Classification of Diseases and Related Health Problems 10th Revision
**DSM–5**: Diagnostic and Statistical Manual of Mental Disorders
**QOL**: Quality of life
**HRQoL**: Health-related quality of life
**AAP**: The American Academy of Paediatrics
**CRS**: Danish Civil Registration System
**CPR-number**: Danish civil registration number
**CES-D**: Centre for Epidemiological Studies Depression Scale
**VDS**: Visual Digital Scale
**STAI-T**: Spielberger’s State-Trait Anxiety Inventory
**SD**: Standard deviations
**GEE**: Generalized Estimating Equation model

# List of papers

## Study I

Lykke C, Ekholm O, Schmiegelow K, Olsen M, Sjøgren P. **All-cause mortality rates and home deaths decreased in children with life-limiting diagnoses in Denmark between 1994 and 2014**. *Acta Paediatr* 2018;107:1781-1785.

## Study II

Lykke C, Ekholm O, Schmiegelow K, Olsen M, Sjøgren P. **Anxiety and depression in bereaved parents after losing a child due to life-limiting diagnoses: A Danish nationwide questionnaire survey**. *J Pain Symptom Manage* 2019;58(4):596-604.

## Study III

Lykke C, Ekholm O, Schmiegelow K, Olsen M, Sjøgren P. **End-of-life communication: a nationwide study of bereaved parents' perceptions**. *BMJ Support Palliat Care* 2019 [Epub ahead of print].

# Background

## *Paediatric palliative care: Definitions and classifications*

Paediatric palliative care (PPC) aims at reducing suffering and promoting quality of life for children with life-limiting or -threatening diagnoses and their families. The World Health Organization (WHO) defines palliative care as *"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"*. According to WHO, PPC represents a special, albeit closely related field to adult palliative care; the principles apply to other paediatric chronic disorders[1]:

- *Palliative care for children is the active total care of the child's body, mind and spirit, and also involves giving support to the family.*
- *It begins when illness is diagnosed and continues regardless of whether or not a child receives treatment directed at the disease.*
- *Health providers must evaluate and alleviate a child's physical, psychological, and social distress.*
- *Effective palliative care requires a broad multidisciplinary approach that includes the family and makes use of available community resources; it can be successfully implemented even if resources are limited.*
- *It can be provided in tertiary care facilities, in community health centres and even in children's homes*[1].

The Association for Children´s Palliative Care (ACT) and Royal College of Paediatrics and Child Health (RCPCH) defines PPC in children with life-limiting conditions as "*an active and total approach to care, from the point of diagnosis or recognition, throughout the child's life, death and beyond. It embraces physical, emotional, social and spiritual elements and focuses on the enhancement of quality of life for the child and support for the family. It includes the management of distressing symptoms, provision of short breaks and care through death and bereavement*"[2].

These definitions highlight important generic features of palliative care, especially important is the fact that palliative care is not only defined as end-of-life care. It is rather extending earlier into life-threatening illness trajectories. In addition, the provision of palliative care is increasingly advocated alongside the disease-related treatment, progressively becoming the focus of treatment as the burden of symptoms in adults with cancer increases toward death[3,4]. Also, the definitions highlight the focus of including the patient's family in palliative care interventions. It is inherently patient-focused and responds to the specific needs of the patients and their families[4] not only including symptom management for the patients, but also social, psychological and spiritual care for the patients and their families, extending into bereavement[5]. Thus, an interdisciplinary team of providers is central to palliative care[4].

In addition, ACT and RCPCH have prepared the following overall classification of children with life-limiting and -threatening diagnoses:

***Category 1:*** *Life-threatening conditions for which curative treatment may be feasible but can fail. Where access to palliative care services may be necessary when treatment fails or during an acute crisis, irrespective of the duration of that threat to life. On reaching long term remission or following successful curative treatment there is no longer a need for palliative care services (e.g. cancer, irreversible organ failures of heart, liver, kidney).*

***Category 2*:** *Conditions where premature death is inevitable, where there may be long periods of intensive treatment aimed at prolonging life and allowing participation in normal activities (E.g. cystic fibrosis, Duchenne muscular dystrophy).*

***Category 3*:** *Progressive conditions without curative treatment options, where treatment is exclusively palliative and may commonly extend over many years (e.g. Batten disease, mucopolysaccharidoses).*

***Category 4*:** *Irreversible but non-progressive conditions causing severe disability leading to susceptibility to health complications and likelihood of premature death (e.g. severe cerebral palsy, multiple disabilities such as following brain or spinal cord injury, complex health care needs and a high risk of an unpredictable life-threatening event or episode)*[2].

Also, the European Association for Palliative Care (EAPC) has worked intensively with the development of PPC since 2006, when the "EAPC Task Force on Palliative Care in Children" was established. Through this initiative, the EAPC has produced "IMPaCCT: standards for paediatric palliative care in Europe"[6] and "Palliative care for infants, children and young people: The Facts"[7]. The "IMPaCCT: standards for paediatric palliative care in Europe" clarify definitions and common standards for European countries concerning care in children with life-limiting and terminal illnesses. It declaims that meeting the needs of PPC requires a comprehensive and integrative approach from skilled interdisciplinary teams and recommends that these core standards for PPC should be implemented across Europe[6]. The document: "Palliative care for infants, children and young people: The Facts" aims at examining the state-of-the-art and the needs for PPC. Thus, it documents the importance of PPC and introduces the evidence for policy development together with describing the needs of the children and their families. Furthermore, it provides arguments for integrating palliative care across all health care services and formulates general recommendations for health care policy-makers[7]. The document has become a reference for HCPs working for implementing and improving PPC practices in many parts of the world.

The overall philosophy of PPC is that the child's life; including family life, as far as possible, is not limited by symptoms, treatment and physical frameworks and paediatric palliative care should be targeted to the entire family.

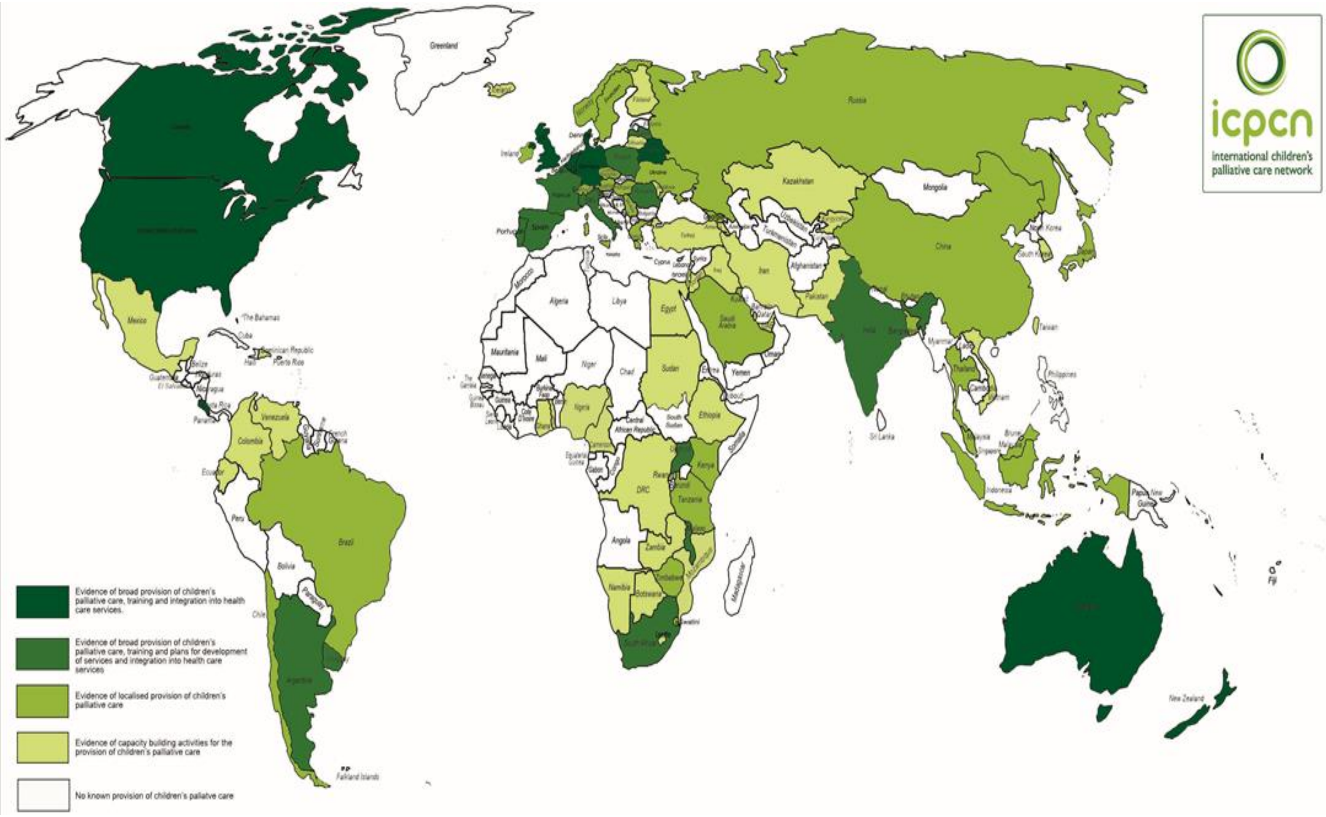
### ***Specialized paediatric palliative care (SPPC) internationally***

WHO's definition on palliative care does not differentiate between basic and specialized palliative care (SPC). However, EAPC has defined SPC as: "*Specialized palliative care is provided by specialised services for patients with complex problems not adequately covered by other treatment options*"[8]. Internationally, there is a distinction between basic and SPC. Basic palliative care can be provided by all HCPs whereas SPC is provided by interdisciplinary teams which work in departments, where palliative care to patients with greater complexity, severity and duration of symptoms are the core function and accordingly the HCPs in these teams have received specialist training and education[9–11].

Looking back in the literature, it has not been easy to trace exactly when the development of SPPC began. A major influence may have been the growing awareness of the benefits and strengths of palliative care for adults, following the opening of St. Christopher's Hospice in London in 1967 by Dame Cicely Saunders.

SPPC services have been developed since the first children's hospice was established at Helen House in Oxford, England in 1982. It included gardens, playrooms, family accommodation and was staffed with an interdisciplinary team[12–15]. Helen House aimed at caring for all children with life-limiting diseases, although most of the children, who were admitted had longer-term trajectories as neurodegenerative and metabolic diseases. Some of the children received end-of-life care; however, the majority of the children received respite care. The entire family including siblings were supported by the staff throughout the disease and bereavement. Thus, Helen House became a role-model for children's hospices worldwide. However, each country and their institutions has developed its own characteristics e.g. involving collaboration with local children's hospitals, hospice care for adults or other models including home or daycare facilities[16]. The hospital-based SPC team at Great Ormond Street Hospital, United Kingdom, was the first of its kind back in 1986. However, the location of SPPCs services varies. Where the United Kingdom has focused on residential hospice teams, the United States has focused on developing hospital-based teams. However, the basic philosophy behind PPC remains the same regardless of the location of care[17].

The need for SPPC globally is unknown. However, a recent study has estimated that more than 21 million children have unmet needs for palliative care and approximately more than eight million of these children need SPC[18]. The International Children's Palliative Care Network (ICPCN) is a global network of organizations and individuals, who since 2005 have reached out to the children with life-limiting and -threatening diseases, to identify children with unmet needs. In November 2018, the ICPCN has updated the estimated levels of PPC globally as follows[19]:



**Level 1:** Evidence of broad palliative care provision for children. Approaching full integration within health care services as well as a national policy to support children's palliative care (E.g. Australia, Canada, Germany, United Kingdom, The Netherlands, United States of America).

**Level 2:** Evidence of broad palliative care provision for children with training available and focused plans for the development of services and integration into health care services (E.g. Argentina, Belgium, **Denmark,** France, India, Italy, New Zealand, South Africa, Uganda)

**Level 3:** Evidence of localized palliative care provision for children and availability of training (E.g. Austria, Brazil, Hungary, Ireland, Japan, Romania, Russia, Sweden, Tanzania, Zimbabwe).

**Level 4:** Evidence of capacity building activities for the provision of children's palliative care. Some localized provision may be available (E.g. Egypt, Finland, Iran, Mexico, Norway Nigeria, Pakistan, Sudan, Turkey, Uruguay, Venezuela).

**Level 5:** No known provision or capacity building activities for children's palliative care[19].

In recent years SPPC has grown world-wide; however, looking at the service provided there still seems to be major gaps globally. As previously written, the need for SPPC globally is not known and an exact estimate of the number of children in need of SPPC is difficult to obtain. Many countries have had challenges in gaining an overview, and in previous studies, it is primarily referred to as uncertain estimates, which are calculated in different ways and therefore, difficult to compare across countries. If we look at some of the countries, which we often associate with, Sweden has a population of approximately 9.5 million inhabitants and about 600 children and adolescents die annually, of whom around half die before the age of one. However, it is unclear how many of these could benefit from SPPC[20]. As the first country in Scandinavia, Sweden established their first and only children's hospice in 2010[20]. Norway has approximately 5.2 million inhabitants and has estimated that between 300-450 children under the age of 18 years die annually. An estimate for the prevalence of children with a "palliative diagnoses" is approximately 3,500[21,22], but estimates on how many could benefit from SPPC is not known. Norway does not have any children's hospices, but various hospitals provide palliative care both in hospitals and at home[21,23] and in 2017, the Norwegian Directorate for Health published national guidelines for palliative care for children and adolescents independently of a diagnosis[24]. Germany has a population of approximately 83 million and it is estimated that there are more than 23,000 children and young adults with terminal diseases out of whom 5,000 die annually[25]. In Germany there are 9 children's hospices distributed throughout the country[26]. In the UK they have a population of approximately 66 million residents, and it is estimated that there are at least 49,000 children under the age of 19 with life-limiting diseases, who may benefit from SPPC[27]. In the UK they had 44 children's hospices in 2014[28]. According to the Foundation "Together for Short Lives" there are 54 Children's hospices around the UK today[29]. Furthermore, paediatric palliative medicine was recognized as a specialty in the UK back in 2009[28].

### *Specialized paediatric palliative care (SPPC) in Denmark*

Denmark has a total population of approximately 5.7 million people, and children below the age of 18 years represent around 20% of the total population. Denmark is characterized by people living in smaller families, typically within two generations; children with their parents, like most countries in the western world. Denmark is a high-income and modern country with a modern welfare state, and it has one of the highest standards of living in the world. The basic principles behind the Danish welfare system is that every citizen has equal rights to social security and free access to health care services including general practitioners, home care and hospital services. Hospital services includes hospital-based palliative care as well as hospice care. A corresponding high tax rate makes it possible to maintain the high level of services.

National guidelines for the provision of palliative care in Denmark are based on WHO's definition[5] and as such emphasize early intervention and holistic, interdisciplinary care including physical, psychological, social and existential care, and family-involvement[10,30] Basic palliative care is provided by HCPs such as general practitioners and non-palliative hospital clinics and home care services. SPC is provided by interdisciplinary teams either at hospitals or hospices, in accordance with clinical guidelines. However, in Denmark SPC is not yet a separate medical specialty[30] and in a recent Lancet Oncology Commission article concerning integration of oncology and palliative care the theoretical and clinical training of physicians according to the curriculum of the Nordic Specialist Course in Palliative Medicine has been termed a special denomination[4].

Previously, PPC has not been a priority in Denmark. No specific national guidelines or policies for children with palliative care needs existed and the population of children with life-limiting diseases was only briefly mentioned in the "National recommendations on palliative care" from 2011, which acknowledged that palliative care for children was a particular challenge[30]. At that time there were limited health care services at the university hospitals using home-based basic palliative care teams for children who mainly had cancer. One example was the Juliane Marie Centre, Rigshospitalet, Copenhagen, which offered basic palliative care at home for children with cancer[31,32]. Another example is the Department of Paediatric oncology and hematology and the Palliative Team at Aarhus University Hospital, who collaborated to support the families, who wished to have their children at home for end-of-life care[33].

From 2015 an increasing attention and interest of SPPC was observed from HCPs and the public[34]. First, a report was published based on a literature study[35]. The purpose of the report was to investigate national and international experiences with the organization of palliative care for children with life-limiting or -threatening conditions and their families[35]. The opening of the first children´s hospice "Lukashuset" in 2015[36] indicated that SPPC was now on the agenda in Denmark and while this project has running, SPPC has developed further. In 2016 all five public healthcare regions in Denmark were upgraded with SPPC teams in order to increase the capacity. In addition, it has recently been decided to allocate money to another children's hospice in Western Denmark with a planned opening in 2020. Also, recommendations regarding PPC have been published by the Danish Health Authority[37] and research in the area is gradually upcoming.

## *Mortality rate and place of death in children in high income countries*

### *Mortality rate*

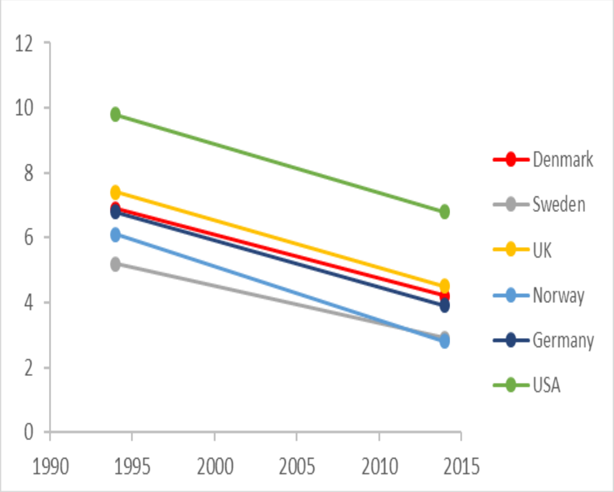
Children contribute about a third of the world's population and their health status is important for every country and society. Global mortality rates among children have been declining since 1990 and through the past several decades there has been a substantial progress in reducing child mortality. According to a report prepared by UNICEF the total number of under-five deaths decreased significantly from approximately 12.6 million in 1990 (35,000 every day) to 5.6 million in 2016 (15,000 every day)[38].

The mortality risk for children aged between 5–14 is about one fifth of the risk of dying for children under-five, however, 1 million children aged between 5–14 still died worldwide in 2016[38].

Striking variations exist across countries[39,40] and WHO proclaims that the inequities in child mortality remains large between high and low-income countries. In 2017, the under-five mortality rate in low-income countries was around 14 times higher than the average rate in high-income countries (69 deaths per 1,000 live births in low-income countries vs 5 deaths per 1000 live births in high-income countries)[41] and causes of death, such as tuberculosis, HIV/AIDS, malaria and malnutrition, which primarily are caused by the living conditions in low-income countries, are no longer or rarely seen in high-income countries.

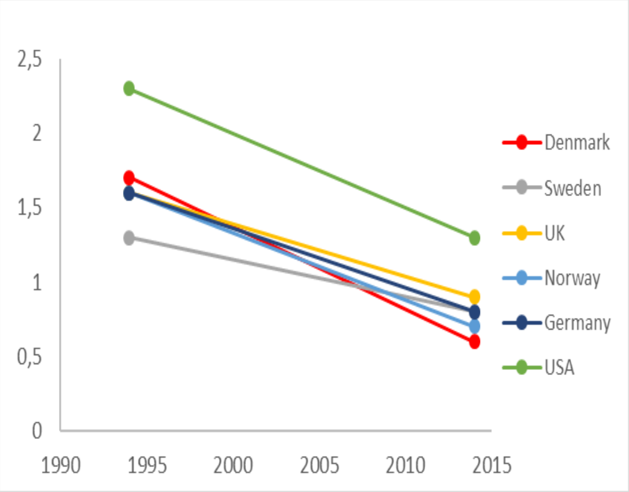
According to WHO the mortality rate in Denmark has decreased from approximately 32 deaths/100,000 in 1950 to 4 deaths/100,000 in 2012[42]. To our knowledge, previous research studying the development of children's mortality across countries over a long-time perspective does not exist. However, WHO has a Global Health Observatory where the probability of death in children under the age of five and children aged between 5-14 years per 1,000 live births is registered[43,44]. The decrease in mortality of children in the age range of 0-14 years in the period 1994-2014 from selected high-income countries, which are comparable to Denmark, is shown below. To our knowledge there is no published data internationally on mortality rates among adolescents in the age group 15-17 years.

**Figure 1: Under 5 years mortality rates in European countries (per 1,000 live births) 1994-2014**



| | Denmark | Sweden | UK | USA | Norway | Germany |
|---|---|---|---|---|---|---|
| 1994 | 6.9 | 5.2 | 7.4 | 9.8 | 6.1 | 6.8 |
| 2014 | 4.2 | 2.9 | 4.5 | 6.8 | 2.8 | 3.9 |
| Decrease % | 39 | 44 | 39 | 31 | 54 | 43 |

**Figure 2: Mortality rates in children aged 5-14 years (per 1,000 live births) 1994-2014**



| | Denmark | Sweden | UK | USA | Norway | Germany |
|---|---|---|---|---|---|---|
| 1994 | 1.7 | 1.3 | 1.6 | 2.3 | 1.6 | 1.6 |
| 2014 | 0.6 | 0.8 | 0.9 | 1.3 | 0.7 | 0.8 |
| Decrease % | 65 | 38 | 44 | 44 | 56 | 50 |

Source: WHO, The Global Health Observatory

As shown above, the mortality rate for all the high-income countries has decreased markedly for children between the ages of 0-14 years in the period 1994-2014. However, the percentage of the decline varies between countries. The USA has in both groups the highest proportion of mortality rates among children and Sweden represents the lowest mortality rate in both groups in 1994. In 2014 the lowest mortality rate under 5 years was identified in Norway closely followed by Sweden. The greatest overall decline in the mortality rate under 5 years was found in Norway. In the age group 5-14 years Denmark had the lowest mortality rate in 2014 as well as the greatest overall decline. According to WHO, the overall average decline of the mortality rate in children aged 0-14 years was found in Norway, followed by Denmark and Germany.

