Hospital-Based Home Care for Children with Cancer

PhD thesis

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SUMMARY

The provision of hospital-based home care (HBHC) for children with cancer is increasing due to technological developments, the costs of health care, and the potential psychosocial benefits of reducing hospitalisations and medical appointments, although the evidence of HBHC and its effects is limited. HBHC for children with cancer has not previously been available in Denmark, and the overall aim of this PhD thesis was to develop and test the feasibility, and investigate the effects of a HBHC programme. The thesis comprises three original papers of which two are based on the HBHC programme and the third is a literature review. The first study (Paper I) describes family members' experiences of HBHC by qualitative interviews with 10 purposefully selected families with various demographic and clinical characteristics using qualitative content analysis. Fourteen parents were included and five children participated in all or part of the interview. The findings indicate that HBHC supports the families throughout the course of treatment by decreasing the strain on the family and their ill child, supporting them in maintaining normality and an everyday life and fulfilling the need for safety. The study highlights the importance of providing HBHC accommodated to the family members' need for safety by using experienced paediatric oncology nurses and having regular contact with the paediatric oncologist.

The second study (paper II) includes 51 children with cancer and examines the feasibility of the HBHC programme with a total of 942 home visits between August 2008 and December 2009. The children in the HBHC programme received part of their treatment and care at home e.g. drawing of blood samples and low-grade-toxicity intravenous chemotherapy. This was provided by hospital-based nurses as a substitute to an outpatient visit or a hospital admission. After each home care visit the families completed an evaluation form assessing their satisfaction with HBHC and their preference for care. The results of this evaluation showed a high satisfaction rate of 94% and a preference for HBHC. There were no adverse events related to the HBHC. A cost analysis, based on the expenses associated with HBHC compared with the standard cost of outpatient visits and inpatient admissions, indicated that HBHC was economically neutral compared to outpatient visits and that expenses were lower compared to inpatient admissions.

The third study (also reported in Paper II) is a non-randomised controlled study comparing HBHC with standard hospital care (SHC) in terms of child self - and parent-reported general and disease-specific health-related quality of life (HRQOL) of the children, the psychosocial impact on the family, and the satisfaction with the provided health care at the paediatric oncology department by using the questionnaire instruments PedsQL^{TM}. Twenty-eight children (44 parents) from the

HBHC programme were included and 47 children (66 parents) were included in the SHC group. The SHC group consisted of a historical and a concurrent group; all children in the two control groups received all their treatment at the same hospital. We found significantly higher scores in the children's general HRQOL (PedsQL Generic Core) (69.2 vs. 60.9 p = 0.04) and physical functioning (67.8 vs. 56.3 p = 0.03) as well as the children reported significantly higher general HRQOL (75.3 vs. 61.1 p = 0.02), psychosocial health, (74.6 vs. 62.4, p = 0.03) and emotional functioning (78.1 vs. 62.2 p = 0.04).

We found