### *Place of death*

Often, home is cited as the preferred place of death end even the public and HCPs consider that a good death should take place at home[45]. However, the information regarding children's preferred place of death varies and is still sparse[45,46]. A systematic review investigating children's preferred place of death according to information from their parents included nine studies from five various countries. The review showed that the majority of parents stated preference for home death in six out of the nine studies. However, significant variations in preference for home death were observed, a study reported 35% preference for home death, whereas other studies did not express any preference. One study found that the number of parents, who preferred home death, increased in the last month of life[45]. However, large cross-national variations in children's place of death has been described in a previous study[47]. The study investigated variations in children with complex chronic conditions in 11 European and non-European countries. The study was based on data from death certificates of all deceased children in the age of 1-17 years, who died in 2008. The study found that children from Belgium and USA with complex chronic conditions, other than malignancies, were less likely to die at home, whereas deaths caused by neuromuscular diseases in South Korea and Mexico were more likely to happen at home than those with malignancies. Furthermore, the study found that boys more often than girls are dying at home in Sweden and Mexico. The wide variations may be related to policies, health system related infrastructures and differences in cultural values in relation to place of death in children[47]. The Nordic countries including Denmark are known to offer high-quality paediatric treatment and care[48]; however, data regarding PPC at home or in hospitals is still sparse. Likewise, data regarding place of death and preferred place of death in Danish children does not exist, which may be considered an essential and basic information for the future planning and organization of PPC.

### *Anxiety and depression in bereaved parents*

In the Palliative Care Dictionary, the definition of psychological distress is "*a range of symptoms and experiences of a person's internal life that are commonly held to be troubling, confusing, or out of the ordinary*", which includes anxiety and depression[49]. The American Psychiatric Association has further defined anxiety as "*Anxiety disorders differ from normal feelings of nervousness or anxiousness, and involve excessive fear or anxiety"*[50] and depression has been defined as "*a common and serious medical illness that negatively affects how you feel, the way you think and how you act more than just sadness"*[51]. Anxiety and depression are both clinical diagnoses and can be diagnosed according to the World Health Organization's International Statistical Classification of Diseases and Related Health Problems 10th revision (ICD-10) [52] and the Diagnostic and Statistical Manual of Mental Disorders (DSM–5)[53]. In Denmark, anxiety and depression is diagnosed by a physician based on the latest ICD-11 criteria. Anxiety and depression are widespread conditions in the general population that greatly affects quality of life (QOL)[54–56].According to WHO's definition, QOL is: "*An individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a* *complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment*" QOL has become increasingly important in health-care practice and in research and the term "health-related quality of life" (HRQoL) narrows QoL to aspects relevant to health. HRQoL is a complex and comprehensive concept. It is a multidimensional concept that can be viewed as a latent construct, which describes both physical, social, and psychological aspects of well-being and functioning[57–59]. However, it has been argued in the literature that the definitions of HRQoL are problematic as some of them fails to distinguish between health and HRQoL or between QOL and HRQoL[60]. However, losing a child may be considered as an extremely burdensome and painful loss, which may challenge the individual's HRQoL/QOL and position in life and may be associated with the risk of developing both anxiety and/or depression.

A previous review focusing on the association between losing a child and subsequent health problems in parents showed that nine out of seventeen studies found an increased risk of illness in bereaved parents including e.g. anxiety and depression. Five studies investigated adverse psychological outcomes including anxiety and depression and agreed that parents who had lost a child had an increased risk of psychological distress compared to non-bereaved parents[61]. A recent systematic review confirmed these findings in parents to children who died from cancer[62]. A recent Danish nationwide study has investigated relatives after the loss of a close one and provided the first comprehensive assessment of incidences of serious mental health conditions in this population. A significantly elevated risk of deliberate self-harm, suicide, and psychiatric illness was shown, especially in the first year after the loss. Loss of a spouse or a child showed higher risk, and younger age, sudden losses and/or a history of mental illness were specific risk factors[63] as well as it has been claimed that spousal and parental caregivers to patients with cancer might experience greater psychological distress than other caregivers[64]. Other Danish studies have found a substantial increase in mortality in bereaved parents[65] as well as an increased risk of psychiatric hospitalization among parents, and especially in mothers, after losing a child[66]. It seems obvious that psychological distress including anxiety and depression in bereaved parents following the loss of a child with a life-limiting diagnose may have a great impact in terms of suffering. However, no Danish studies have formerly investigated anxiety and depression in bereaved parents after the loss of a child with life-limiting diagnoses.

In addition, we have to consider that symptoms normally associated with depression is a common feature in grief and grief is a natural and normal reaction to loss[67,68]. In public "grief" is widely used and describes not only the emotional reactions following the loss of a relative, but also the reactions that may follow, for example, divorce, loss of work, loss of physical function, loosing pets and involuntary childlessness[69]. According to the Textbook of Palliative Medicine and Supportive Care grief is described as a natural and multifaceted response to a loss and losses related to illness involve mourning. Mourning is the expression of grief and represents the process of dealing with the loss[70]. The work of grieving has been described as a process of "relearning the world"[71,72]. The Danish National Center of Grief describes grief as the reactions a person may experience after a loss of a close relative. At the same time, they recognize that people who have experienced other types of loss can undergo reactions very similar to those that may occur following the loss of a close relative.[69]. However, grief and depression share some common characteristics and grieving persons may experience e.g. symptoms of depression as fatigue, intense sadness, social isolation, sleep and appetite disturbances and/or cognitive deficits. However, there is a clear distinction between depression and grief. Depression is a mental disorder and grief is a natural and normal reaction to a loss which does not involve a clinical diagnosis[73]. However, the type of grief may vary in its duration, its intensity and in the way it is expressed and experienced[73,74]. Most bereaved experience that their suffering after losing a loved one, more or less heals over time and they adjust in the long run to their life without their loved one. For some, however, the grief will be more intense and persistent and may appear as complicated or prolonged grief[75,76]. In fact, prolonged grief has recently been introduced as a separate diagnostic category in the WHO's diagnostic manuals ICD-11 as a grief response, which has been persisting for an atypically long period of time following a loss. An evaluation of the grief-reaction cannot be made until 6 months after the loss[52,77,78]. Previous research has estimated that in a representative German population 7% of bereaved people are suffering from complicated grief[79].

### *Communication between healthcare professionals and parents*

Skillful communication has for a long time been considered as a key pillar in practicing medicine[80–82] and good communication has been integral to the development of meaningful relationships between individuals as well as an critical aspects of the therapeutic alliance[83]. However, the construct of "good communication" varies among individuals and according to different definitions communication can simply be defined as a process where information is exchanged between individuals. To achieve effective communication adjusted transmission of information is necessary, but it is not sufficient; trust and human relations are also essential elements[83]. Thus, in a recent textbook, Palliative Care in Pediatric Oncology, "good communication" in this medical setting requires a synergy of trust building and effective information sharing, with the goal of building up meaningful relationships that can inform and guide the illness experience for both children, families and the HCPs[84]. Although skillful communication is very important across all fields of medicine it seems to be particular essential at the intersection of paediatrics and palliative care[82,85]. Previous research has shown that a central component of PPC is the communication between patients, families, and HCPs[86] and the parents satisfaction with the care may strongly be related to the communication skills of the HCPs[87]. Empathetic, accurate and timely communication from HCPs to parents about the child's disease and prognosis including the shift from curative to palliative treatment, has been proposed by the children and their parents as a prerequisite for providing high quality PPC[82,85,88–91]. In contrast, inaccurate and inconsistent communication has in the literature been associated with increasing distress for both the parents and the dying children[85,92–94].

The Institute of Medicine and the American Academy of Paediatrics (AAP) has gathered some of these concepts to promote empathetic and effective communication between families and HCPs in paediatrics and palliative care[95–98]. The AAP has published three domains in communication between families and HCPs; Informativeness, Interpersonal sensitivity and Partnership building to advocate for the promotion and to improve effective communication among HCPs, patients and families in PPC[99] (Table 1). The first domain, informativeness, includes the quantity and quality of the healthcare information provided to the patient or family by the physician. The second domain, interpersonal sensitivity, is the rational behavior that reflects an HCPs interest in addressing and understanding the concerns and feelings of the family. The behavior can be verbal or non-verbal and the HPC should allow the concerns of the child or the family members to be heard. The third and last domain, partnership building, is the extent to which the HCP invites the child and the parents to share their ideas, concerns and expectations. When this is carried out with empathy and with a desire to build up a partnership the family including the patient might be more comfortable by sharing their questions, beliefs, fears and values with the HCPs[99]. According to AAP, HCPs who have the ability to meet all three domains have the skills to encourage a shared decision-making and will ensure that difficult conversations about the diagnoses, treatment, prognoses and end-of-life care issues corresponds to the goal of care for the child and the family[84]. In Denmark there is no formal education or training in end-of-life communication in the education of HCPs and in Danish medical schools teaching in palliative medicine is generally sparse and mainly deals with pain management and general aspects of adult palliative care[100]. Therefore, it is likely that end-of-life communication and transition to SPPC can be a huge challenge for HCPs in the Danish healthcare system with the potential consequence that parents and children with life-limiting diagnoses experience increasing distress. Thus, it seems likely that HCPs may benefit from education in end-of-life communication with the children and their families.

Table 1. Important domains of communication for HCPs, children, and parents[99]

| | |
|---|---|
| Informativeness | The quantity and quality of health information provided by the physician to the patient and family |
| Interpersonal sensitivity | The relational behaviors that reflect an HCPs interest in eliciting and understanding the feelings and concerns of the family; these behaviors can be verbal or nonverbal and allow the child's or family member's concern to be heard |
| Partnership building | The extent to which the HCP invites thee parents and child to share their concerns, ideas, and expectations; when this is conducted with empathy and a desire to build rapport, the patient and family might be more comfortable sharing their questions, fears, beliefs, and values with the HCP |

### ***Summary of the background***

Worldwide SPPC services have been developed since the first children's hospice St. Christopher's Hospice in London was established in 1982. The need for SPPC globally is unknown. However, a recent study has estimated that more than 21 million children have unmet needs for palliative care and approximately more than eight million of these children need SPPC. In recent years SPPC has grown worldwide; however, looking at the services provided in terms of quality and capacity there still seems to be major gabs globally.

Previously, PPC has not been a major priority in Denmark and no specific national guidelines or policies for children with palliative care needs have been launched. However, since 2015 an increasing attention and interest in SPPC has been observed from HCPs and the public. A report examining the organization of palliative care for children with life-limiting or -threatening conditions and their families has been published[35] and the opening of the first children´s hospice "Lukashuset" announced that SPPC now was on the agenda in Denmark. In 2016 all five regions in Denmark were upgraded with SPPC teams in order to increase the capacity of SPPC. In addition, it has recently been decided to allocate funding to one more children's hospice in Western Denmark with a planned opening in 2020. Also, recommendations regarding PPC has been published by the Danish Health Authority. Thus, although PPC expands in Denmark we have no knowledge about the population of children and parents who potentially could benefit from SPPC. Further, previous Danish studies have found a substantial increase in mortality in bereaved parents as well as an increased risk of psychiatric hospitalization among parents, especially in mothers, after losing a child. Thus, it seems obvious that psychological distress including anxiety and depression in bereaved parents following the loss of a child with a life-limiting diagnose may have a great impact in terms of suffering. However, no Danish studies have formerly investigated anxiety and depression in bereaved parents after the loss of a child with life-limiting diagnoses.

Skillful communication seems to be particularly important at the intersection of paediatrics and palliative care. Inaccurate and inconsistent communication has in the literature been associated with increasing distress for both the parents and the dying children. In Danish medical schools there is no formal education or training in end-of-life communication of HCPs. Therefore, it is likely that end-of-life communication and transition to SPPC can be a huge challenge for HCPs with the potential consequence that parents and children with life-limiting diagnoses experience increasing distress. In order to organize future SPPC in Denmark based on the needs of the parents a basic estimation of numbers, diagnoses and places of deaths in children with life-limiting diagnoses is warranted. Furthermore, knowledge about how the bereaved parents are affected during their child's illness and after their loss and their needs of communication with the HCPs is crucial to achieve and seem to be key issues for future planning of SPPC in Denmark.

# Overall aim

This PhD thesis aims at investigating causes and places of death in children and the needs and distress of the bereaved parents to promote future planning, organization and interventions of SPPC in order to improve care of children with life-limiting diagnoses and their families.

### *Study aims*

The overall aim compromises of three specific aims:

### *Study I*

To investigate causes and places of death in Danish children below 18 years of age.

### *Study II*

To investigate anxiety and depression in bereaved parents after losing a child with a life-limiting diagnosis.

### *Study III*

To investigate bereaved parents' perception of end-of-life communication with HCPs during their child's life-limiting disease and imminent death.

# Methods

***Study I*** was a register-based study identifying causes and places of death in children under the age of 18 years, who died in the period 1994-2014[101]. ***Study II and III*** were parts of a nationwide cross-sectional questionnaire survey, which assessed bereaved parents' experience of anxiety and depression (***study II)*** and their needs for information and communication with HCPs concerning their child's life-limiting diagnosis and imminent deaths (***study III)***. As the same method was used ***in Study II and III***, it will be described collectively.

## *Study I*

In the period 1994-2014 data on all deceased children below 18 years were obtained from the Danish Register of Causes of Death[102,103]. As the classification of causes of deaths in the register has been managed in accordance with WHO's guidelines, and since 1994 by the ICD-10[103,104], 1994 was judged to be a relevant starting point. The most recent available data was from 2014, and therefore, the period 1994-2014 was used. The Danish Register of Causes of Death covers all deaths among Danish citizens dying in Denmark. The electronic death certificate was launched in Denmark in 2007[103]. Unfortunately, this change involved a temporary increase in missing death certificates and in the case of missing certificates the children´s death causes were coded as R99 (ill-defined and unknown cause of mortality). In 1994-2007, 6% were attributed to ill-defined and unknown causes of mortality which increased to 21% in 2007-2010 before it again declined in 2011-2014 to 12%.

Due to considerable variation in the prevalence of the children´s diagnoses by age, the children were divided into two main groups (infants below 1 year and children aged 1-17 years). Most infant deaths can be classified into two categories; perinatal and malformations/deformations/ chromosomal abnormalities. Therefore, all the remaining groups were merged into a category named "others". The distribution in children aged 1-17 years were more evenly. In this group we maintained the largest groups: external causes, neoplasms, neurological diseases and malformations/deformations/chromosomal abnormalities as they comprised at least 10 deaths per year. We merged the remaining groups into "others".

We calculated the annual crude death rate by dividing the total number of deaths by the population, who lived in Denmark (0-17 years) multiplied by 100,000. The mortality rate in infants were calculated as the total number of deaths under the age of one per 1,000 live births.

In the age group 1-17 years the cause-specific mortality rate was calculated by dividing the total number of deaths by the Danish population and multiplying by 100,000. All analyses were performed using SAS version 9.4.

### Study II and III

From ***study I***, we extracted 951 Danish children, who died due to life-limiting diagnoses in the period 2012-2014. To identify the children who potentially could benefit from SPPC a Directory of life-limiting conditions was used. The Directory was based on diagnoses of children receiving palliative care in five children hospices and a tertiary specialist paediatric palliative care service in the UK[105]. As SPPC is well-established in the UK and a new clinical discipline in Denmark the Directory was used to identify the Danish children, who potentially could benefit from SPPC. The diagnoses from the Directory was matched with the causes of death in the Danish Register of Causes of Death and we identified 402 Danish children with life-limiting diagnoses. The parents of these 402 children were identified through the Danish Civil Registration System (CRS). All individuals with a residence permit in Denmark have a unique civil registration number (CPR-number) stored in the CRS, which contains information on e.g. date of birth and death, gender and identity of parents. Parents with a Danish CPR-number and non-protected postal address were eligible.

#### Assessments

As our intention was to investigate bereaved parent's experiences during the care, treatment and loss of their child we decided to use a modified version of the questionnaire "To lose a child". The original questionnaire has been used in parents, who lost a child due to malignancies in Sweden[106]. A translated version of this questionnaire has recently been used in Norway[107]. The fact that Denmark and Sweden are similar in language, culture and healthcare systems as well as the fact that the comprehensive content easily could be modified to comprise parents, who had lost a child due to a life-limiting disease greatly influenced on the choice of this questionnaire. The original questionnaire contains 129 questions divided into three sections. The first part of the questionnaire covers demographics of the parents and their views on the care received during the child's disease. The second part contains the parents' views of the support and care received by themselves after the child's death. The third part covers the parents' well-being at the time of the survey, which meant 3-5 years after their loss. The questionnaire also included qualitative questions that enabled the parents to elaborate on their responses in more details.

To make the questionnaire applicable we translated the questionnaire from Swedish into Danish according to a revised version of the manual of European Organization for Research and Treatment of Cancer[108]. Independently, two native speaking Danes translated the questionnaire. One of them was an HCP (CL) and the other was a non-professional, who had lived in Sweden for several years. After the forward translation the versions were compared, and any discrepancies were solved between the two translators. A final discussion and adjustment of the translation was made by the research group. Finally, a native Swedish speaker (OE) from the research group, who speaks fluently Swedish and Danish and has many years of experience in processing questionnaire data made the final linguistic corrections. Due to our population of all children with life-limiting diagnoses we changed the wording of some of the questions as part of the translation. For example, each time “last month” was used as part of the child’s disease it was changed to “end-of-life time”, since other life-limiting diagnoses than cancer diagnoses in children may have more unpredictable trajectories. We also excluded all questions which were directly associated with cancer diagnoses as “How old were you when your child felt ill with cancer?” and “Did your child’s disease reappear (recur) after having disappeared?”. Because of the thorough processing of the questionnaire a back-ward translation according to the translation manual was not considered necessary. Our final version included 122 questions (Please, see Appendix 2). To ensure that the questions and the response categories was understood as intended and was appropriate for the use in the Danish population of bereaved parents who lost a child to life-limiting diagnoses the questionnaire was prior to the survey face validated in three bereaved parents. The questionnaire was adjusted according to their responses. In order to have at least one representative parent for each child the questionnaire was separately sent to mothers and fathers. Together with the questionnaire we sent an introductory letter, which briefly explained the objectives of the study and a folder explaining the study in more depth. A phone number was at the disposal of the parents for further information. We tested the content of the questionnaire by considering the first 20 parents as pilots and after receiving and analyzing the responses of the first 20 questionnaires, which did not involve further revision, they were all included in the total sample of the study. If the parents did not respond within three weeks one reminder was sent. All the bereaved parents were invited to participate in the survey and to complete the questionnaire between April and June 2017.

Because of the comprehensive nature of the questionnaire this thesis will only present parts of the questionnaire and future studies will focus on other sections.

***Study II*** presented the demographics of the children and their parents and the parents' responses to questions assessing anxiety, depression and well-being. To identify depression-related symptoms in the bereaved parents the Centre for Epidemiological Studies Depression Scale (CES-D) was used. The Center for Epidemiological Studies-Depression (CES-D) scale has been used extensively world-wide to quantify depression in different populations[109]. There is an extensive body of studies demonstrating the sound psychometric properties of CES-D, including high internal consistency, fair stability, good concurrent, convergent, and discriminant validity in a variety of samples[110–113]. Reliability tests suggest that the CES-D is consistently capturing depression and that this is a reliable screening instrument for depression[109]. Thus, the CES-D scale is a well-known and validated 20-item measure using 4-point Likert scale where 1 indicates "never" and 4 indicates "most of the time". It measures symptoms of depression in nine different domains: sadness, loss of interest, appetite, sleep, thinking/concentration, guilt, tired, movement and suicidal ideation[114]. The CES-D is a useful assessment tool for epidemiologic studies of depression and is widely used for the screening and assessment of depressive symptoms and is consistent with the DSM-IV diagnoses of major depression[114]. The CES-D has formerly been used in a Danish population of women with breast cancer[115]. According to the guidelines of CES-D we summarized the responses by giving a score of 0-3. A score of 16 or higher reflects risk of clinical depression. More precisely, a total score of 16-23 indicates moderate and a total score of 24-60 indicates severe depression[114]. Responders with more than four missing items were excluded.

The parents' evaluation of anxiety and depression during their child's illness (according to their memory) and at the time of the survey were evaluated on a 7-point Visual Digital Scale (VDS). The VDS is a very easy scale for the parents to administer and covers a single question measuring anxiety and depression by asking: "Did you suffer from anxiety/depression during your child's illness?" and "have you felt anxiety/ depression during the last month?". The responses comprising ranging from 1 (never) to 7 (all the time). We used cut-off scores; 1-2 indicates "no or mild", 3-5 "moderate" and 6-7 "severe" anxiety or depression. The VDS for anxiety and depression has been thoroughly tested for face validity in Sweden and has been used in previous research projects by the research group of Clinical Cancer Epidemiology[116–120]. Furthermore, the VDS of depression and the CES-D has in several Swedish studies been found to correlate to a high degree in depression[118,121,122]. Likewise, VDS of anxiety has shown to correlate to a high degree with the widely used Spielberger's State-Trait Anxiety Inventory (STAI-T)[118,121–123]. To investigate the feasibility of using the VDS for measuring anxiety and depression in the context of cancer research and palliative care settings in Sweden a previous study made a thorough validation to compare the properties of VDS of anxiety and depression with the two traditional psychometric scales CES-D and STAI-T[122]. Non-paramedic correlations (Spearman's) were calculated for the VDS questions and for the two scales. Sensitivity and specificity, and positive and negative predictive values were calculated for the VDS questions with CES-D and STAI-T for comparison. Cut-off points between 2 and 3 on the VDS questions of anxiety and depression provided the best balance between sensitivity and specificity. Thus, values between 2 and 3 indicates moderate or high risk of having symptoms of anxiety and depression. Missing rates were obtained in 7% using the STAI-T and 9% using the CES-D, compared to VDS (Anxiety 3%, depression 2%). The concurrent validity of the VDS of anxiety and depression was confirmed by their good correlation to the CES-D and STAI-T and the high response rate found according to the VDS of anxiety and depression vs CES-D and STAI-T further illustrated validity advantages. Based on the validation VDS may have a role as a screening tool in research and possibly also in clinical settings[122].

The VDS was also used for measuring the parents self-assessed physical health and well-being at the time of the survey with the categorization; 1-2 "worst", 3-7 "moderate or best". The VDS for physical health and well-being at the time of the survey has been face validated in bereaved parents, who lost a child due to cancer in Sweden[121,122].

Questions used for anxiety and depression and the parents' physical health and mental well-being, please see appendix 2: 17, 18, 101, 102, 103, 104, 111 and 113).

The parents' civil status, education and residential area used in the study were based on the parents' self-report according to the questionnaire. Residential area was identified by using the Nordregio classification of urban and rural areas dividing the 98 municipalities in Denmark into four groups: intermediate, urban, peripheral and rural. The classification is based on 14 indicators such as population in rural areas and villages with less than 1,000 inhabitants, population per square kilometer, percentage of the workforce with basic education and average distance to motorway[124]. Parental gender, and the diagnoses and age of the child were gained through the Danish Register of Causes of Death.

Results gained from this study regarding the bereaved parents' grief have not been included in the article about anxiety and depression in bereaved parents. However, I have decided to include the results in this thesis as anxiety and depression are common features in grief and grief is a normal reaction when parents lose a child (question included, please see appendix 2: 110).

***Study III*** presented demographics of the children and their parents and included the parents' perceptions of the communication with HCPs in charge of treatment and care for their child (questions included, please see appendix 2: 22, 24, 25, 27, 43, 46, 59, 65, 67 and 70).

### *Data analyzes*

We used descriptive statistics including frequency in percentages for categorical variables and means, median and standard deviations (SD) for continuous variables. P-values were calculated by $\chi^2$-tests and the significance threshold was set at 0.05.

When examining the association between parental gender and the psychological outcomes scores according to a 7-point Visual Digital Scale, p-values were estimated using linear regression models, where we also used Generalized Estimating Equation (GEE) with allowance for clustering within each child.

In S***tudy II*** we investigated the associations between depression, civil status, education, parental gender, and the diagnoses and age of the child assessed by a logistic regression model, where we used GEE with allowance for clustering within each child. The effect of clustering must be taken into account to allow for the likelihood that the parents of the same child could respond similarly, because they have been exposed to the same experience. However, we found it interesting to stratify the analysis by parental gender, as we assumed that there could be some gender differences. Data on potential risk factors as parental civil status, sex, and age of the children and primary causes of death were obtained from the CRS. Highest level of completed education was self-reported.

The association between various background variables obtained from administrative registers (diagnosis of the child, the residential area of the parents, age and gender of the parents and the child, respectively) and non-response were assessed by multiple logistic regression. Our results are presented as odds ratios with 95 % confidence intervals. All P-values were calculated by $\chi^2$ tests; adjusted for clustering within the child. We used SAS version 9.4 to perform all analyses.

### *Ethics*

Research in palliative care has always faced ethical and moral challenges in conducting research involving human suffering[125]. Thus, it has been argued that withholding research in this population is even more problematic[126] and an over-protective health care culture may cause that the patients and their families are denied choosing whether they want to participate in research or not. In PPC a tension exists between the desire to enhance palliative and end-of-life care and the need to protect the children and their families from untoward burdens[127]. Thus, it can be unethical to assume that patients and families should not be offered the opportunity to participate purely because the patients have advanced diseases[126]. Previous research has demonstrated that most of the bereaved parents felt positively affected by research participation, both due to personal matters and as regards having the opportunity to help others[106,128–130]. A recent systematic review investigating the benefits and burdens of PPC and end-of-life care research showed that patients and family members more heavily emphasized the benefits whereas the burdens were more prominently emphasized by the researchers and the clinicians[127]. Parents have described benefits as it was helpful to get the chance to ‘‘tell their story’’[128]. Also, themes as relief[131] and positive meaning making[128,132] have been identified. Some parents have described therapeutic benefits[129,133] and a hope for other parents or families to benefit from their participation[134–136]. However, researchers and clinicians’ burden have primarily been characterized by a desire to protect the potential individuals in a vulnerable situation[135]. Also, potential emotional impact on the researchers have been described as a burden[137,138]. In research the key issues may primarily be whether the research is justifiable in terms of the balance between possible benefits and harm to the individuals involved. It is a sensitive task to study a nationwide sample of bereaved parents, who lost a child due to life-limiting diagnoses and ethical concerns do exist surrounding this research agenda. However, the involvement of children and their families in health care research are essential to improve clinical care for future patients and families using PPC services. As we wanted to investigate bereaved parents’ perspectives on losing a child due to life-limiting diagnoses the parents were the only source of information. However, contacting the parents several years after their loss must be done with respect and by careful approach. Therefore, we discussed thoroughly how we could contact the parents during the preparation of this study. Potential harm we could inflict upon the bereaved parents was carefully weighed against the benefits for children and their families.

Especially, ethical considerations must be considered before a non-response survey, since the bereaved parents, who declined to participate in the original survey were approached. Our questionnaire in the original survey was long and extensive and we assumed that it could be demanding for the parents to participate. Thus, we wanted to give the parents the opportunity to tell why they did not want to participate and at the same time give them the option of either respond to the original questionnaire or respond to the non-response. Re-approaching participants have been investigated and recommended in previous studies. However, we did not re-approach the participants by a reduced version of the questionnaire[139–142] or by a short phone interview[143]. We developed a specific questionnaire based on comments from participating parents to enhance the knowledge on how to approach the bereaved parents in future studies. An approach which has been used in previous studies investigating reasons for accepting or declining participation in randomized clinical trials[144,145]. It was, of course, important that the parents were approached without increasing the response burden, particularly in relation to survey recipients feeling coerced or harassed and therefore, no reminder was sent. However, this is the first Danish study to include all parents who have lost a child with a life-limiting diagnosis and, therefore, it was important that the parents' perspectives on the survey was evaluated so future research in bereaved parents can be organized due to the parents' experiences and wishes. Ultimately, this approach will hopefully contribute to higher response rates.

However, due to the emotive nature of our questionnaire, a phone number for counselling were given to the parents prior to their participation and all questionnaires were assigned with a serial number to ensure participation anonymity. Ethical principles applied in this project are based on the Helsinki declaration on medical research in human subjects[146] and the study was assessed by the Danish Ethics Committee (H-16021831) and the Danish Data Protection Agency (2012-58-0004).

# Results

## Study I

### *Mortality rates and death causes*

During the observation period 1994-2014 the all-cause mortality rate in children aged 0-17 years decreased by 52% (1994: 57.1, 2014: 27.4/100 000 children) in Denmark. The mortality rate declined in all age groups in children 1-17 years of age (Figure 3). The all-cause mortality rates were higher among boys than girls (Figure 4). The decline in infant deaths by 26% (from 5.5/1 000 live births in 1994 to 4.0 in 2014) reflected a lower mortality rate related to congenital malformations, deformations and chromosomal abnormalities (by 68%) and perinatal death by 30%. Perinatal deaths constituted 61% of all deaths (Figure 5).

**Figure 3: Age-specific mortality rates among Danish children 1-17 years of age (per 100,000 children)**

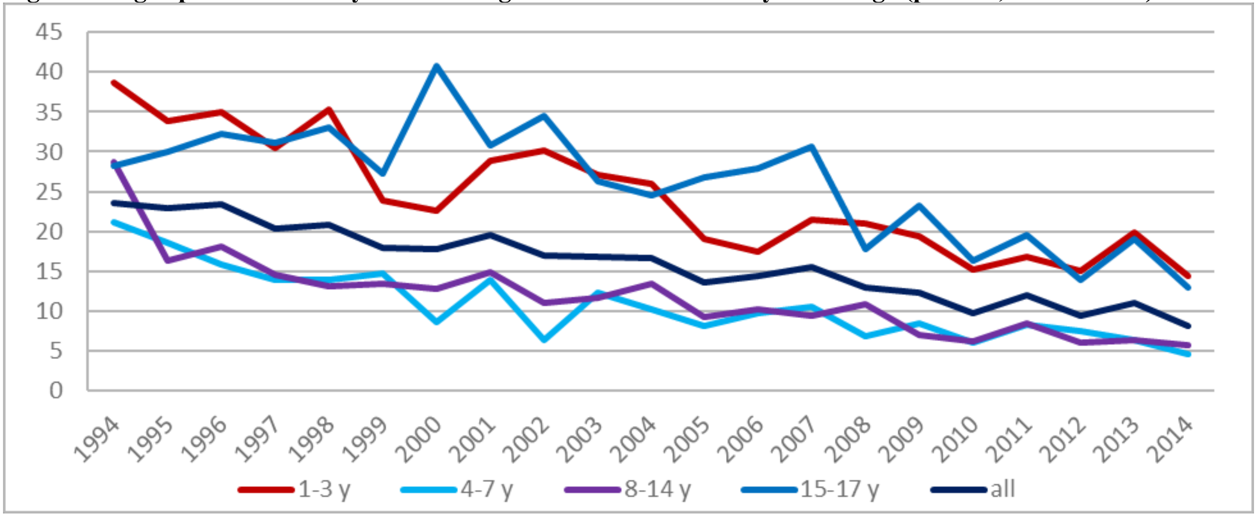


**Figure 4: All-cause mortality rate and the distribution between boys and girls 0-17 years of age (per 100,000 children)**

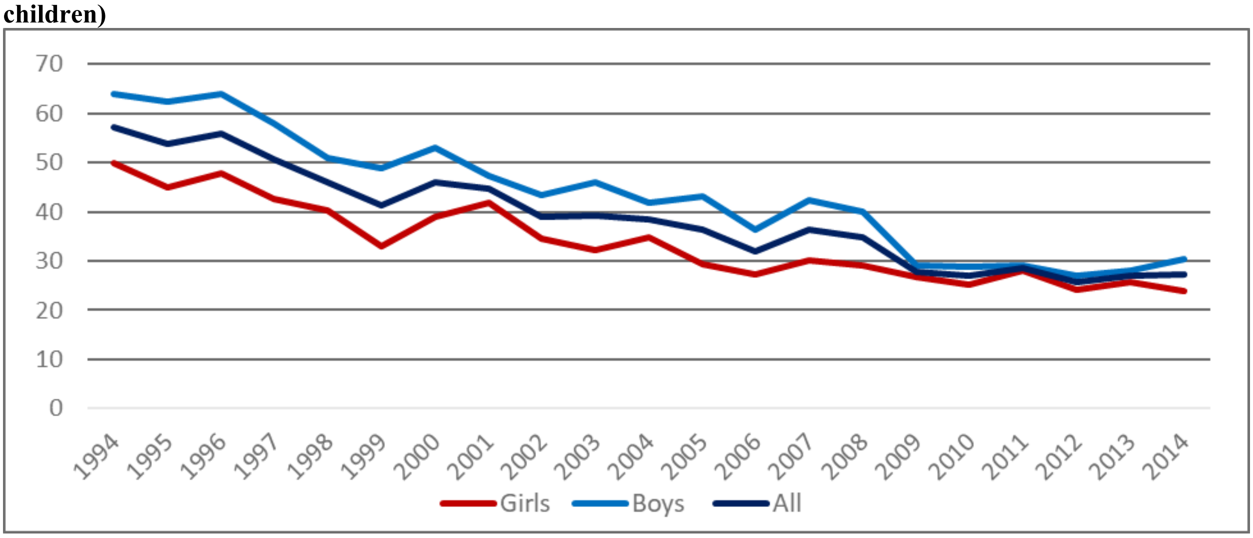
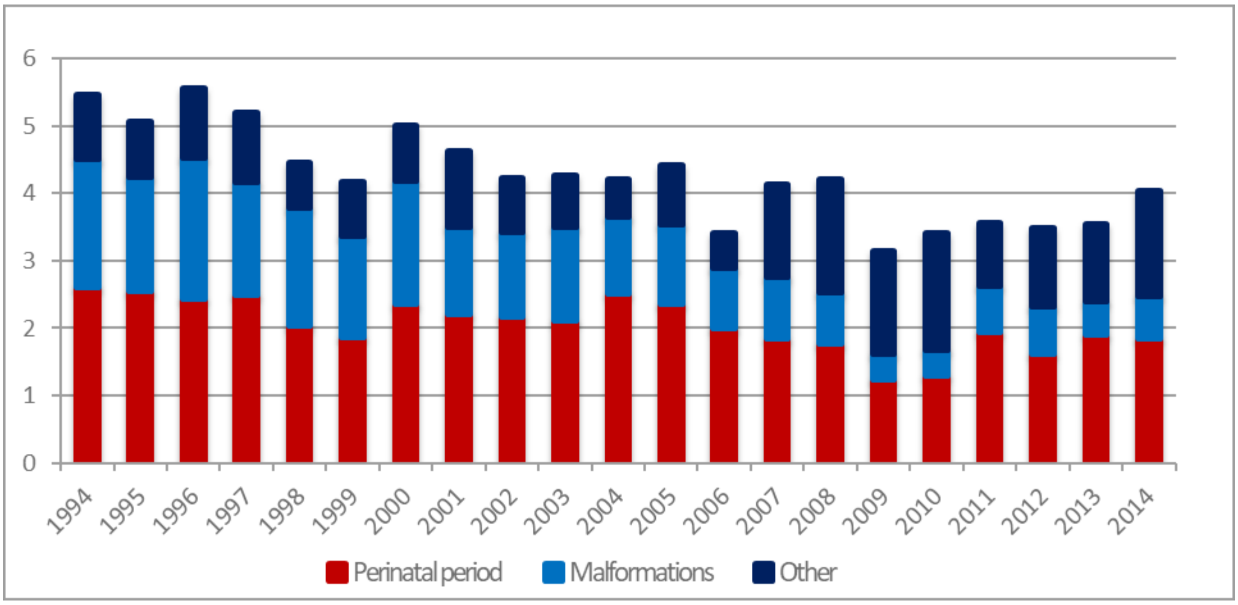
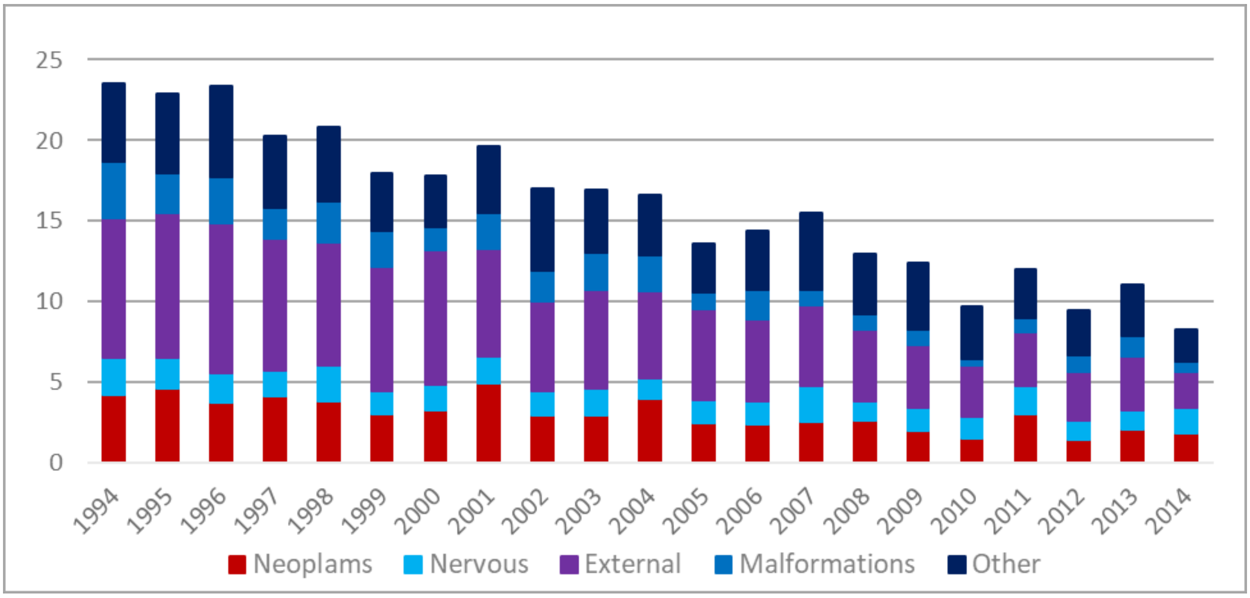


Figure 5: Cause-specific mortality rate in infants (per 1,000 live births) in Denmark 1994-2014



In the age group 1-17 years a substantial over-all decrease was found (65%). A decline in deaths related to external causes by 75% and a decrease by 57% in deaths related to neoplasms was observed (Figure 6).

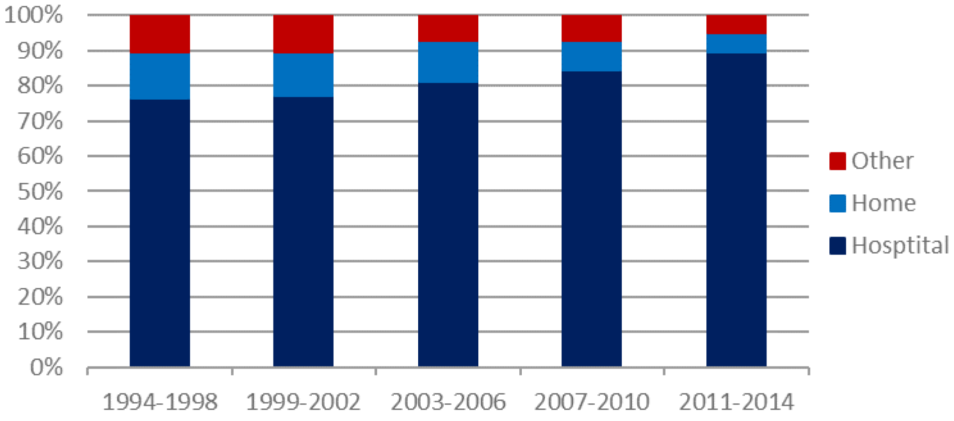
Figure 6: Cause-specific mortality rate among 1-17 years (per 100,000 children) in Denmark 1994-2014



***Place of death***

During the observation period 1994-2014 the relative proportion of hospital deaths increased by 17% (76% in 1994-1998 to 89% in 2011-2014), whereas the relative proportion of home deaths and death in other places than hospitals or home decreased by more than 50% (13% in 1994-1998 to 6 % in 2011-2014) in Denmark. The most pronounced difference regarding age was observed in the age group 4-7 years, where the proportion of deaths in hospitals increased from 56% to 85% during the observation period (data not shown). The highest proportion of home deaths was observed in the age group 8-14 years, which was stable throughout the observation period. The distribution of place of death in children between 1994 and 2014 are shown in figure 7.

**Figure 7: Place of death among children under the age of 18 in Denmark. 1994-2014 Percentage.**



## *Study II and III*

### *Response rates and characteristics of the participants*

In total, 402 Danish children with life-limiting diagnoses were identified. The parents of these 402 children were included in the study. Caused by e.g. unknown paternity, emigration from Denmark, death or protected address contact information of some of the parents were not reachable. Thus, 743 bereaved parents were invited to participate in the questionnaire survey. In all, 193 parents, 136 mothers and 57 fathers completed a questionnaire. These represented parents of 152 children (38% of the total population of children who died with a life-limiting diagnose in the period 2012-2014). Seventy-nine % of the children were represented with one parent and 21% of the children were represented with both parents. Of the parents, who responded to the questionnaire, boys and girls were equally distributed. Children, who died within the first year of life, were represented by 56%. Characteristics of the children, in whom at least one parent has responded to the questionnaire, are shown in table 2.

Totally, 99.5% of the parents were biological, 87% were married and 90% had shared custody during the child's illness. Eighteen% had divorced after the child's death. Eighty-three % were actively participating in the care of the child, 72% of the mothers and 42% of the fathers had sick leave during the child's disease trajectory, 68% stated to be religious and 67% had higher education than upper secondary or vocational school. Characteristics of the participating bereaved parents are shown in table 3.

**Table 2. Characteristics of the children, in whom at least one parent has answered the questionnaire. Number of individuals (%).**

| | **N (%)** |
|---|---|
| **Identified children** | 402 |
| **Number of children represented** | 152 (37.8) |
| **Children represented by both parents** | 41 |
| | |
| **Gender** | |
| Girls | 96 (49.7) |
| Boys | 97 (50.3) |
| | |
| **Age** | |
| 0-31 days | 72 (37.3) |
| 32-364 days | 36 (18.7) |
| 1-10 years | 46 (23.9) |
| 11-17 years | 39 (20.2) |
| | |
| **Death causes** | |
| Neoplasms | 41 (21.2) |
| Diseases of the nervous system | 24 (12.4) |
| Congenital malformations, deformations and chromosomal abnormalities | 46 (23.8) |
| Conditions originating in the perinatal period | 55 (28.5) |
| Other | 27 (14.0) |

**Table 3. Characteristics of the survey respondents. Number of individuals (%).**

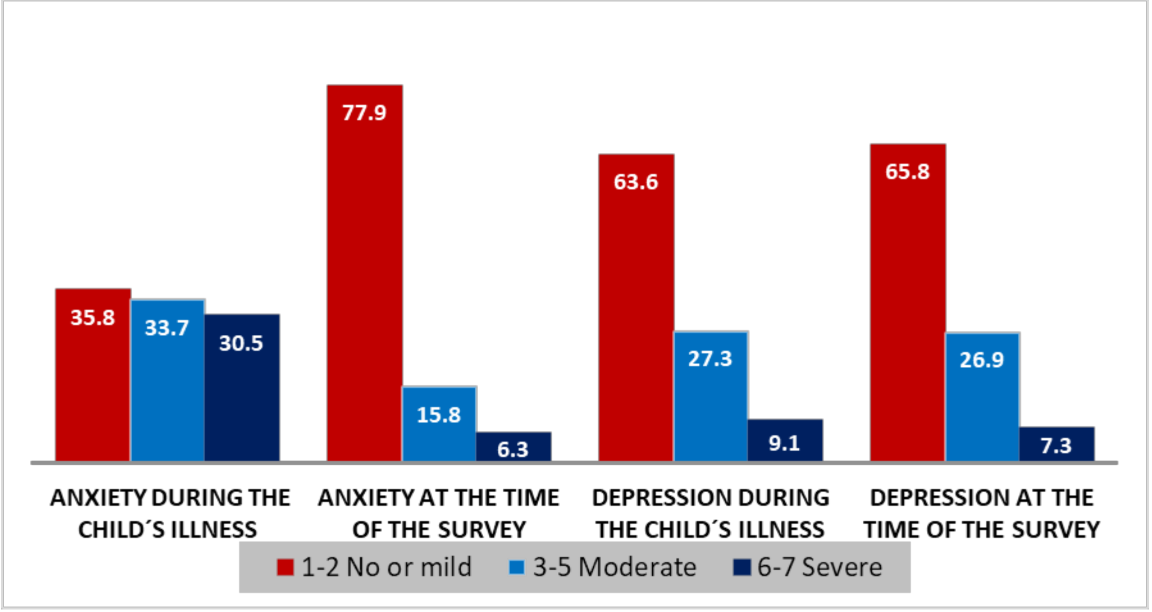
| | **Mothers** | **Fathers** |
|---|---|---|
| **Number of invited parents** | 391 | 352 |
| **Number of respondents** | 136 (34.8) | 57 (16.2) |
| | | |
| **Age** | | |
| <35 years | 35 (25.7) | 10 (17.5) |
| 35-44 years | 63 (46.3) | 23 (40.4) |
| ≥45 years | 38 (27.9) | 24 (42.1) |
| | | |
| **Civil status today** | | |
| Married | 103 (75.7) | 46 (80.7) |
| Not Married | 31 (22.8) | 9 (15.8) |
| Not answered | 2 (1.5) | 2 (3.5) |
| | | |
| **Education level** | | |
| Basic, upper secondary or vocational school | 29 (21.4) | 19 (33.3) |
| Higher education | 95 (69.9) | 37 (64.9) |
| Not answered | 12 (8.8) | 1 (1.8) |
| | | |
| **Lost more than one child** | | |
| Yes | 17 (12.5) | 5 (8.8) |
| No | 118 (86.8) | 51 (89.5) |
| Not answered | 1 (<1) | 1 (1.8) |
| | | |
| **Religiousness** | | |
| Religious | 100 (73.5) | 32 (56.1) |
| Not religious | 36 (26.5) | 24 (42.1) |
| Not answered | 0 (0.0) | 1 (1.8) |

## *Study II*

### *Anxiety and depression in bereaved parents*

During the child´s illness 65% of mothers and 63% of fathers according to their memory reported moderate to severe anxiety according to VDS. At the time of the survey (3-5 years after the loss), 24% of the mothers and 16% of the fathers reported moderate to severe anxiety. No statistically significant differences were found in anxiety between mothers and fathers.
During the child´s illness 35% of the mothers and 39% of the fathers according to their memory reported from moderate to severe depression according to VDS. At the time of the survey (3-5 years after the loss), 34% of the mothers and 35% of the fathers still reported moderate to severe depression (Figure 8). No statistically significant differences between mothers and fathers in self-reported depression neither during the child's illness nor at the time of the survey.

**Figure 8: Anxiety and depression in bereaved parents during the child's disease and at the time of the survey (3-5 years after the loss) according to a Visual Digital Scale (VDS).**



According to VDS 64% of the bereaved parents experienced moderate to worst possible physical health, 61% experienced moderate to worst mental well-being and 52% experienced moderate to worst possible quality of life at the time of the survey (table 4 and 5).

**Table 4. Physical health, mental well-being and quality of life by gender of the parents according to a 7-point Visual Digital Scale.**

| **Physical health during the last month** | | **Mean (SD)** | **Median** | **N** | **P-value** |
|---|---|---|---|---|---|
| Score range 1-7/7 | **Mothers** | 5.0 (1.31) | 5 | 134 | 0.519 |
| | **Fathers** | 4.9 (1.27) | 5 | 55 | |
| **Mental well-being during the last month** | | | | | |
| Score range 1-7/7 | **Mothers** | 5.0 (1.31) | 5 | 134 | 0.703 |
| | **Fathers** | 4.9 (1.42) | 5 | 56 | |
| **Overall quality of life during the last month** | | | | | |
| Score range 1-7/7 | **Mothers** | 5.3 (1.18) | 5 | 134 | 0.255 |
| | **Fathers** | 5.1 (1.29) | 5 | 57 | |

**Table 5: The distribution in physical health, mental well-being and quality of life of the parents according to a 7-point visual digital scale.**

| **Physical health during the last month** | **N (%)** |
|---|---|
| Cut-off scores | |
| 1-2 Worst | 6 (3.2) |
| 3-5 Medium | 115 (60.9) |
| 6-7 Best | 68 (36.0) |
| **Total** | **189 (100.0)** |
| **Mental well-being during the last month** | |
| Cut-off scores | |
| 1-2 Worst | 9 (4.7) |
| 3-5 Medium | 107 (56.3) |
| 6-7 Best | 74 (39.0) |
| **Total** | **190 (100.0)** |
| **Overall quality of life during the last month** | |
| Cut-off scores | |
| 1-2 Worst | 5 (2.6) |
| 3-5 Medium | 93 (49.0) |
| 6-7 Best | 92 (48.2) |
| **Total** | **190 (100.0)** |

According to CES-D mothers reported lower prevalence of depression than fathers at the time of the survey. No statistically significant relationship between religious belief and depression among the parents was found. Neither did we find any statistically significant associations between the child's death cause, age of the child and the parents' gender and severe depression (CES-D>23). However, at the time of the survey the results of a multiple logistic regression analysis showed that bereaved parents with basic, upper secondary or vocational education had

6.92 (95% CI: 2.74-17.47) times higher odds of reporting severe depression than bereaved parents with higher education. Furthermore, married bereaved parents had 0.29 (95% CI: 0.11-0.78) times lower odds of reporting severe depression than unmarried bereaved parents at the time of the survey.

Finally, 49% of mothers and 54% of fathers reported that they never received psychological support during end-of-life care of their child and 64% of the parents experienced that their mental health had deteriorated after the loss of their child. In all, 29% of the parents answered “no not at all” to the question of whether or not they have adapted to their grief. Out of the 29% of the parents 82% indicated moderate to severe depression according to the VDS. There was no association between the level of depression and whether or not the parents had received psychological support during end-of-life of their the child.

## *Study III*

### *Bereaved parents’ perceptions of communication about end-of-life care issues*

Totally, 59% received the information about their child’s incurable illness through conversation with a physician and in 2% of the cases the child was present. Thirty % of the parents reported that they received information that their child was incurable immediately after birth. However, 15% received the information within the last 24 hours before the child died and 12% did not receive any information. Nineteen % of the parents realized that their child was going to die only a few hours before death and 11% did not realize the child’s imminent death before it actually happened.

In total, 75% of the parents found that the information given by the HCPs in relation to their child’s disease was given in a satisfactory manner and 80% of the parents were satisfied with the information given about the treatment received by their child. However, information regarding how the disease and treatment could affect the child’s mental and physical health was found inadequate by 48% and 33% respectively, and information regarding how the parents could take part in the care of their child during the end-of-life period was not received by 34%.

In all, 79% of the parents reported that the information about their child’s disease was incurable was given in an appropriate manner. However, 42% of the parents reported that none from the attending staff told them that the child was imminently dying. In all, 43% reported that the death of their child was “a shock” and 31% of the parents experienced that they felt deprived taking leave with the child in the way they wished.

### *A survey for non-responders*

We investigated the association between diagnosis, gender and age of the child and age and residential area of the parents and non-response. We found a significant association between the age of the mothers and non-response. Mothers under the age of 35 years showed to have 1.56 (95% CI: 0.94-2.57) times higher odds of non-response than mothers in the age between 35-44 years. Conversely, mothers aged 45 years or older had 0.45 (95% CI: 0.22-0.94) times lower odds of non-response than mothers aged 35-44 years. We observed the same tendency regarding the fathers, but the association was not statistically significant (probably due to a lack of statistical power). No other statistically significant associations were observed.

However, caused by our relatively low response rate among the bereaved parents we decided to undertake a post-hoc non-response survey as we wanted to investigate and identify reasons for a lack of response. A self-administered questionnaire with 14 questions was conducted based on reactions from participating parents (please see appendix 3). We pilot-tested the questionnaire in 15 bereaved parents, who all provided written feedback. We revised the questionnaire before it was sent together with a version of the original questionnaire to the non-participating parents. Hereby, parents were given the opportunity to fill in either the original questionnaire or the short non-response questionnaire. Due to ethical considerations no reminder was sent to the parents. Sixteen parents participated in the original questionnaire survey and 51 parents participated in the non-response survey. The non-response showed that 51% of the parents “completely or partly agreed” that the questionnaire was too extensive. Sixty-seven % “completely or partly agreed” that it was emotionally too demanding to participate and 77% “completely or partly agreed” that they did not have the energy to participate. Finally, 51% of the bereaved parents “completely or partly agreed” that this survey was important.

# Discussion

### *Study I*

Our study in Danish children under the age of 18, who died due to life limiting diagnoses, has an observation period of 20 years. The opportunity in Denmark to use national registry data is demonstrated in this study by the long-term overview of causes and places of death in children. The all-cause mortality rate decreased with more than 50% during the observation period from 1994-2014. The most pronounced decline was found regarding congenital malformations. Denmark was the first country worldwide to offer all pregnant women first-trimester risk assessment for Down syndrome combined with an ultrasound screening for foetal abnormalities in the gestational age of 18-20 weeks[147]. This resulted in a substantial reduction of infants born with Down syndrome[148]. In the same period folic acid supplements were found to prevent the development of congenital anomalies[149,150] and primarily due to improved pregnancy and birth care a general decline of maternal mortality was observed in the western world[151]. A general decline, which still continues regarding perinatal mortality[152] as well as the cure and survival rates for childhood cancers have greatly improved in Europe including Denmark during the past 40 years[153]. In our study we also identified a remarkable decline in mortality due to neoplasms, perinatal deaths and external causes as a general effort to prevent accidents also has contributed to a decline in in the mortality of Danish children[154]. However, the over-all decline in all diagnoses in children may be a general expression of e.g. improved prevention, access to healthcare, expertise in treatment and reduced smoking and the abuse of other substances. Whether the massive decline in the Danish child mortality through the past 20 years has found a steady level may be revealed in the future.

HCPs and the public consider that a good death takes place at home and home is frequently cited as the preferred place of death[45]. However, the relative proportion of hospital deaths increased by 17%, and home deaths decreased with more than 50% during our study period. This may be due to more aggressive treatment attempts continuing to the very end of life, striving for a cure or prolonging life. This may involve an increasing number of deaths in hospitals, as well as it may actually save or prolong lives in children. However, the downside may be that some children are deprived the opportunity to die in their own homes surrounded by their families and loved ones. Previous studies have found large cross-national variations in children's place of death[47,155,156]. A systematic review found that in six out of nine studies the majority of parents expressed preference for death at home. Other studies found significant variations in preference of home death ranging from 0-35%[45]. Our study found a relative decline of more than 50% of home deaths over a long period of time. This finding does not necessarily indicate that it has become more difficult for Danish children to die at home; however, the decline may, as mentioned above, reflect that children with life-limiting conditions receive more aggressive treatments for longer periods of time as in-patients. Thus, maybe the development of PPC appears to be lacking behind the development of curative treatment in Denmark as Kreicbergs concluded in a recent editorial[48] (please see appendix 1). However, even though death at home may become a choice for many, empirical research on preferred place of death in children found only meagre evidence for the often-repeated claim that most parents and children would prefer home as the place of death. Also, studies point out that preferences for place of death may change through the illness trajectory[45,157]. Which aspects there may be important in deciding the relevant place of death must also include the perspectives of siblings and other family members. Research on siblings needs and experiences of death of a brother or sister showed that siblings wished to be informed about the imminent death[158] and that they wanted to be close and involved in the care[159]. However, as their role shifted from being playmates to companions followed by a more supportive role the siblings reported growing feelings of frustration and helplessness[159]. A recent study described both difficult times and moments of relief for the siblings following the death of a brother or a sister in hospital or at home[160]. However according to a recent study end-of-life care at home is only feasible if the parents make extraordinary efforts[161].What is most important for the children, siblings and families may be to have ongoing discussions about priorities and options for current and future care including issues surrounding preferred place of death.

In Denmark there is no research in children's and their families' end-of-life care decisions, advance care planning, early integration of PPC and curative treatment and withdrawal of curative treatments[162,163]. Thus, there might be an unmet need for earlier PPC interventions both in hospitals and at home for selected children and families. Studies have shown that children with complex chronic medical conditions may benefit from early introduction of PPC, advance care planning and medical decision-making as well as supportive care to maintain quality of life[164–167]. However, it may be difficult to predict the children's disease trajectories and this uncertainty is a significant challenge for paediatricians. Therefore, the goals of care may for long periods almost always be both supportive and curative in nature[168]. Early integration of PPC, sometimes already at the time of diagnosis or soon thereafter, may introduce PPC as a natural part of the treatment so that PPC and end-of-life care not will be perceived as major changes[168]. However, research has found that even in disease trajectories with a more predictable course, the integration of PPC and curative treatment still occurred to late resulting in missed opportunities to control pain and other symptoms[90]. Barriers for earlier introduction of PPC has been identified including family and HCP discomfort and resistance[167]. However, a study in paediatric oncology demonstrating a high degree of symptom-related suffering early in the trajectories showed that only a few children and parents expressed negative attitudes toward early integration of PPC. The results indicated that children with cancer and their families may benefit from early PPC integration[169]. As the majority of Danish children died in hospitals the HCPs have a very important role in identifying children and their families who potentially could benefit from PPC, and early integration may help to ensure that especially children in the palliative phase of diseases are exposed to a minimum of suffering by applying more aggressive symptom management[17]. Previous studies have also indicated, that children receiving PPC had fewer hospital admissions and were more likely to die at home[170,171]. Thus, the current shortage of PPC may to some extent explain the low percentage of home deaths found in Denmark.

### *Study II*

To our knowledge this is the first study of its kind to investigate anxiety, depression and well-being in a national sample of bereaved parents, who lost a child with a life-limiting diagnosis. This study indicated that bereaved parents reported high levels of anxiety and/or depression after losing a child due to life-limiting diagnosis and that the parents suffered from depressive symptoms many years after the loss.

During the child's disease a substantial proportion of the bereaved parents reported high levels of moderate to severe anxiety. However, according to the parents' responses the level of anxiety decreased markedly 3-5 years after their loss. However, the reported high prevalence of anxiety may likely be associated with increased distress due to the child's end-of-life trajectory[172]. According to DSM-5 and ICD-11 definitions some of the bereaved parents may even have developed posttraumatic stress disorders[52,173], which depending on their psychological resilience could be either reduced on a sustained basis or makes them vulnerable to crises and stressors later in life, that in turn could be associated with long-standing depressive disorders years after the distressing and traumatic period has ended[174]. However, as we have no diagnosis or incidence posttraumatic stress disorder in the parents participating in our study, other studies e.g. of accident victims have reported a high incidence of depression one-year post-trauma among individuals with no diagnosis of posttraumatic stress disorders[175]. Thus, the findings could indicate that anxiety and depression in the aftermath of trauma could be conceptualized as a general traumatic stress construct.

Previous studies have found that anxiety in general was more prevalent among women than in men[176,177]. However, in our study we did not find any statistically significant association between the parent's gender and anxiety. In our study, the reported score of anxiety in the bereaved parents was considerably higher than their score of depression according to the VDS during the child's disease. At the time of the survey, 3-5 years after the child's death, anxiety was reduced substantially, whereas depression remained virtually unchanged. The study is based on self-report by the parents and the parents were not clinically diagnosed by a physician or phycologist. However, more than one-third of the parents reported moderate to severe depression according to the CES-D both during the child´s disease trajectory and at the time of the survey. A recent systematic review based on all English and Spanish validation studies in the general populations or primary care settings using the CES-D scale for depression found a median prevalence of major depression around 8.8%[178]. However, a previous study found that 7-9 years after the loss of a child both anxiety and depression decreased to levels similar to non-bereaved parents. The non-bereaved parents were selected from the general population, where the children were matched for sex, birth date and residential area to the deceased children[179]. However, another study investigating bereaved parents showed that 18 years after the loss, the parents still reported poor well-being and high depressive symptoms and episodes compared to non-bereaved parents[180].

The bereaved parents' relatively high score of depression at the time of the present survey may be associated with their low ratings of their quality of life and general well-being. A systematic review of psychosocial co-morbidities among parents of children with cancer found that the parents had elevated rates of anxiety, depression, poor psychological well-being, prolonged grief, and poor quality of life and physical health[181]. Although, the psychosocial co-morbidities in the review were diversely defined and assessed, the bulk of suffering including the low levels of quality of life was in line with the findings of the present study. Finally, in our study it may be particularly noteworthy that the reported and pronounced lack of psychological support may have contributed to the parents over-all deteriorated condition[182,183].

Our study showed, that parents who were unmarried or had lower education had more severe depression. This is to some extent consistent with a previous study, which found that mothers with lower education had a lower capability to access support after losing a child as well as being more likely to report higher levels of anxiety and depression[184]. A recent questionnaire survey preformed in the US was in consistency with our study showing that mothers with lower education appeared to report higher levels of anxiety and depression and they had lower capability to access support following their loss of their child[184]. We are aware that the socioeconomic environment in the US is highly different from Denmark. However, it is obvious even in a welfare state as Denmark that parents with lower education (which is a strong predictor for low household income) may be more exposed to higher comorbid problems. Finally, the higher odds for depressive symptomatology in unmarried parents could also be explained by the marital disruption as our study found that 18% of the parents had divorced between the death of the child and the time of our survey. However, our study does not identify whether it was the loss of the child that caused the divorce and it may just be a part of the generally high divorce rate found in Denmark (1994: 43.66%, 2014: 54.39%). On the other hand, a mixed-methods study has demonstrated that positive dyadic coping between couples after losing a child with a life-limiting diagnose seems to be helpful during grief - not only for the couple but also for the individual[185]. Religion most commonly refers to ways in which humans relate to the divine. However, religion is a central marker of individual identity. It provides meaning and a sense of belonging and it influences human traditions and their behaviors[186]. Whether religious beliefs may be beneficial in the process of coping with the loss of a loved one has been investigated in a systematic review, which showed that most studies indicated a positive effect[187]. Similarly, a study has found that bereaved parents regularly attending church experienced less anxiety and depression[188]. A Swedish study was consistent with our results indicating that religious beliefs were not associated with scores of anxiety and/or depression. The same study found that losing children 9 years or older implied an increased risk of anxiety and depression, especially in the fathers[179]. In our study these findings could not be confirmed as we did not find any association between the age of the child and the parents’ reported levels of anxiety and depression.

Even though, our intention with this study was to investigate anxiety and depression in the bereaved parents rather than their experience of grief it is most likely that their experience of depression was associated with grief and that the distinction between the two can be difficult for the parents themselves and the HCPs to draw. At the time of the survey, 3-5 years after their loss, one-third of the bereaved parents reported that they had “not at all” adapted to their grief and the majority of those parents indicated moderate to severe depression. An aspect in this context is conceptually to distinguish depression from prolonged grief disorder and a key consideration is to which extent the symptoms are specifically related to the loss of the child versus more generalized depression. Diagnostic Criteria for DSM-5 Persistent Complex Bereavement-Related

Disorder and ICD-11 Prolonged Grief Disorder are available[52,173]; however, the questionnaire used in this study was not designed to discriminate between prolonged grief and depression according to these concepts and definitions. Earlier research has shown that parents' grief after the loss of a child could be more intense and complicated than e.g. after the loss of a parent or a spouse[189,190]. Furthermore, bereaved family members have elevated risks of developing complicated grief[79] as well as other mental health problems including anxiety and depression lasting nearly a decade after their loss[62,179,180,191]. Another study found that parents, who experienced their grief as resolved, had significantly less impairment of their mental health than parents who experienced their grief as unresolved[191]. Although, grief and mourning processes are a normal and universal part of the natural healing processes that enables all individuals to live with the reality of their loss, the symptoms of grief and depression may be difficult to distinguish. This could involve a clinical dilemma if the parents are being clinically diagnosed as depressed, but not offered adequate treatments, because their reaction is misinterpreted as "natural" or on the other hand are offered treatments with no effect. As this study was based on self-report this study does not clarify whether the bereaved parents suffered from clinically diagnosed anxiety, depression or complicated grief; however, we have to acknowledge based on the psychometric properties of the used assessment tools that the bereaved parents were suffering and had unmet needs. Recall bias may, of couse, influence reliability of reporting from an devastating, incomprehensible and chaotic period of life after 3-5 years[192,193]. Complicated grief and major depression could be associated with cognitive dysfunction, including memory, executive function and attention[194,195] and frequent, lengthy and chronic states of depression may involve impairing effects on brains function[196]. Previous research has demonstrated lower attention and cognitive performance in individuals with complicated grief compared to control participants[195]. However, other studies found that complicated grief comprised cognitive deficits in the attention and concentration but did not differ from control participants with regard to executive functioning and memory[195,197]. Thus, the results from the present study calls for skilled professionals, who are capable of making clinical distinctions between grief and depression, so that the parents who are at risk of developing either depression or complicated grief are directed to timely and accurate support and treatment[73].

***Study III***

In our study the majority of the parents found the information regarding the child´s illness and treatment satisfactory. However, 42% of bereaved parents reported that none from the attending staff told them that their child was imminently dying. The communication and relationship between the HCPs and the parents during end-of-life care have shown great impact on parental satisfaction, well-being, post-loss bereavement process and quality of life[82,198,199]. However, communication with the informal caregivers has often been perceived as poor or inadequate and the HCPs have often felt insecure and stressed in communicating end-of-life care issues[198]. In spite of the fact, that one of the major tasks for HCPs are to support and care for dying children and their families, studies have consistently shown that HCPs find the communication about end-of-life issues distressing and difficult[92,200,201]. In accordance with the primary goal of optimizing the child's chances of cure most physicians are generally be educated and trained to diagnose and treat children, and they may feel uncomfortable, reluctant or poorly educated to inform and discuss issues related to death and dying with the informal careers. Therefore, they may have a tendency to underestimate or avoid communication surrounding end-of-life care issues[202–204]. The majority of the bereaved parents in our study reported that they wanted accurate and timely information about their child's life-limiting disease and imminent death, and they reported, that they wanted physicians to disclose immediately, when curatively intended treatment was exhausted. However, the parents also reported, that the HCPs communicated these issues too late and one-third of the parents felt they were deprived of the possibility of taking leave with the child as they wished. The majority of parents in this study was satisfied with the information they received in relation to the child's treatment, but the parents reported unmet needs for information and support regarding end-of-life care and imminent death. The child's death was reported as "a shock" in almost half of the parents. However, poor memory retention of received information may of course be associated with the distress affecting parents caring for their imminently dying child and studies have indicated that parents receiving difficult and complex information about a child's disease understand and retain less than half[85,205]. The fact that the child's death was perceived as "a shock" in 43% of the parents does not necessarily mean that the information was delivered in an insensitive or inappropriate way by the HPCs but may also reflect the parents' unbearable loss. The term "a shock" used in the questionnaire "To lose a child" by Kreicbergs et al - and also in our modified version - is not a medical term, but is a common language expression, which is widely used as an emotional reaction to an unexpected, sudden, and usually unpleasant experience or event[106]. Almost one third of the parents in our survey reported that they did not say a final goodbye to their child in the way they wished. Some parents whose children are dying may experience anticipatory grief as they prepare for the death. Anticipatory grief contains elements of anticipation of death and future absence of the child, separation anxiety, denial and relational losses. In general, studies concerning prevalence of clinically significant pre-death symptoms ranged in the caregivers from 12.5 to 38.5%[206]. This prevalence may be even higher in parents losing a child.

The publications from AAP and the Institute of Medicine[95–98] and the three domains identified by AAP[99] corresponds with the goals of care for children and their families[84]. AAP states that HCPs, who have the capability to meet all three domains, Informativeness, Interpersonal and Partnership building, have the skills to encourage shared decision-making and will ensure that difficult conversations concerning diagnoses, treatment, prognoses and end-of-life care issues correspond to the goal of care for the child and the family. Hereby, the tree domains correspond very well with the questions in our survey as the questions clarify the quality and quantity of the information given by the HCPs. Further, the questions explore the HCPs interest in eliciting and understanding the feelings and concerns of the parents and explore whether the HCPs allow the parents to be comfortable with sharing their questions. However, nearly one third of the parents in our study reported they received the information, that their child was incurable sick within the last 24 hours of the child's life. Further, 42% of the parents reported that none from the attending staff told them that the child was imminently dying. It seems likely that even though the HCPs undoubtedly strive to communicate timely and effectively several barriers may hinder the best of intensions, when communicating with parents about children's life-limiting diagnosis or imminent death. Indeed, this is a sensitive area of practice and these trajectories may have strong and penetrating impact on the HCPs and they may use emotional, physical, spiritual and problem-solving efforts and strategies to continue to perform this endeavor effectively, while protecting their own well-being[207]. However, in addition continuing education and training in end-of-life communication of the HCPs could be beneficial and strengthen their professional skills.

Parents confidence in HCPs may be diminished when communication is inconsistent and delivered inadequately[208]. In addition, the distress in parents increases if the HCPs avoid communicating about their child's end-of-life care. Thus, parents' satisfaction with treatment and care has been demonstrated to be closely associated with the communication skills of physicians[209–213] and research has demonstrated benefits of optimized communication for families, patients and HCPs[82]. However, some parents find it very difficult to talk about discontinuation of treatment and the child's imminent death, and it is therefore important that the parents are prepared to receive this kind of information[211,214]. Parents hope to the very end and if the parents have unrecognized or unaddressed anger or fear they may be dissatisfied with the amount and quality of information even if it has been given in a detailed, empathic and meticulous way[99]. In addition, previous studies have shown, that parents receiving more prognostic information felt more hope, even though the prognosis was poor[215–218]. Early implementation of PPC as an integrated part of the curative treatment may help to establish common clinical pathways and destigmatize PPC as it will not be perceived as a major and often sudden change at the end-of-life[168]. It is essential that clinicians offer the opportunity to discuss issues related to end-of-life care in line with information about diagnosis and prognosis and decision-making preferences[219]. The bereaved parents in our study reported that they would have preferred the information to be disclosed immediately when curatively intended treatment was exhausted. However, in some situations, unpredictable disease progression and sudden death can make it extremely difficult for HCPs to inform the parents timely and accurately. Further, uncertainty related to prognostication of various diagnoses may also be one of the challenges[219]; however, PPC providers must realize, that this is unavoidable in caring for seriously ill children, and uncertainty related to prognostication should not be a barrier for initiating PPC[220]. Therefore, it is very important that HCPs have the knowledge and the skills to communicate about death, end-of-life care and transition to SPPC[212]. Improved education and training of HCPs in communication could help overcoming some of the barriers in providing PPC[216,221–225].

### *Organizational and clinical implications*

The results presented in this thesis may reflect that more aggressive and effective treatment attempts to save lives may deprive some terminally ill children the option of dying in their own homes. In order to give the best possible support and help to the families during the child’s illness and imminent death timely involvement of home-based care may facilitate and improve the opportunity to communicate and plan location of care and preferred place of death. Constructive use of this opportunity requires a certain amount of structure, capacity and dedication from the HCPs working in the field. The concept of Advanced Care Planning (ACP) where the purpose is to clarify the patients’ and families wishes for treatment and care in the end-of-life, and on this basis organize the treatment so their wishes are fulfilled to the greatest possible extent should be an integral part of PPC. However, it requires true and respectful cooperation within the interdisciplinary team of HCPs to ensure a strong, caring, supportive and coherent network for the entire family.

The new knowledge of the present thesis regarding diagnoses and age distribution of the children in question may by predicting trajectories inform the basis for organizing SPPC. Thus, neonatal care units should definitely be involved in the planning as nearly one-third of the children died within the first year of life. However, additional new studies investigating the children's and parents' perspectives and wishes on their preferred place of care and wishes on the level of end-of-life care and their preference concerning ultimate place of death will be crucial for the further planning and organization of SPPC in Denmark.

A very important finding is that the bereaved parents reported prolonged depression 3-5 years after their loss. This indicates the need of specific interventions directed towards the parents. A more systematic clinical practice including screening and follow-up visits may ensure that the parents get the help and support during the child's illness trajectory and after the loss. Thus, if the parents show symptoms of clinical depression following screening it must be diagnosed so they can get the timely support and treatment. Likewise, psychological interventions including family and/or couples' therapy and bereavement care may advantageously be integrated in the SPPC approach. Also, facilitating different frames for the families to bond with other families in similar situations gives the opportunity to share thoughts, feelings, experiences and establish mutual support.

Finally, HCPs strives to communicate effectively and timely with parents of children with life-limiting diagnoses. However, it seems likely that some barriers may hinder even the best of intentions. Therefore, educational programs including communication training and continuous supervision may serve to qualify the HCPs working in SPPC and hereby enable them to protect and support the affected families and themselves better.

### ***Strengths and limitations***

All background data of the children and their parents were acquired through national registers. The strengths of register-based research are the unique method of understanding and describing relationships in health and diseases. Denmark as well as the other Nordic countries have a very special position globally to access register information about all their national citizens. All the information provides unique possibilities for combining data and investigating e.g. hospitalizations, diagnoses, development of a disease over time, causes and places of death of all citizens with permit residents. This information has been established as an administrative and regulatory fundament. Thus, there is no underlying social selection or recall bias in these databases. In this PhD study, the registers gave us the valuable information about the children's all-cause mortality and places of death as well as the unique opportunity to combine the dead children with their surviving parents[226].

In study I, the relatively high proportion of death certificates coded as unknown and ill-defined causes of mortality after the introduction of electronic death certificates in 2007 is notable and should be considered as a study limitation. Thus, this indicates that after 2007 the cause-specific mortality rates may be somewhat underestimated. However, the study has demonstrated new and reliable knowledge of all-cause mortality over a time span of 20 years and place of death among Danish children under the age of 18 years.

To identify the bereaved parents for the questionnaire survey in study II and III, the children were selected based on their diagnoses. A Directory of life-limiting diagnoses was used to identify the children who potentially could befit from SPPC[105]. To our knowledge this Directory has not been used in previous research to identify children with life-limiting diagnoses in other countries than UK. Thus, classification of life-limiting diagnoses in children have never previously been made and the diagnoses listed in the Directory are based on children, who have been in contact with SPPC in the UK (where SPPC is a well-established part of the national health care system). By using the Directory, we developed a "real life" overview of the children according to diagnoses, who potentially could be expected to be in need of receiving SPPC in Denmark. However, we are certainly aware that this may lead to selection bias as not all children with life-limiting diagnoses needs SPPC and some children not listed may benefit from SPPC. Also, it is possible that very rare diagnoses may not have been captured.

The questionnaire used in this study has formerly been used in bereaved parents who lost a child due to cancer in Sweden where the questionnaire also has undergone face-validity. However, to try to ensure that all questions was understood as intended by the bereaved parents in Denmark the questionnaire was face-validated in 3 bereaved parents. However, even though the Swedish population is very similar to the Danish, content validation of the Danish translation of the questionnaire may be recommended in the future. The VDS was used to capture self-reported anxiety and depression and the widely used assessment tool, CES-D[109], was also used to screen for depression. It is important to notice that the assessment tools merely screen for symptoms of anxiety and depression reported by the bereaved parents. However, caused by the thorough validation of these tools we considered their use as a strength in the present study[122].

However, we must be aware of the bereaved parents reporting of moderate to severe depression as both depression and prolonged grief by the associated cognitive deficits may affect the representativeness negatively[194–197].

The strengths in our cross-sectional design is the broad range of bereaved parents that allowed us to find coherent patterns in their experiences during their child's illness trajectory and imminent death. The patterns demonstrate valuable knowledge for improving the care for children with life-limiting diagnoses and their parents. Studies II and III were cross-sectional designs, which did not allow for drawing causality; however, our use of a self-administered questionnaire presumably reduced the risk of interview bias.

It is well-known that through the last decade the response rates in health surveys have been declining, which has been considered as an increasing problem for the validity of health and epidemiological surveys[227,228]. Non-response bias may jeopardize the validity of the results of questionnaire data, which underpins the importance of performing non-response surveys[229–231]. Therefore, due to the expected limited number of responding parents', we undertook a post-hoc non-response survey, which we believe have strengthened our study[139–141]. Of course, ethical considerations by doing a non-response must be considered, since the parents, who declined to participate in the questionnaire survey are re-approached. The questionnaire, "To lose a child", is long and many questions may be sensitive and demanding for the parents. Our hypothesis was that it might seem demanding, overwhelming and exhausting to fill in the questionnaire and it could be assumed that it was the most vulnerable parents, who declined to participate. Therefore, and in order to raise response rates in future surveys we wanted to give them the opportunity to tell why they had chosen not to participate. Our results indicated that the primary reasons for non-response were that the parents did not have the energy and found it too emotionally demanding to participate. However, it is important to note that the low response rate in the non-response survey requires careful interpretation. However, the response rate alone may be a poor indicator of non-response bias[232]. Non-response analyses can be used to assess the validity of the outcomes and a high non-response rate may not necessarily impact the representativeness of the survey[232].

A reason for our relatively low response rate may be due to the fact that both mothers and fathers individually received the questionnaire. More than 80% lived as couples and one representative for the family may have responded to the questionnaire on behalf of the family. Furthermore, as both mothers and fathers of the same child in some cases may have filled out the questionnaire together it could be questioned whether this was done independently. Finally, from previous research it is well known that females are more likely to participate in questionnaire surveys[233,234]. This was also observed in our study. Thus, all analyses were (initially) stratified by gender.

# Conclusion

This is the first PhD thesis in Denmark to provide an overview of causes and places of death in children and to assess bereaved parents' needs and distress during their child's disease, imminent death and after the loss. In **study I**, a national overview of causes and places of death in children under the age of 18 years showed that the all-cause mortality rate decreased more than 50% in the period 1994-2014. Almost two-third of the children died within the first year of life. Regarding place of death, we found that the relative proportion of hospital deaths increased, whereas home deaths decreased, which may reflect more aggressive treatment attempts to save lives. However, the downside may be that some children have been deprived of the opportunity to die at home. This study has added new and important knowledge since relevant causes of death and distribution of age and diagnosis now may underlie the future planning and organization of SPPC, just as the place of death qualifies the intervention in relation to one's own home vs hospital.

In **study II,** we found that bereaved parents, who lost a child with a life-limiting diagnosis reported high levels of anxiety and/or depression. However, 3-5 years after the loss of the child, anxiety had decreased markedly in both mothers and fathers, whereas the level of depression was unchanged in the same period. Being unmarried or having lower education were associated with severe depression. Although bereaved parents' experience of depression may be difficult to distinguish from grief, the results indicated that there is a need for interventions to support and treat parents during their child's disease and after the loss. **Study III** showed that parents wanted accurate and timely information regarding their child's life-limiting disease and imminent death. HCPs communicated late about issues related to end-of-life care and some parents felt that they were deprived taking leave with their child in the way they wished. Thus, parents' need for information and support may not be sufficiently met, which should raise awareness of the necessity for improved education and training of HCPs in communication skills.

We certainly hope and believe that the new knowledge gained from this study will inform future organization and planning of SPPC in Denmark in order to improve care for children with life-limiting diagnoses and their families.

# Future perspectives

As the majority of Danish children die in hospitals, HCPs have a very important future role in identifying children and their families who potentially could benefit from PPC, and early integration of PPC and curative treatment may especially help to ensure that children entering the palliative phase of diseases are exposed to a minimum of suffering by applying more aggressive symptom management. Thus, early integration of PPC and curative treatment may be considered already at the time of diagnosis or soon thereafter in children with life-limiting diagnoses. This may foster new common clinical pathways and destigmatize PPC. Likewise, home care capacity must be expanded and improved for selected children and families. Thus, 24-hour access to SPPC specialists should reduce hospital admissions for dying children and enable the children to spend more time and die at home according to their and their family's wishes.
As demonstrated in this PhD thesis, parents losing children have unmet needs for support and care both during the child's disease trajectory and after their loss. To optimize and target interventions for both the children and their parents, it is crucial that more research is supported and initiated in Denmark. Through our questionnaire survey we have received unique and extensive material from bereaved parents. Unfortunately, due to the time frame of this project, we have not been able to process all the parents' responses. Important topics such as parents' communication with their children about their imminent death, physical symptoms in the children, the parents' feeling of guilt and other psychosocial issues need to be analysed in further details. We consider this future work extremely important so that PPC can be based on the needs and wishes of the children and their families. Additionally, qualitative data from our study in the form of explanatory comments as well as interviews, could be used supplementary to the questionnaire survey including those parents who participated and filled in questionnaires. This data could promote a deeper and more detailed understanding of the bereaved parents' needs.
Further, this thesis is the first to specifically investigate palliative care in Danish children with both malignant and non-malignant diagnoses. An increasing amount of attention and interest in PPC has been observed in HCPs, politicians and the public after the publication of a report investigating national and international experiences with the organization of palliative care for children with life-limiting or -threatening conditions[35] and after the establishment of the first Danish children's hospice [36] in 2015. Therefore, it is noteworthy that the data used in this study is based on bereaved parents, who lost a child without access to SPPC as it was not established in Denmark at that time. When SPPC has been further developed and established it would be

valuable to study the integration of basic palliative care and the SPPC to strengthen and develop the area for the benefit of the affected children and their families. Likewise, clinical intervention studies targeting the children's symptomology as well as support to siblings and bereavement care interventions also needs increasing attention.

Even though there has been an increasing interest in SPPC in terms of developing clinical practice and research internationally, there is still very little consensus on how different interventions of SPPC should be designed. More widespread cooperation across countries and common strategies to develop national and international guidelines to improve the quality of SPPC must therefore also be considered.

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# Paper I-III

## Paper I

Lykke C, Ekholm O, Schmiegelow K, Olsen M, Sjøgren P. **All-cause mortality rates and home deaths decreased in children with life-limiting diagnoses in Denmark between 1994 and 2014**. *Acta Paediatr* 2018;107:1781-1785.

## Paper II

Lykke C, Ekholm O, Schmiegelow K, Olsen M, Sjøgren P. **Anxiety and depression in bereaved parents after losing a child due to life-limiting diagnoses: A Danish nationwide questionnaire survey**. *J Pain Symptom Manage* 2019;58(4):596-604.

## Paper III

Lykke C, Ekholm O, Schmiegelow K, Olsen M, Sjøgren P. **End-of-life communication: a nationwide study of bereaved parents´ perceptions**. *BMJ Support Palliat Care* 2019 [Epub ahead of print].

# I

## *All-cause mortality rates and home deaths decreased in children with life-limiting diagnoses in Denmark between 1994 and 2014*

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**REGULAR ARTICLE**

# All-cause mortality rates and home deaths decreased in children with life-limiting diagnoses in Denmark between 1994 and 2014

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**Keywords**
Cause of death, Diagnoses, Location of death, Paediatrics, Palliative care

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## ABSTRACT

**Aim:** Specialised paediatric palliative care has not previously been a priority in Denmark. The aim of this study was to support its development and organisation, by examining why and where children died using official national data for 1994–2014.

**Methods:** We obtained data on 9462 children who died before the age of 18 from the Danish Register of Causes of Death. The causes of deaths were listed according to the codes in the International Classification of Diseases.

**Results:** The all-cause mortality rate decreased by 52% over the study period, and infants below one year accounted for 61% of all deaths. The decline in infant mortality (26%) primarily reflected fewer deaths due to congenital malformations and chromosomal abnormalities (68%) and perinatal deaths (30%). In children aged one year to 17 years, the substantial decrease (65%) was due to external causes (75%) and neoplasms (57%). The relative proportion of hospital deaths increased, while home deaths decreased.

**Conclusion:** All-cause mortality rate decreased markedly, and the relative proportion of hospital deaths increased. The results may reflect more aggressive and effective treatment attempts to save lives, but some terminally ill children may be deprived of the option of dying at home.

## INTRODUCTION

Since the early 1990s, the global mortality rates among children have been steadily declining and today they are generally low. According to the World Health Organisation, 5.9 million children under the age of five died worldwide in 2015 and the mortality rate has decreased significantly from approximately 32 deaths/100 000 in 1950 to four deaths/100 000 in 2012 (1). However, striking variations exist across continents, countries and regions (2,3). The mortality rate among children in European countries and North America has declined markedly over the last few decades, partly as a result of specialisation and advances in medicine (4).

The total population in Denmark is 5.3 million, and children below 18 years of age represent 20% of the population. Denmark is a high-income country with a modern welfare state, and it has one of the highest standards of living in the world. The basic principle of the Danish welfare system is that all citizens have equal rights to social security and free access to public services, including health care. Previously, specialised palliative care (SPC) for children and their families has not been a priority in Denmark, but recent years have seen emerging awareness and interest in this area by health professionals and the public (5). To support sound decision-making regarding the development and organisation of paediatric SPC in Denmark, this study aimed to examine why and where children under the age of 18 died during a long observation period.

**Abbreviation**
SPC, Specialised palliative care.

## METHODS

We obtained data on 9462 children who died below the age of 18 years in 1994–2014 from the Danish Register of Causes of Death, which covers all deaths of Danish citizens

**Key notes**
- Specialised paediatric palliative care has not previously been a priority in Denmark, and we examined why and where 9462 children died using official data for 1994–2014.
- The all-cause mortality rate decreased by 52%, 61% of the deaths occurred before the age of one, and home deaths became less common.
- The 26% decline in infant mortality primarily reflected fewer deaths due to congenital malformations, chromosomal abnormalities and perinatal deaths.

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in Denmark (6). The classification of the causes of death during the study period was performed in accordance with guidelines from the World Health Organisation, and since 1994, the register has used the International Classification of Diseases, Tenth Revision (ICD-10) (7,8). In 2007, electronic death certificates were introduced in Denmark and this resulted in an increase in the number of missing death certificates (7). All deaths with a missing death certificate were coded as ill-defined and unknown cause of mortality (ICD-10 code R99). The total numbers of deaths attributed to code R99 were 6% for 1994–2007, and these rose to 21% for 2007–2010 before reducing to 12% for 2011–2014.

Due to substantial variations in the prevalence of diagnoses by age, we divided the children into two groups, which were infants below one year and children between one year to 17 years of age. As the majority of deaths in infants can be classified into the two main categories—perinatal deaths and deaths due to malformations, deformations and chromosomal abnormalities—we merged the remaining groups into a single category termed others. In children one year to 17 years of age, the distribution appeared more even. Thus, we retained the largest groups: neoplasms, neurologic, malformations, deformations and chromosomal abnormalities and external causes, which generally comprised of at least 10 deaths per year. The remaining groups were merged into others.

The annual crude death rates were calculated by dividing the number of deaths by the population aged 0–17 years living in Denmark and multiplying them by 100 000 for each year. The infant mortality rate was calculated as the number of deaths below one year of age per 1000 live births. The cause-specific mortality rates among children aged one year to 17 years old were calculated by dividing the number of deaths by the population living in Denmark and multiplying them by 100 000 for each year. The Statistical Application System, version 9.4 (SAS Institute Inc, Cary, NC, USA) was used to perform all the analyses.

## RESULTS

### Mortality rates and diagnoses

During this period, the all-cause mortality rate among children of 0–17 years of age decreased by 52% from 57.1 deaths/100 000 children in 1994 to 27.4 in 2014. The mortality rate declined in all age groups from 1994 to 2014. Figure 1 shows the decline in all-cause and age-specific mortality rates among children aged one year to 17 years, and Figure 2 shows the decline all-cause mortality infants below the age of one.

The decline in infant mortality by 26% from 5.5/100 000 live births in 1994 to 4.0 in 2014 primarily reflected fewer deaths related to congenital malformations, deformations and chromosomal abnormalities. We found a decline of 68% from 1.9/100 000 live births in 1994 to 0.6 in 2014, and perinatal deaths declined by 30% from 2.6/100 000 live births in 1994 to 1.8 in 2014. Deaths in the perinatal period constituted 61% of the total number of deaths.

In children one year to 17 years, there was a substantial decrease of 65%, which reflected a decline in deaths related to external causes such as accidents, assaults or self-harm by 75%, from 8.7/100 000 children in 1994 to 2.2 in 2014. Furthermore, a marked decrease in deaths related to neoplasms was observed from 4.2/100 000 children in 1994 to 1.8 in 2014. The mortality rate and the distribution in diagnoses are shown in Figures 2 and 3.

### Place of death

During the observation period, the relative proportion of deaths at hospitals increased by 17% from 76% in 1994–1998 to 89% in 2011–2014, whereas the relative proportion of home deaths decreased by more than 50%, from 13% in 1994–1998 to 6% in 2011–2014. Deaths in places other than hospitals or home also decreased by more than 50%, from 11% in 1994–1998 to 5% in 2011–2014 (Fig. 4).

The over-all mortality rate related to neoplasms decreased by 60%, but the relative proportion of hospital deaths increased by 24%, from 61% in 1994–1998 to 81% in 2011–2014, whereas home deaths decreased by 50%, from 37% in 1994–1998 to 18% in 2011–2014.

The most pronounced difference with regard to age was seen in the age group four to seven years, where the relative proportion of hospital deaths increased from 56% to 85%. The highest and most stable relative proportion of home deaths was found in the age group eight years to 14 years: 19% in 1994–1998 to 17% in 2011–2014.

## DISCUSSION

In this study, the all-cause mortality rate in children decreased by 52% during a substantial observation period of 20 years. The most striking decline was found with regard to congenital malformations, deformations and chromosomal abnormalities. In 2000, a new screening method was launched internationally, which provided the first-trimester risk assessment for Down syndrome and other serious chromosomal abnormalities, (9). Due to the recommendations from The Danish National Board of Health in 2004, Denmark became the first country in the world to offer all pregnant women first-trimester risk assessment for Down syndrome combined with ultrasound screening for foetal abnormalities in weeks 18–20 (10). After the implementation of the national screening programme, the number of infants born with Down syndrome and the number of invasive procedures were substantially reduced in Denmark (11). In the same period, folic acid supplements were further recommended during pregnancy as studies had shown that they prevented the development of congenital anomalies of the central nervous system (12,13). Finally, there was a general decline of maternal mortality in the western world primarily due to improved pregnancy and birth care (14).

In general, perinatal mortality rates declined in Europe during the last decades of the twentieth century and that decline continues today (15). Furthermore, survival and cure rates for childhood cancers in Europe, including

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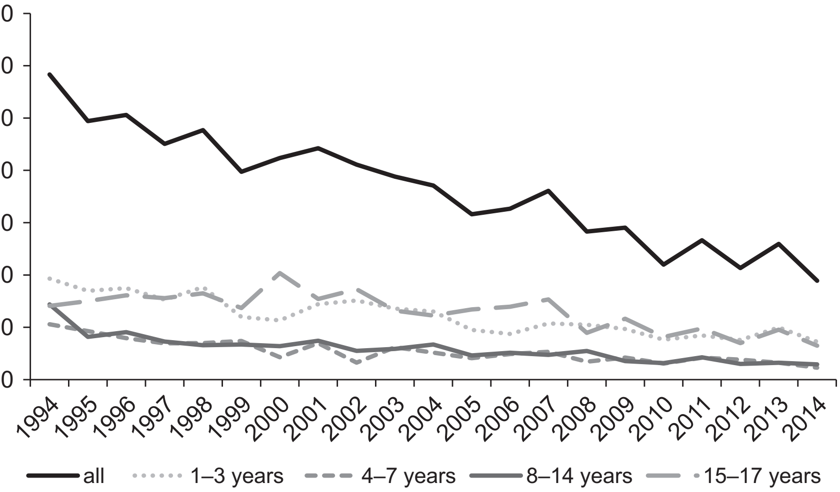

**Figure 1** Age-specific mortality rates (per 100 000 children) among children aged one year to 17 years in Denmark 1994–2014.

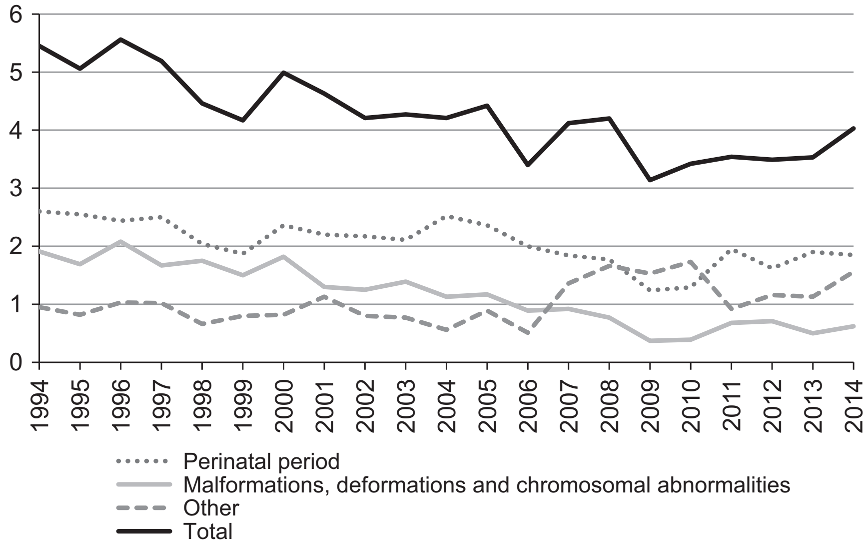

**Figure 2** Cause-specific mortality rate (infants) in Denmark (per 1000 children) 1994–2014.

Denmark, have also greatly improved over the past 40 years (16). Thus, in the present study, we also found remarkable declines in perinatal deaths and deaths due to neoplasms and external causes. A general effort to prevent accidents has resulted in fewer deaths among children in Denmark, as in most European countries (17).

Healthcare professionals, and even the public, consider that a good death takes place at home and home is often cited as a preferred place of death (18). During the observation period, we found that the relative proportion of deaths in hospitals had increased by 17%. The increasing percentage of deaths in hospitals may be due to more aggressive treatment attempts that continue to the very end of life and strive for cures or to prolong life, especially in children. This may involve more deaths in hospitals, but it may actually also prolong or save lives and contribute to decreasing mortality. The downside may be that children with life-threatening or life-limiting diseases are deprived of the opportunity to die at home surrounded by their loved ones. However, information regarding the preferred place of death in children varies and is still sparse (19). A systematic review on the preferred place of death for children and adolescents with life-threatening and life-limiting conditions included nine studies from four different countries. In six of the studies, the majority of the parents expressed the preference for a home death. The other studies showed significant variations regarding the preference for home deaths, ranging from 0% to 35% (19). In our study, a relative decline of more than 50% was seen in home deaths. This does not necessarily mean that it has become more difficult for children in Denmark to die at home. The decline could also be because children with life-limiting

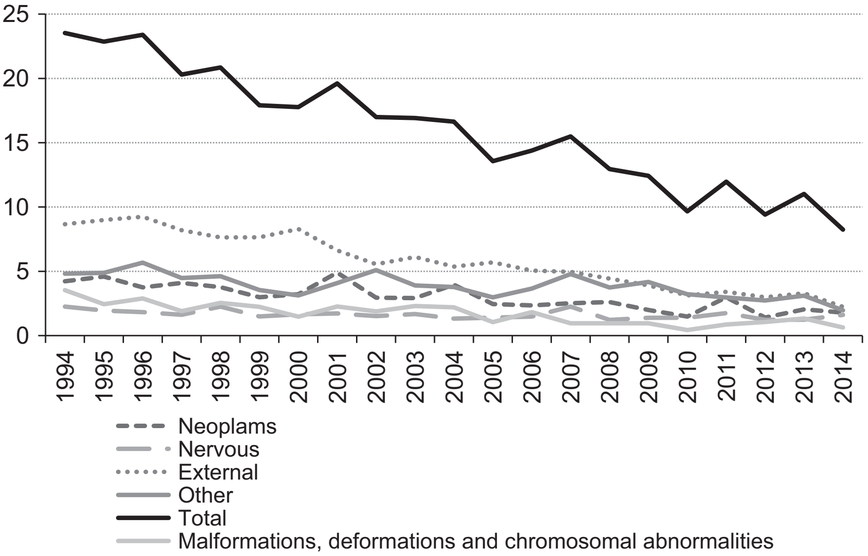

**Figure 3** Cause-specific mortality rate (one year to 17 years) in Denmark (per 100 000 children) 1994–2014.

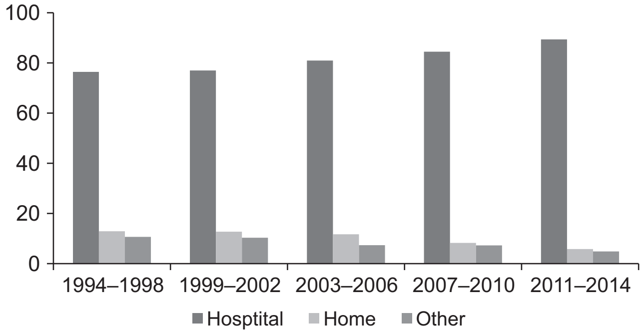

**Figure 4** Place of death among children in Denmark. Percentages.

conditions now receive more aggressive treatments, which require them to be inpatients, and so are more likely to be in hospital at the end of their life. However, we have no knowledge about end-of-life care decisions for children with life-threatening diseases in Denmark, and therefore, more research in advance care planning and decision-making concerning the withdrawal of curative treatments are needed in various diagnoses (20,21). Thus, there may be an unmet need for extended specialised palliative home care for selected children and families.

A previous study with a much shorter observation period than ours found large cross-national variations in the place of death for children in 11 countries (22). Another study found that children in Belgium and the Netherlands had significantly higher chances of dying at home than, for example, children in Italy (23). Furthermore, an increase in the proportion of home deaths in Belgium was noted, from 35.6% in 2003 to 42.1% in 2008. In Italy, the proportion of home deaths increased from 21.7% to 31.7% during the same period (22,23). According to a review by Knapp et al., Belgium, New Zealand and Italy were judged to have the highest capacity of paediatric palliative home care worldwide (24).

Previous studies have indicated that children with complex chronic conditions who receive SPC have fewer hospital admissions, are more likely to die at home (25,26) and that the number of home deaths increased with the increasing capacity of SPC (26). The different levels of paediatric SPC development can probably explain some of the country variations regarding the prevalence of home deaths in children, including the low percentage of home deaths in Denmark. SPC for children is a new area in Denmark, and the first hospice for children was established in Denmark in 2015 (27). In 2016, all five healthcare regions in Denmark were upgraded to establish and strengthen the capacity of SPC teams for children. This approach may bring about increasing rates of home deaths for children with life-threatening and life-limiting diseases.

The relatively high amount of death certificates that were coded as ill-defined and unknown cause of mortality after 2007 is notable and is a study limitation. This means that the cause-specific mortality rates after 2007 may be somewhat underestimated. However, our study has provided a long-term overview and new knowledge of the all-cause mortality and place of death in Danish children below 18 years of age.

## CONCLUSION

This study provided a national overview of the causes and places of death of 9462 Danish children from 1994 to 2014. Our results showed that the all-cause mortality rate decreased 52%, and almost, two-thirds died in the first year of life. With regard to the place of death, the relative proportion of deaths in hospitals increased and home deaths and deaths in other places decreased. New awareness gained from this study, and the rising attention paid to SPC for children, may change current practice and empower children and their families to choose the place of care and death according to their wishes and needs. The overview of the causes and places of death has provided valuable new knowledge, which may provide the basis for future support in the planning and organisation of paediatric SPC in Denmark.

## FUNDING

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## CONFLICT OF INTEREST

None to declare.

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# II

## *Anxiety and depression in bereaved parents after losing a child due to life-limiting diagnoses: a Danish nationwide questionnaire survey*

*Original Article*

# Anxiety and Depression in Bereaved Parents After Losing a Child due to Life-Limiting Diagnoses: A Danish Nationwide Questionnaire Survey

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## Abstract

**Context.** Losing a child is the most burdensome event parents can experience involving risks of developing anxiety and depression.

**Objectives.** To investigate anxiety and depression in bereaved parents during their child's life-limiting illness and imminent death and three to five years after the loss to target future interventions.

**Methods.** A Danish nationwide cross-sectional questionnaire survey. From 2012 to 2014, a register-based study identified causes of deaths of 951 children aged zero to 18 years. Potential palliative diagnoses were classified according to previously used classification. A total of 402 families were included. A modified version of the self-administered questionnaire "To lose a child" was used. Non-response surveys identified reasons for lack of response.

**Results.** In all, 136 mothers and 57 fathers completed a questionnaire, representing parents of 152 children (38%). Sixty-five percent of mothers and 63% of fathers reported moderate-to-severe anxiety during the child's illness. However, three to five years after their loss anxiety had decreased markedly. Thirty-five percent of mothers and 39% of fathers reported moderate-to-severe depression during the child's illness; three to five years after the loss they were suffering equivalently from depression. The Center for Epidemiologic Studies Depression Scale indicated that severe depression was significantly associated with lower education and being unmarried.

**Conclusion.** The reporting of anxiety during the child's illness and prolonged depression in bereaved parents three to five years after the loss indicates a potential need for psychological interventions. In the process of implementing specialized pediatric palliative care in Denmark, our findings should be considered for future treatment programs. J Pain Symptom Manage 2019;58:596–604. © *2019 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

***Key Words***

*Anxiety, depression, pediatric, bereavement, parents, palliative care*

## Introduction

Losing a child is considered the most burdensome event parents can experience and the risk of developing anxiety and/or depression may be expected to be high. Previous Danish studies found an increased risk of psychiatric hospitalization and mortality in bereaved parents.[1,2] A review focusing on the association between losing a child and the subsequent health status of parents found in nine of 17 studies an increased risk of developing anxiety and depression.[3] Thus, psychological distress in terms of anxiety and

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depression seems to have high impact on suffering in bereaved parents.

Since 2015, specialized pediatric palliative care has been a priority in Denmark, which includes establishment of both hospices and hospital-based teams. Palliative care in this study are based on the World Health Organization's (WHO) definition of pediatric palliative care[4] and specialized palliative care is based on the Recommendations from the European Association for Palliative Care.[5] To target future interventions for parents during their child's life-limiting illness and after their loss, it seems highly relevant to investigate bereaved parents' experiences including anxiety and depression. We hypothesized that anxiety and depression would decline over time and that potential risk factors as the child's age and diagnosis, the parents age, civil status, education, and religious belief could influence anxiety and depression.[6] Potential risk factors impacting parental bereavement outcomes after the death of a child with a life-limiting disease have previously been studied[7] and the findings indicated that the child's age and diagnosis,[6] the educational level of parents,[8] and their religious belief[9] may influence anxiety and depression, which seemed to decline over time.[6] Thus, the aim of this study was to investigate anxiety and depression in bereaved parents during the child's life-limiting illness and imminent death and three to five years after the loss to target future interventions in specialized pediatric palliative care.

## Methods

### Participants and Settings

In a recent nation-wide study, we investigated the mortality rate, causes, and places of death for children less than 18 years of age, who died in Denmark in the period 1994 to 2014.[10] The data were obtained from the Danish Register of Causes of Death, which covers all deaths of citizens in Denmark.[11] The classification of the primary causes of death during the study period was performed in accordance with guidelines from the WHO; and since 1994, the Register has used the International Classification of Diseases, Tenth Revision.[12,13] From the Danish Register of Causes of Death, 951 children, who died in Denmark in the period 2012 to 2014, were identified. A directory of life-limiting conditions elaborated in Wales were used to identify those children, who could benefit from specialized pediatric palliative care. The directory was recorded through diagnoses of patients under the care of five children hospices and a tertiary specialist palliative care service in the U.K.[14] As specialized pediatric palliative care is a new clinical discipline in Denmark, the directory was used to identify Danish children, who potentially could benefit from the intervention. The diagnoses in the directory were matched with the causes of death in the Danish Register of Causes of Death and 402 children were identified. In Denmark, individuals with residence permit have a unique civil registration number stored in the Danish Civil Registration System.[15] This register contains information on, for example, date of birth and death, sex, identity of parents, municipality of residence, and civil status. Through this register, we identified the parents of the 402 children. Parents were eligible if they had a Danish civil registration number and a Danish non-protected postal address. Of 804 eligible parents, contact information was reachable for 743 and they were invited to participate. Contact information was not available for 61 parents due to, for example, death of the parents, unknown paternity, protected address, or emigration from Denmark.

### Data Collection and Assessment

As we wanted to investigate bereaved parent's experiences during the child's illness, imminent death and at present, a modified version of the comprehensive questionnaire "To lose a child" was chosen. The questionnaire has been face-to-face validated and formerly been used in parents, who lost a child because of malignancies in Sweden.[16] The fact that Sweden and Denmark are very similar in culture, language, and health care systems as well as the fact that the content could be easily be modified to comprise parents who lost a child to life-limiting diseases influenced our choice of this questionnaire. The original questionnaire contains 129 questions, which are divided into three parts. The first part covers demographics and the parent's views on the care given during the child's illness, the second part includes the parents' views of the professional care received by themselves after the child's death, and the third part covers the parent's well-being at present. We translated the questionnaire from Swedish into Danish according to a revised version of the manual of European Organization for Research and Treatment of Cancer.[17] Independently, a health care professional and a non-professional translated the questionnaire from Swedish into Danish. A discussion and adjustment of the translation was made by our research group. The wordings of some of the questions were changed in the forward translation, for example, each time "last month" during the child's illness was used, it was changed to "end-of-life time," because other life-limiting diagnoses in children than cancer may often have more unpredictable trajectories. Finally, specific questions related to cancer trajectories, for example, "Did your child's illness reappear (recur) after having disappeared" were deleted. As the questionnaire was modified, a back-ward translation according to the translation manual was not made. The final version included 122 questions. This study presents the demographics of the parents and their responses to questions assessing anxiety, depression, and psychological well-being.

To identify depression-related symptoms, the Centre for Epidemiological Studies Depression (CES-D) Scale was used. The CES-D Scale is a well validated 20-item measure using a four-point Likert scale, where 1 is "never" and 4 is "most of the time."[18] The CES-D Scale responses were summarized according to the guidelines by giving a score of 0 to 3. A score of 16 or more reflects risk of clinical depression. More specifically, a score of 16 to 23 indicates moderate and 24 to 60 indicates severe depression.[18] Responders with missing values on more than four items were excluded.

In addition, the single-item, seven-point Visual Digital Scale (VDS) was used to measure the parent's subjective evaluation of anxiety and depression at present and during the child's illness and death according to their memory. The VDS for anxiety and depression has been thoroughly tested for face validity and has been used in several research projects by the research group of Clinical Cancer Epidemiology.[19–23] Furthermore, the VDS of depression has been shown to correlate well with the CES-D Scale.[21,24,25]

The VDS was also used for measuring the bereaved parents self-assessed well-being. Cut-off scores for VDS were used; 1 to 2 indicates "no or mild," 3 to 5 "moderate," and 6 to 7 "severe" anxiety or depression. Questions referring to the parents' well-being were categorized as 1 to 2 "worst," 3 to 5 "moderate," and 6 to 7 "best."[24,26]

A pilot survey and in-depth interviews with tree bereaved parents focusing on comprehensibility and usability were performed before the questionnaire was finally approved. No further adjustments were made after pilot testing.

At least one representative parent for each child was preferred and, therefore, the questionnaire was sent to mothers and fathers separately. The questionnaire and an introductory letter, which briefly explained the objectives of the study were sent including a folder explaining the study in more depth. Parents not responding within three weeks received one reminder. All parents were invited to fill the questionnaire between April and June 2017. After receiving and analyzing the responses of the first 20 questionnaires, which did not give rise to further revision, they were included in the total sample.

### Other Variables of Interest

The Nordregio classification of urban and rural areas was used to divide the 98 Danish municipalities into the following four types of municipalities: urban, intermediate, rural, and peripheral. The classification is based on 14 indicators as population per square kilometer, population in rural areas and towns with less than 1000 inhabitants, percentage of the workforce with basic education, and average distance to motorway.[27] Finally, information on education, status of employment through the child's illness, loss of more than one child, and religiousness were self-reported in the present study.

### Statistical Analyses

Descriptive statistics included percentages for categorical variables and means, SDs, and medians for continuous variables.

The associations between the potential risk factors (parental sex, civil status, education, primary causes of death, and age of the children) and severe depression (CES-D Scale >23) were assessed by a logistic regression model using a Generalized Estimating Equation, with allowance for clustering within each child. The effect of clustering has to be taken into account to allow for the likelihood that parents of the same child could respond similarly, because they have been exposed to the same experience. However, we found it interesting to divide the results into mothers and fathers in the results section, as we assumed that there might be differences. Data on potential risk factors (parental sex, civil status, primary causes of death, and age of the children) were obtained from the Danish Civil Registration System and education was reported by the parents in the questionnaire.

The association between potential explanatory factors (sex, age of the parents and the child, primary causes of death of the child, and the residential area of the parents) and non-response were assessed by logistic regression analysis. The results from the logistic regression models are presented as odds ratios with 95% CIs. All *P*-values were adjusted for clustering within the child. The Statistical Application System, version 9.4 (SAS Institute Inc, Cary, NC) was used to perform all the analyses.

## Results

### Characteristics of the Sample

In all, 136 mothers and 57 fathers completed a questionnaire, representing parents of 152 children (38%). There was an equal distribution between boys and girls (Table 1).

In all, 99.5% were biological parents, 87% were married, and 90% shared the custody at the time of the child's illness. Eighteen percent of the parents had divorced after the child's death. Sixty-seven percent had higher education than upper secondary or vocational school and 68% stated to be religious. Bereaved

*Table 1*
**Characteristics of the Children**

| *N* (%) | Children |
|---|---|
| Identified children | 402 |
| Number of children represented | 152 (37.8) |
| Children represented by both parents | 41 |
| Age | |
| 0−31 days | 72 (37.3) |
| 32−364 days | 36 (18.7) |
| 1−3 yrs | 14 (7.3) |
| 4−7 yrs | 21 (10.9) |
| 8−10 yrs | 11 (5.7) |
| 1113 yrs | 18 (9.3) |
| 14−17 yrs | 21 (10.9) |
| Sex | |
| Girls | 96 (49.7) |
| Boys | 97 (50.3) |
| Death causes | |
| Neoplasms | 41 (21.2) |
| Diseases of the nervous system | 24 (12.4) |
| Congenital malformations, deformations, and chromosomal abnormalities | 46 (23.8) |
| Conditions originating in the perinatal period | 55 (28.5) |
| Other | 27 (14.0) |

parents to children with congenital malformations, deformations and chromosomal abnormalities, conditions originating in the perinatal period, and cancer were more likely to participate (Table 2).

### *Anxiety and Depression*

During the child's illness, 65% of the mothers and 63% of the fathers according to their memory scored moderate-to-severe anxiety using VDS. At the time of the survey (three to five years after the loss), 24% of mothers and 16% of fathers scored moderate-to-severe anxiety (Fig. 1). There were no statistically significant differences in anxiety between mothers and fathers (Table 3).

During the child's illness, 35% of mothers and 39% of fathers according to their memory scored from moderate-to-severe depression using VDS. At the time of the survey (three to five years after the loss), still 34% of mothers and 35% of the fathers scored moderate-to-severe depression (Fig. 1). There were no statistically significant differences between mothers and fathers with regard to self-reported depression neither during the child's illness nor at the time of the survey (Table 3).

At the time of the survey, 61% of the parents scored moderate-to-worse mental well-being and nearly 52% assessed their overall quality of life as moderate-to-worst possible using VDS (Fig. 2).

At the time of the survey, mothers had lower prevalence of moderate-to-severe depression (33%) than fathers (44%) according to the CES-D Scale (Table 4). No statistically significant association between depression and religious belief in the parents was found. Furthermore, there were no statistically significant associations between the parent's sex, the child's death cause, the age of the child, and severe depressive symptomatology (CES-D Scale >23). However, results from multiple logistic regression analysis showed that parents with lower education (i.e., basic, upper secondary, or vocational school) had 6.92 (95% CI: 2.74 to 17.47) times higher odds of having severe depressive symptomatology than parents with higher education. Furthermore, married parents (at the time of the survey) had 0.29 (95% CI: 0.11 to 0.78) times lower odds than unmarried parents of having severe depressive symptomatology (Table 5).

Finally, 71% of the mothers and 66% of the fathers reported that their mental health has deteriorated after losing a child and 49% of the mothers and 54% of the fathers answered that they never had had access to psychological support during their child's end-of-life time (data not shown).

### *Non-response*

The associations between diagnosis, sex, and age of the child and age and residential area of the parents and non-response were analyzed. The non-responder

*Table 2*
**Characteristics of Bereaved Parents After Losing a Child due to Life-Limiting Diagnoses**

| *N* (%) | Mothers | Fathers |
|---|---|---|
| Number of invited parents | 391 | 352 |
| Number of respondents | 136 (34.8) | 57 (16.2) |
| Age | | |
| <35 yrs | 35 (25.7) | 10 (17.5) |
| 35−44 yrs | 63 (46.3) | 23 (40.4) |
| ≥45 yrs | 38 (27.9) | 24 (42.1) |
| Civil status today | | |
| Married | 103 (75.7) | 46 (80.7) |
| Not Married | 31 (22.8) | 9 (15.8) |
| Not answered | 2 (1.5) | 2 (3.5) |
| Education level | | |
| Basic, upper secondary, or vocational school | 29 (21.4) | 19 (33.3) |
| Higher education | 95 (69.9) | 37 (64.9) |
| Not answered | 12 (8.8) | 1 (1.8) |
| Status of employment through the child's illness[a] | | |
| Employed | 36 (26.7) | 34 (59.7) |
| Leave | 97 (71.7) | 24 (42.2) |
| Unemployed, studying, or other | 18 (13.2) | 3 (5.3) |
| Residential area | | |
| Countryside and small town | 79 (58.1) | 35 (61.4) |
| Medium to large sized city | 56 (41.1) | 22 (38.6) |
| Not answered | 1 (<1) | 0 (0) |
| Lost more than one child | | |
| Yes | 17 (12.5) | 5 (8.8) |
| No | 118 (86.8) | 51 (89.5) |
| Not answered | 1 (<1) | 1 (1.8) |
| Religiousness | | |
| Religious | 100 (73.5) | 32 (56.1) |
| Not religious | 36 (26.5) | 24 (42.1) |
| Not answered | 0 (0) | 1 (1.8) |

[a] Can give more than one answer in the same question.

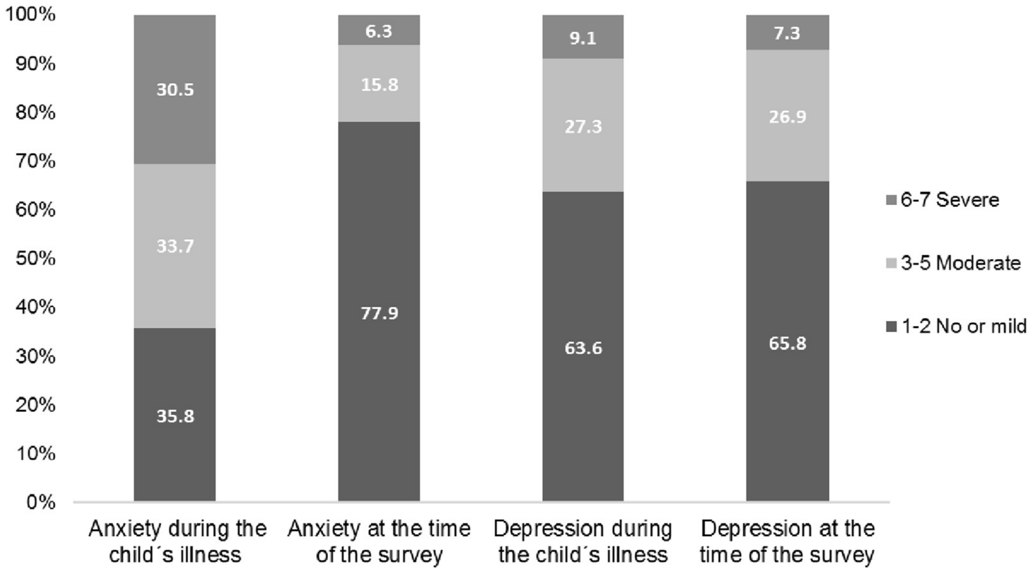

Fig. 1. Anxiety and depression in bereaved parents during the child's illness and after the loss according to VDS, %. VDS = Visual Digital Scale.

analysis revealed a significant association between mothers' age and non-response. Mothers less than 35 years of age had 1.56 (95% CI: 0.94 to 2.57) times higher odds of non-response than mothers aged 35 to 44 years. Furthermore, mothers aged 45 years or older had 0.45 (95% CI: 0.22 to 0.94) times lower odds of non-response than the reference group. The same tendency was observed in fathers, but the association was not statistically significant.

Furthermore, because of the low response rate, a post-hoc non-response survey to identify reasons for lack of response was performed. First, a self-administered questionnaire with 14 short questions based on reactions from participating parents was constructed. The questionnaire was pilot-tested by 15 bereaved parents, who all provided written feedback. The questionnaire was sent to all non-participating parents. For ethical reasons, no reminders were sent. Fifty-one parents participated in the questionnaire survey. Fifty-one percent of these parents "completely or partly agreed" that the questionnaire was too extensive, 63% "completely agreed" that they did not have energy, and 67% "completely or partly agreed" that it was emotionally too hard to participate. However, 51% "completely agreed" that the survey was important and 40% "completely disagreed" that they received the help they needed during the illness and after the child's death (data not shown).

*Table 3*

**Anxiety and Depression According to VDS**

| | Mean (SD) | *N* | *P*-value |
|---|---|---|---|
| Feelings of anxiety during your child's illness (1 = never and 7 = always) | | | |
| Fathers | 3.6 (2.06) | 57 | 0.246 |
| Mothers | 4.0 (2.38) | 130 | |
| Feelings of anxiety at the time of the survey? (1 = never and 7 = always) | | | |
| Fathers | 1.7 (1.31) | 55 | 0.138 |
| Mothers | 2.1 (1.66) | 135 | |
| Feelings of depression during your child's illness (1 = never and 7 = always) | | | |
| Fathers | 2.5 (1.78) | 57 | 0.952 |
| Mothers | 2.5 (1.84) | 130 | |
| Feelings of depression at the time of the survey? (1 = never and 7 = always) | | | |
| Fathers | 2.5 (1.74) | 57 | 0.630 |
| Mothers | 2.4 (1.70) | 136 | |

VDS = Visual Digital Scale.

## *Discussion*

To our knowledge, this is the first study to investigate anxiety, depression, and well-being in a national sample of parents, who lost a child due to life-limiting diagnoses. Our study indicated that the parents reported to recall high levels of anxiety and/or depression during the child's illness and still reported prolonged depression three to five years after their loss.

Previous studies have found that most anxiety disorders are more prevalent in women than in men.[28,29] However, no statistical sex differences in anxiety were observed in our study. Recall bias may, of course, influence reliability of reporting from an incomprehensible, devastating and chaotic period of life after three to five years;[30,31] however, the reported

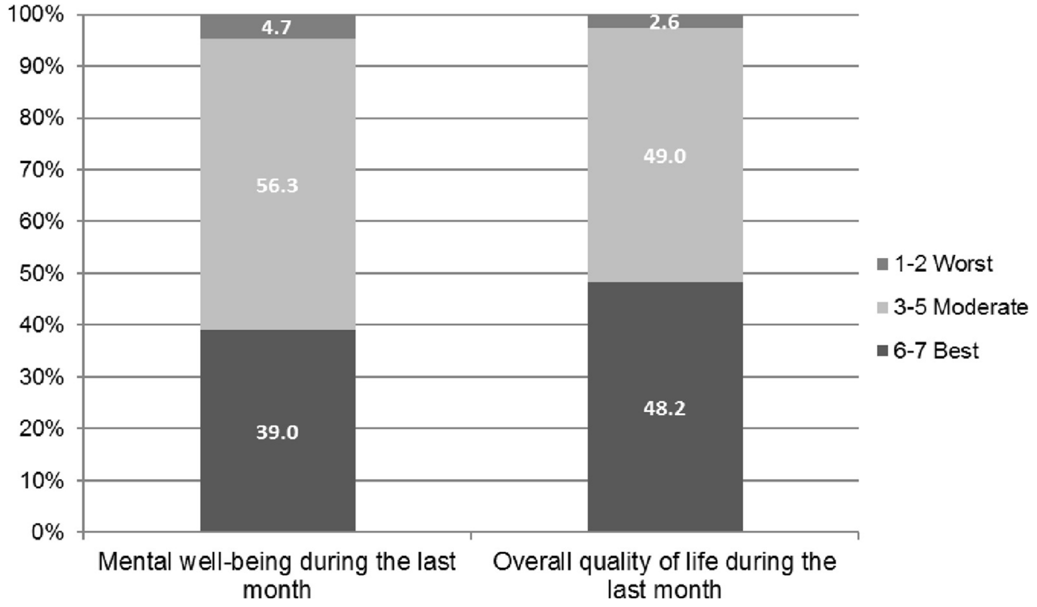

Fig. 2. Mental well-being and quality of life in bereaved parents at the time of the survey according to VDS, %. VDS = Visual Digital Scale.

high prevalence of anxiety may likely be associated with increased distress because of the child's end-of-life trajectory.[32] Some of the parents may even have developed posttraumatic stress disorders,[33,34] which depending on their psychological resilience may be either significantly reduced on a sustained basis or making them even more vulnerable to stressors and crises later in life, that in turn may be associated with long-standing depressive disorders many years after the traumatic and distressing period has ended.[35] Thus, these findings may indicate that anxiety and depression in the aftermath of trauma may be conceptualized as a general traumatic stress construct. In Denmark, depression is mainly diagnosed by a physician based on the WHO's International Classification of Diseases, 11th Revision, criteria.[34] The parents in this survey were not clinically diagnosed, but exclusively screened for depression based on self-report. According to the median prevalence of 8.8% in the general population using the CES-D Scale,[36] we found high levels of moderate-to-severe depression in the bereaved parents. However, another aspect in this context is conceptually to distinguish prolonged grief disorder from depression. A key consideration is the extent to which certain symptoms are specifically about the loss of the child vs. more generalized depression. Diagnostic Criteria for International Classification of Diseases, 11th Revision, Prolonged Grief Disorder and Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) Persistent Complex Bereavement-Related Disorder are available; however, our study is not designed to discriminate between depression and prolonged grief according to these concepts and definitions.[37]

We found based on recall that the reported anxiety scores for both mothers and fathers were considerably higher than their depression scores during the child's illness. However, anxiety was reduced substantially at the time of the survey, whereas depression remained unchanged. Although populations, settings and designs differ between a previous study found that anxiety and depression in bereaved parents decreased to levels similar to non-bereaved seven to nine years after losing a child.[6] However, another

*Table 4*

**Depression of the Parents According to CES-D**

| | Mothers, $n = 136$ | Fathers, $n = 57$ | *P*-value |
|---|---|---|---|
| Total scores mean (SD) | | | |
| CES-D (score range 0–60) | 14.1 (12.7) | 13.8 (10.1) | 0.867 |
| Cut-off scores $n$ (%) | | | |
| 0–15, No to mild depressive symptomatology | 89 (66.9) | 32 (56.1) | |
| 16–23, Moderate depressive symptomatology | 17 (12.8) | 14 (24.6) | |
| 24–60, Severe depressive symptomatology | 27 (20.3) | 11 (19.3) | |

CES-D = Center for Epidemiologic Studies Depression.

*Table 5*

**OR for Severe Depression (CES-D >23) in Bereaved Parents Three to Five Years After Losing a Child With a Life-Limiting Diagnose**

| | Crude OR (95% CI) | P-value | Adjusted[a] OR (95% CI) | P-value |
|---|---|---|---|---|
| Sex | 1.00 (0.51–1.96) | 0.994 | 1.93 (0.76–4.91) | 0.157 |
| Women vs. men (ref) | | | | |
| Child's age | 1.04 (0.99–1.10) | 0.089 | 1.08 (1.02–1.15) | 0.019 |
| Education | | | | |
| Basic, upper secondary, or vocational school vs. higher education (ref) | 5.50 (2.50–12.1) | <0.001 | 6.92 (2.74–17.47) | <0.001 |
| Civil status | | | | |
| Married vs. not married (ref) | 0.25 (0.11–0.58) | 0.001 | 0.29 (0.11–0.78) | 0.028 |
| Death causes | | | | |
| Certain conditions originating in the perinatal period | 0.22 (0.06–0.75) | 0.217 | 0.59 (0.14–2.43) | 0.805 |
| Congenital malformations, deformations, and chromosomal abnormalities | 0.40 (0.13–1.27) | | 1.15 (0.24–5.64) | |
| Diseases of the nervous system | 0.38 (0.09–1.48) | | 0.60 (0.11–3.39) | |
| Neoplasms | 0.58 (0.18–1.86) | | 1.04 (0.20–5.30) | |
| Other | Ref | | Ref | |

OR = odds ratio; CES-D = Center for Epidemiologic Studies Depression Scale.

[a] ORs adjusted for variables shown in the table.

study found that 18 years after the loss, bereaved parents reported more depressive symptoms and poorer well-being than non-bereaved parents 18 years after the loss.[38]

At the time of the survey, it is likely that the high score of depression found in our study may be associated with low ratings of well-being and quality of life in the parents. A systematic review of psychosocial comorbidities among bereaved parents of children with cancer found that the parents had elevated rates of anxiety, depression, prolonged grief, poor psychological well-being, poor physical health, and poor quality of life.[39] Although, the particular psychosocial comorbidities assessed in the studies of the review were diversely defined and assessed the bulk of suffering including the low levels of quality of life was in line with our findings. However, in our study, it may be noted that the reported lack of psychological support both during the child's illness and after the child's death could have contributed to some of the parents deteriorated condition. Previous studies have shown positive effects of cognitive behavioral therapy for treating[40] and preventing depression[41] and anxiety.[42–44] Thus, depending on the clinical diagnosis, both pharmacologic and non-pharmacologic interventions or a combination of both may be beneficial before and after loss.

We did not find any association between the level of depression and religious belief. A systematic review has formerly concluded that religious beliefs can be helpful in the process of coping with loss,[9] and reported that bereaved parents attending church regularly had less anxiety and depression after loss.[45] However, another study was more consistent with our findings indicating that religious beliefs were not associated with the risk of developing high levels of anxiety and depression.[6] The study found that the loss of a child aged 9 years or older implied an increased risk of anxiety and depression, especially in fathers.[6] Our study could not confirm this finding as we did not find any association between the diagnosis and age of the child and the parents' levels of anxiety and depression. However, lower education and being unmarried were found to be associated with more severe depression. Socioeconomic and marital status have not been studied widely in parental bereavement. However, a recent questionnaire survey from the U.S. found in consistency with our study that mothers with lower education appeared to report more anxiety and depression and had lower capability to access support after their loss.[8] Although the socioeconomic environment in the U.S. is highly different from Denmark, it is obvious even in a welfare state like Denmark that parents with lower levels of education associated with lower levels of household income may have greater risk of comorbid problems.

Finally, the higher odds in unmarried parents for depressive symptomatology could also be explained by marital disruption as our study showed that 18% of the parents got divorced between the death of the child and time of the survey. However, our study could not identify whether the loss of the child caused the divorce. On the other hand, a mixed-methods study demonstrated that dyadic coping between couples after the death of a child due to a life-limiting illness seemed to be helpful for the parents to work through their grief—not only as a couple, but also individually.[46]

### *Strengths and Limitations*

The data of the children and their parents were acquired through national registers. The strength of the registers is the unique opportunity to combine data of decreased children and surviving parents.[47]

The relatively low response rate may preclude the ability to generalize the study's findings as it is possible that the most vulnerable parents may be the ones who declined to participate. Further to study a nationwide sample of parents, who lost a child due to life-limiting diagnoses is a sensitive task and, indeed, ethical concerns are prevailing. However, previous researches have demonstrated that most bereaved parents felt positively affected by their participation, both personally and for the opportunity to help others after losing their child.[16,48,49] Finally, it is well known that females are more likely to participate in questionnaire surveys.[50,51] This finding was also reflected in the present survey, which involved an over-representation of mothers.

## Conclusion

Parents losing a child with life-limiting diagnosis recalled high levels of anxiety and/or depression during the child's illness and death. Three to five years after the loss, the self-reported level of anxiety decreased markedly, whereas the level of depression remained unchanged. Especially, unmarried parents and parents with lower education were associated with reporting more severe depression. The reported experience of anxiety and prolonged depression years after loss indicates the need for interventions to support and treat parents during their child's life-limiting illness and after the loss. Future studies should inform who is at risk and may identify resilience factors that protect parents from psychosocial comorbidities and potential family disruption.

## Disclosures and Acknowledgments

The authors have no financial or other conflict of interest to disclose.

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Ethical approval: Caused by the emotive nature of this questionnaire, contact information for counseling was given to the parents before participation. To ensure anonymity for anyone other than the research group, all questionnaires carried a serial number. The study protocol was approved by the Danish Data Protection Agency (2012-58-0004) and the Danish Ethics Committee (H-16021831).

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III

# *End-of-life communication: a nationwide study of bereaved parents' perceptions*

# End-of-life communication: a nationwide study of bereaved parents' perceptions

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## ABSTRACT

**Objective** To investigate bereaved parents' perception of end-of-life communication with healthcare professionals after losing a child due to life-limiting diagnoses.

**Methods** A national register identified the causes of death of 951 children aged 0–18 years during the period 2012–2014. A previously described classification of life-limiting diagnoses identified 402 children. A modified version of the self-administered questionnaire 'To Lose a Child' was distributed to the parents of these 402 children, capturing their perceptions of communication with the healthcare professionals throughout the child's disease trajectory and imminent death.

**Results** A total of 193 bereaved parents, representing 38% of the identified children, participated in the study. Overall, 98% of the parents expressed the view that physicians should immediately disclose when curatively intended treatment options were exhausted. Some 79% of parents reported that information about their child's incurable illness was given in an appropriate manner; however, 42% said that information about the child's imminent death was given too late. Finally, 31% felt deprived of the option to say goodbye to their child in their preferred manner, and 56% said that their child's death was "a shock".

**Conclusions** Parents request accurate and timely information. However, a substantial number of the parents surveyed reported that healthcare professionals communicated too late about palliative care and end-of-life issues. Even though healthcare professionals strive to communicate effectively with dying children and their parents, barriers were identified that may hinder even the best of intentions. National guidelines addressing communication issues and improved education of healthcare professionals should form part of any future agenda.

## INTRODUCTION

Communication between patients, families and healthcare professionals is an essential component of palliative care.[1] Parental satisfaction with the care provided for children with life-limiting diseases and imminent death may reflect the way healthcare professionals communicate about palliative care issues.[2] Studies have shown that parents who make decisions for their child with advanced cancer consistently indicate the need for truthful delivery of information in non-technical language to build up trust and a relationship[3 4] which may enable the families to take part in decisions on treatment goals and care on an well-informed basis.[5 6] Thus, open, accurate and timely communication about disease and prognosis has been proposed as a prerequisite for providing high-quality palliative care,[7 8] whereas inconsistent and inaccurate communication has been associated with increasing distress for the dying child and the parents.[7 9] However, previous studies have demonstrated that healthcare professionals may feel uncomfortable and distressed when communicating about end-of-life issues.[10 11] They may feel reluctant or poorly educated, and underestimate the parents' need for support, information and understanding of end-of-life care issues.[12 13]

Several studies have explored parental experiences with end-of-life communication with healthcare professionals. However, most of these studies have focused on the parental experiences of children dying in paediatric intensive care units.[14–16]

Since 2015, specialised paediatric palliative care has been a major priority in Denmark, and includes the establishment of both hospice- and hospital-based teams. However, educational programmes

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involving specialised training in end-of-life communication with children and their families have not yet been implemented. Therefore, we hypothesised that communication surrounding end-of-life care issues may be problematic and that barriers for communication should be identified. To target the support and care for the informal caregivers, our aim was to investigate bereaved parents' perception of end-of-life communication with healthcare professionals after losing a child due to life-limiting diagnoses.

## METHODS

Children who died from life-limiting illnesses durign the period 2012–2014 were identified through the Danish Register of Causes of Death. The parents of 402 children who potentially could benefit from specialised paediatric palliative care[17–19] were identified through the Danish Civil Registration System, a national register containing basic personal information on every individual with a residence permit in Denmark. The register contains information such as an individual's unique personal identification number, date of birth and death, gender, and parents' identity.[20] Parents were eligible if they had a Danish personal identification number and a non-protected postal address.

### Data collection

A modified version of the questionnaire 'To Lose a Child' was used. The questionnaire has formerly been used in parents who have lost a child due to malignancies in Sweden.[21] The fact that Sweden and Denmark are similar in culture, language and healthcare systems highly influenced the choice of this particular questionnaire. The original version contains 129 questions and includes questions about the parents' demographics, their view on the treatment and care received by their child, the professional support they received after the child's death, and their perceptions of their own present well-being. The questionnaire was translated from Swedish into Danish according to a revised version of the European Organisation for Research and Treatment of Cancer approach.[22] In the forward translation we changed the wording of some questions since life-limiting diagnoses other than cancer often may have different disease trajectories, and we excluded specific questions related to cancer. Following modification, the final version of the questionnaire comprised 122 questions. For the modified version, a backward translation according to the manual did not make sense. For this study we included all the questions that focused on parents' perceptions of communication with healthcare professionals throughout the child's disease trajectory and imminent death (tables 1–3). Future studies will focus on other sections of the questionnaire.

The questionnaire was validated face-to-face with three bereaved parents. To test the content of the questionnaire the first 20 patients were considered as pilots. After a successful trial the 20 pilot patients were included in the final study population.

In order to have at least one representative parent for each child the questionnaire was sent separately to mothers and fathers. The questionnaire and an introductory letter, which briefly explained the study objectives, was sent together with an information folder that explained the study in greater detail. Contact information, including a telephone number to call if the parents had any queries or wanted to talk, were included in the material. A reminder was sent after 3 weeks to non-respondents. The data collection period was from April to June 2017.

### Data analysis and ethics

The data were analysed descriptively and presented as percentages. P values were calculated by $\chi^2$ tests and the significance threshold was set at 0.05.

The association between potential explanatory factors (gender, age of the parents and the child, the child's diagnosis, and the parent's residential area) and non-response were assessed by logistic regression. The results are presented as odds ratios with 95% confidence intervals. All p values were calculated by $\chi^2$ tests (adjusted for clustering within the child). SAS version 9.4 was used to perform all the analyses.

**Table 1** Information regarding the child's incurable illness and the realisation of the child's imminent death

| Question | Right after the birth or immediately afterwards | Never received such information | During the 24 hours before death | A few days to a week before death | Two weeks or more before death | Respondents (n) |
|---|---|---|---|---|---|---|
| When did you receive the information that your child's illness was incurable? (%) | 30 | 12 | 15 | 13 | 30 | 179 |
| | **I didn´t realise it until it happened** | **A few hours before death** | | | | |
| When did you realise on a purely rational basis that your child was going to die? (%) | 11 | 19 | 31 | 13 | 26 | 186 |

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**Table 2** Parental perceptions of the adequacy of information provided by healthcare professionals

| IInformation topic | | Incomplete (%) | Adequate (%) | Total (%) | Respondents (n) | P value |
|---|---|---|---|---|---|---|
| The illness | Mothers | 26 | 74 | 100 | 128 | 0.578 |
| | Fathers | 22 | 78 | 100 | 54 | |
| | All | 25 | 75 | 100 | 182 | |
| The treatment | Mothers | 22 | 78 | 100 | 128 | 0.569 |
| | Fathers | 19 | 82 | 100 | 54 | |
| | All | 20 | 80 | 100 | 182 | |
| How the illness and treatment would affect the child's physical health | Mothers | 35 | 65 | 100 | 125 | 0.289 |
| | Fathers | 28 | 72 | 100 | 54 | |
| | All | 33 | 67 | 100 | 179 | |
| How the illness and treatment would affect the child's mental health | Mothers | 51 | 49 | 100 | 123 | 0.189 |
| | Fathers | 41 | 59 | 100 | 54 | |
| | All | 48 | 52 | 100 | 177 | |
| How you could help in the care of your child during the end-of-life period | Mothers | 34 | 66 | 100 | 125 | 0.74 |
| | Fathers | 32 | 68 | 100 | 53 | |
| | All | 34 | 66 | 100 | 178 | |
| What you should do in the case of an emergency | Mothers | 42 | 58 | 100 | 124 | 0.414 |
| | Fathers | 36 | 64 | 100 | 53 | |
| | All | 40 | 60 | 100 | 177 | |

To study a nationwide sample of bereaved parents who had lost their child due to a life-limiting diagnosis is a sensitive task. Indeed, ethical concerns exist around performing this research. However, previous research has demonstrated that most bereaved parents felt positively affected by their participation, both personally and as regards having an opportunity to help others.[21 23 24] Due to the emotive nature of the questionnaire, contact information for counselling was given to the parents prior to participation. To ensure participant anonymity outside the research group, all questionnaires were assigned a serial number. This study was approved by the Danish Ethics Committee (H-16021831) and the Danish Data Protection Agency (2012-58-0004).

## RESULTS

### Sample characteristics

In total, 136 mothers and 57 fathers completed the questionnaire, representing the parents of 152 children (38% of the total population of children who died due to life-limiting diagnoses during the period 2012–2014). Some 79% of the children were represented by one parent and 21% were represented by both parents. The proportion of boys and girls were

**Table 3** Bereaved parents' perspectives on issues regarding end-of-life care

| Question | | Yes (%) | No (%) | Total (%) | Respondents (n) | P value |
|---|---|---|---|---|---|---|
| Was the information that your child's illness was incurable given in what you would consider to be an appropriate manner? | Mothers | 78 | 22 | 100 | 128 | 0.482 |
| | Fathers | 83 | 18 | 100 | 57 | |
| | All | 79 | 21 | 100 | 185 | |
| Did any member of the attending staff tell you that your child did not have long to live? | Mothers | 56 | 44 | 100 | 131 | 0.387 |
| | Fathers | 62 | 38 | 100 | 55 | |
| | All | 58 | 42 | 100 | 186 | |
| How applicable is the following statement to what you felt when your child died? "My child's death came as a shock." | Mothers | 44 | 56 | 100 | 129 | 0.759 |
| | Fathers | 42 | 58 | 100 | 57 | |
| | All | 43 | 57 | 100 | 186 | |
| Did you take leave of your child in the manner that you wanted to *before* he/she died? | Mothers | 69 | 31 | 100 | 131 | 0.892 |
| | Fathers | 70 | 30 | 100 | 56 | |
| | All | 69 | 31 | 100 | 187 | |
| Did you take leave of your child in the manner that you wanted to *after* he/she died? | Mothers | 88 | 12 | 100 | 129 | 0.061 |
| | Fathers | 97 | 4 | 100 | 57 | |
| | All | 92 | 8 | 100 | 186 | |

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**Table 4** Characteristics of the children in the study cohort

| Characteristic | n (%) |
|---|---|
| Identified children | 402 |
| Children represented | 152 (38) |
| Children represented by both parents | 41 |
| Age at death | |
| 0–31 days | 72 (37) |
| 32–364 days | 36 (19) |
| 1–3 years | 14 (7) |
| 4–7 years | 21 (11) |
| 8–13 years | 29 (15) |
| 14–17 years | 21 (11) |
| Cause of death | |
| Neoplasms | 41 (21) |
| Diseases of the nervous system | 24 (12) |
| Congenital malformations, deformations and chromosomal abnormalities | 46 (24) |
| Conditions originating in the perinatal period | 55 (29) |
| Other | 27 (14) |

equally distributed, and 56% of the children died within the first year of life (table 4).

Of 804 bereaved parents, contact information was obtained for 743 individuals. For reasons such as unknown paternity, death of the parents, emigration, or protected address, contact information was not available for 61 parents. In the study cohort, 99.5% were biological parents, 87.0% of the parents were married at the time of the child's diagnosis, and 83.0% participated actively in the care of the child during the child's illness (table 5).

**Table 5** Characteristics of the bereaved parents after losing a child due to a life-limiting diagnosis

| Characteristic | Mothers (n (%)) | Fathers (n (%)) |
|---|---|---|
| Invited parents | 391 | 352 |
| Respondents | 136 (35) | 57 (16) |
| Age (years) | | |
| <35 | 35 (26) | 10 (18) |
| 35–44 | 63 (46) | 23 (40) |
| ≥45 | 38 (28) | 24 (42) |
| Current civil status | | |
| Married | 103 (76) | 46 (81) |
| Unmarried | 31 (23) | 9 (16) |
| Not answered | 2 (2) | 2 (4) |
| Education level | | |
| Basic, upper secondary or vocational school | 29 (21) | 19 (33) |
| Higher education | 95 (70) | 37 (65) |
| Not answered | 12 (8.8) | 1 (2) |
| Status of employment through the child´s illness* | | |
| Employed | 36 (27) | 34 (60) |
| Leave | 97 (72) | 24 (42) |
| Unemployed, studying or other | 18 (13) | 3 (5) |

*Multiple answers were permitted.

### Parents’ perception of communication with healthcare professionals regarding end-of-life care issues

In total, 59% of the parents received information about their child’s incurable illness from a physician; 30% received the information immediately after the child's birth and 15% received the information during the final 24 hours before the child died. A few (12%) of the parents never received this information. Furthermore, 11% of the parents did not realise or understood that their child was going to die until the event occurred, and 19% only realised that the child’s death was imminent a few hours before they died (table 1).

In total, 75% of the parents found the information received from the healthcare professionals regarding their child’s illness satisfactory, and 80% found the information about the treatment satisfactory. However, the information about how the illness and treatment would affect the child’s physical and mental health was judged inadequate by 33% and 48% of parents, respectively. One-third (34%) of parents did not receive information on how they could access end-of-life care, and 40% did not know what to do in the case of an emergency (table 2).

In total, 98% of the parents expressed the view that physicians should immediately disclose when curatively intended treatment options were exhausted, and 79% of the parents reported that information about their child’s incurable illness was given in an appropriate manner. However, 42% said that the information about their child's imminent death was given too late, and 31% of the parents said that they were unable to take leave of their child in their preferred manner. Finally, 43% of the parents said that their child’s death was “a shock” (table 3).

## DISCUSSION

Our study found that a substantial number of the bereaved parents reported that healthcare professionals communicated too late about their child’s incurable illness and imminent death, although the general information provided regarding illnesses and treatment were found to be satisfactory in the vast majority of cases. The relationship and communication between healthcare professionals and the families during end-of-life care have been shown to have a great impact on parental satisfaction, their quality of life, as well as the outcomes of post-loss bereavement.[25 26] A review of parents’ perceptions of end-of-life care of their child found that communication and the relationship between the informal caregivers and the healthcare professionals were generally poor or inadequate, and that healthcare professionals often felt uncomfortable and inadequate when communicating about end-of-life issues.[25] Most physicians are generally trained to diagnose and treat, and their primary goal is to optimise

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the chances of a cure. In our study, the majority of the bereaved parents were satisfied with the information given to them regarding their child's treatment; however, a substantial number reported unmet needs regarding information and support during their child's illness and imminent death, and 43% indicated that the death of their child was "a shock". Nevertheless, the distress affecting parents caring for an imminently dying child may be associated with poor memory retention of information, and it has been demonstrated that the majority of parents receiving complex and difficult information about their child's illness and treatment understand less than half of the given information.[7 27] The fact that the child's death was reported as "a shock" by a substantial number of the parents does not necessarily mean that the information was not given by the healthcare professionals in a sensitive way but may certainly also reflect the unbearable loss. "A shock" used in the original questionnaire by Kreicbergs *et al* and in the present modified version of the questionnaire is a common and widely used expression to describe an emotional reaction to a sudden, unexpected, and usually unpleasant event or experience.[21] Almost one-third of the parents reported that they did not get to say their final goodbye to their child in the way that they wished. Some parents whose children are dying may experience anticipatory grief as they prepare for the death. Anticipatory grief contains elements of separation anxiety, anticipation of death and future absence of the child, denial and relational losses. In general, studies concerning the prevalence of clinically significant predeath symptoms in caregivers range from 12.5% to 38.5%.[28] This prevalence may be even higher in adults who lose a child.

The importance of high-quality communication as an essential aspect of providing optimal care for children with life-limiting diagnoses and their families has been increasingly recognised in recent years. The American Academy of Paediatrics and the Institute of Medicine have published statements to promote effective communication between healthcare professionals and families in paediatrics and palliative care.[29–31] The American Academy of Paediatrics has identified three important domains in the communication between healthcare professionals and families: informativeness, interpersonal sensitivity and partnership building.[3] Healthcare professionals who meet these domains encourage shared decision-making, engage in difficult conversations about diagnosis, prognoses, treatment and end-of-life issues, and correspond continuously with the goals of care for the patient and family.[32] Models based on the fundamental elements of communication outlined by the American Academy of Paediatrics have been developed to promote effective communication between healthcare professionals and the families.[33] However, even though healthcare professionals strive to communicate effectively with the families, several barriers may hinder even the best of intentions. Communicating with parents about their child's life-limiting diagnosis or imminent death is undoubtedly a difficult task, and it is well-known that healthcare professionals may feel uncomfortable and uncertain discussing issues related to palliative care, death and dying.[12 13] Indeed, this is a delicate and sensitive area of practice that has been shown to have a powerful and lasting impact on health professionals. They use physical, emotional, spiritual and problem-solving strategies and efforts to continue to perform this endeavour effectively and to protect their own well-being.[34] From the parental perspective the majority wish and hope to the very end that their child will survive or at least that their health will improve, and even when they are given very detailed, meticulous and empathic information, parents, who have unrecognised or unaddressed feelings of fear and anger, may be dissatisfied with the content, amount and quality of information provided by healthcare professionals.[3]

It is increasingly recognised that specialised paediatric palliative care requires specific skills and knowledge,[29] and timely communication including advanced care directives to avoid futile and burdensome treatment. Therefore it is important that healthcare professionals have the skills to communicate about end-of-life care, death and the transition into palliative care.[35] The parents' confidence in healthcare professionals may be diminished when communication is delivered in an uncoordinated and inconsistent manner.[14] Thus parents' distress is increased if healthcare professionals avoid communication about the child's imminent death, and their satisfaction with the treatment and care offered is associated with physicians' communication competencies.[35 36] However, it is also important that the parents are prepared to receive and understand the information given regarding the child's imminent death.[36 37] The bereaved parents in our study expressed the wish that information be disclosed immediately when curatively intended treatment options were exhausted. However, there may be situations where, for example, sudden death and unpredictable disease progression make it extremely difficult for healthcare professionals to provide the parents with accurate information in a timely manner, particularly in advance. In addition, healthcare professionals' knowledge of the child's diagnosis and imminent death may vary depending on the diagnosis and/or prognosis, and the optimal timing regarding information provision may often be difficult to predict. Thus, specialised paediatric palliative care providers must realise that uncertainty may be an integral part of the care pathway for seriously ill children, and that an uncertain prognosis should not be a barrier for initiating specialised paediatric palliative care.[38]

### Strengths and limitations

We have studied a nationwide sample of bereaved parents who have lost a child due to a life-limiting

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diagnosis. It is certainly a difficult task to study a vulnerable population; however, we believe that we have obtained valuable information, which may provide a basis for addressing the needs of the parents in terms of communication with healthcare professionals. In the present study, data on the bereaved parents were acquired through national registers. The strength of the registers is the unique opportunity to pool data on children who have died with surviving parents.[39]

We must acknowledge that the low number of participating parents may have precluded our ability to generalise our findings since the most vulnerable parents may be the ones who declined to participate. Further, recall bias may of course also influence reporting during a devastating and chaotic period in the parents' lives.[40] Due to the expected limited number of responding parents we undertook a post-hoc non-response questionnaire survey. We constructed a self-administered questionnaire that comprised 14 short questions. The questions aimed to clarify some of the reasons for the relatively high level of non-response. Whether the parents found it too mentally demanding to participate in the study, or they could not devote the time or did not find the study relevant, were reasons for non-participation that were covered by the questions. The questionnaire was sent to non-participating parents and no reminder was sent on ethical grounds. In total, 51 parents completed the short questionnaire, and 63% 'completely agreed' that they did not have the energy to participate and 67% 'completely or partly agreed' that it was emotionally too difficult. However, 51% 'agreed' that the survey was very important.

As we have included all the children who died of any life-limiting diagnosis our results regarding the parents' need for communication and support may vary depending on the child's diagnosis and disease trajectory. However, we certainly believe that our results demonstrate the challenges that healthcare professionals are exposed to in communicating with parents about their children's life-limiting illness and imminent death, as well as the importance of providing high-quality education and support to healthcare professionals working in the field.

Finally, limitations concerning the impact of the Danish culture and healthcare system, and the education of medical professionals in our country, which may differ from that in other countries, must also be taken into consideration.

## CONCLUSIONS

This study showed that parents want empathetic, accurate and timely information about their child's life-limiting illness and imminent death. A substantial number of bereaved parents were of the opinion that healthcare professionals communicated too late about palliative care and end-of-life issues, and a substantial number reported that they felt deprived of the option of saying goodbye to their child in their preferred manner. Healthcare professionals are exposed to great challenges in communicating with parents about their children's life-limiting illness and imminent death, and even though healthcare professionals strive to communicate effectively with the children and their parents, several barriers on the sides of both parents and professionals may hinder even the best of intentions. However, the present study clearly demonstrated that the parents' need for information and support were not sufficiently met, and the study results may raise awareness of the importance of providing improved education and training for healthcare professionals working with children with life-limiting diagnoses and their parents. As the data were collected via a self-administered questionnaire, which made it impossible to question the parents in more detail regarding complicated and emotional matters, future research should incorporate qualitative research methodology in order to achieve a deeper and more detailed understanding of the bereaved parents' experiences of end-of-life communication. Research on how end-of-life communication influences parents' decision-making regarding the setting of the child's treatment may also be considered. Consequently, in order to improve practice, national guidelines on high-quality end-of-life communication should be considered as a part of the future agenda of specialised paediatric palliative care.

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# Appendix 1

## *Why and where do children die?*

*By Ulrika Kreicbergs*

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# Why and where do children die?

Child morbidity and mortality have changed for the better in most industrialised countries. This can mainly be attributed to screening programmes, improved paediatric care and preventive measures such as reducing accidents and providing vaccination programmes. But child deaths remain a reality that can never be totally avoided. Incurable, life-threatening conditions will always pose medical and ethical challenges. When and where to offer treatment and, or, palliative care is debatable. The Nordic countries offer high-quality paediatric diagnosis and treatment, as shown by registry data, but data on palliative care at hospital or at home are sparse, as is our knowledge on the preferred location of death.

These issues are addressed in an interesting study by Lykke et al. (1) in this issue of *Acta Paediatrica*. The authors analysed why and where children died in Denmark from 1994 to 2014. They identified 9462 children who died before the age of 18 from the Danish Register of Causes of Death and found a 52% decrease in child mortality during the study period. Most were under the age of 1, and this was mainly due to fewer deaths from chromosomal abnormalities, perinatal deaths and congenital malformations. The decrease was more pronounced after that age, mainly due to a decline in death by external causes, including accidents, and neoplasms.

The most striking study finding was the dramatic decrease in child mortality over the last two decades in a well-established industrialised, high-income, welfare country such as Denmark. Whether this downward trend has reached a plateau remains to be seen. Although the findings will not be exactly the same in other developed countries, due to differences in legislation, ethics and culture – particularly with regard to prenatal diagnoses, perinatal intervention and abortion – we can assume they reflect general trends in paediatrics. As the authors point out, Denmark was the first country in the world to offer pregnant women first-trimester risk assessments for Down syndrome and ultrasound screening for foetal abnormalities in weeks 18–20. They suggest that these procedures, together with improved birth care and folic acid supplements to prevent congenital neurological anomalies, are the main factors driving decreases in infant mortality. However, the measures and outcomes the authors describe are based on sophisticated resources that are not available in most countries and the debate continues about what perinatal efforts should be made to select and preserve life.

Another notable observation was the high rate of hospital deaths, which continuously increased over the study period, but detailed information was probably not available in the registry. It would be useful to make the distinction between deaths in intensive care units, ordinary clinical ward or palliative care facilities, as this would provide a more accurate reflection of policies and practice. The high rate of hospital deaths in Denmark could be attributed to a strong intent to cure, as well as the statistical inclusion of infants under one year, who were excluded from a similar study of 11 countries by Hakanson et al. (2). The ample availability of high-tech equipment managed by skilled staff in specialised neonatal and intensive care units may reinforce the intent to cure and offer the prospect of therapeutic advances, but it can also lead to overtreatment and suffering. The price for the decrease in child mortality is paid by seriously ill children, their parents and staff. Aggressive treatment may cause hospital deaths and long-lasting sequelae, and there are reasons to believe that the strong intent to cure delays decisions about palliative care and could even reduce the need for it. According to the authors, the highest capacity of paediatric palliative home care in the world is in New Zealand, Italy and Belgium. Whether this has a bearing on the intent to cure and mortality rate is unknown, but it is unlikely.

The authors readily admit that their study did not permit conclusions about palliative care and end-of-life decisions, as data on the timing and underlying reasons for the shift from curative to palliative care could not be extracted. A Swedish study of children with malignancies found that decisions about discontinuing curative treatment varied greatly, depending on the child's diagnosis. Children with poor prognosis received palliative treatment at an early stage of their disease unlike those with a better prognosis. Notably, a higher rate of children with brain tumours died at home than those with leukaemia (3).

Lykke et al. (1) noted that home deaths among children aged 8–14 remained stable over the study period, but decreased among children aged four to seven years, as reflected by the substantial increase in hospital deaths. Although this may suggest that older children had a greater say about where to die, there are no data on children's preferred locations. We know that parents generally prefer that children die at home (4), but this cannot be seen as the gold standard, given the lack of reliable knowledge about children's wishes.

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We also know that children and their parents want open, honest information about the seriousness of the disease, including the shift from curative to palliative treatment (5–7). Despite this, healthcare professionals find it extremely challenging to communicate bad news (8), and this can have a great impact on family decisions about the type of care and location of death. Parents who are informed and aware of their child's impending death are more likely to choose palliative care and death at home (9).

The study by Lykke et al. permits several important conclusions. One is that child mortality decreased, which is encouraging and presumably not limited to Denmark. Another is the contrasting increase in hospital deaths, which may reflect a shortage of palliative care facilities in Denmark. Moreover, the study demonstrates how useful national registry data could be for making decisions about the allocation of existing and future resources and the organisation of paediatric care and treatment. Decreased mortality would seem to suggest that fewer facilities for end-of-life care are required, but should not be construed to mean there is less need for palliative care in hospitals or at home. In fact, the high rate of deaths in hospitals, beyond that caused by aggressive treatment, presumably reflects a shortage of paediatric palliative resources, not just for end-of-life care, but also for protracted curative treatment and, or, severe sequelae. In summary, the study provides convincing proof of the efficiency, not to say success, of modern paediatric care. However, this does not remove the need for palliative resources, particularly at home. In general, it appears that the development of paediatric palliative care lags behind paediatric curative treatment in Denmark. Whether this is also true for other developed countries is unknown, and this uncertainty should prompt similar studies to the one conducted by Lykke et al.

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# Appendix 2

## *Forældre der har mistet et barn*

- *En spørgeskemaundersøgelse*

Due to the extensive nature of the questionnaire, it has been removed from the printed version of the thesis. The questionnaire can be requested by contact to Camilla Lykke, camilla.charlotte.lykke@regionh.dk.

# Appendix 3

## *Non-response spørgeskema*

***Markér venligst hvor enig eller uenig du er i følgende udsagn ved at sætte tydelige X'er inden for boksene ☐:***

| | *Jeg ønskede ikke at deltage i undersøgelsen fordi…* | Helt enig | Delvist enig | Hverken eller | Delvist uenig | Helt uenig |
|---|---|---|---|---|---|---|
| 1 | … jeg fik den hjælp jeg havde behov for under og efter mit barns sygdomsforløb | ☐ | ☐ | ☐ | ☐ | ☐ |
| 2 | … skemaet var for langt og for omfattende | ☐ | ☐ | ☐ | ☐ | ☐ |
| 3 | … jeg havde ikke overskud til at deltage | ☐ | ☐ | ☐ | ☐ | ☐ |
| 4 | … det ikke er muligt at beskrive tabet af mit barn gennem en spørgeskemaundersøgelse | ☐ | ☐ | ☐ | ☐ | ☐ |
| 5 | … det er for hårdt følelsesmæssigt at deltage | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6 | ... jeg synes at skemaet var for konfronterende | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7 | … jeg ikke var blevet informeret om undersøgelsen før jeg fik tilsendt spørgeskemaet med posten | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8 | … jeg ikke synes at undersøgelsen var relevant for mig | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9 | … jeg ikke fik nok information om undersøgelsen | ☐ | ☐ | ☐ | ☐ | ☐ |
| 10 | … jeg synes at spørgsmålene var svære at besvare | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11 | … jeg ikke synes at skemaet fokuserer på de spørgsmål der er vigtige for mig | ☐ | ☐ | ☐ | ☐ | ☐ |
| 12 | … jeg ikke mener, at denne undersøgelse er vigtig | ☐ | ☐ | ☐ | ☐ | ☐ |
| 13 | … jeg allerede har været med i mange undersøgelser igennem mit barns sygdomsforløb | ☐ | ☐ | ☐ | ☐ | ☐ |
| 14 | Andre årsager eller kommentarer (skriv gerne):<br>______________________________<br>______________________________<br>______________________________ | | | | | |

**Tusind tak for din deltagelse**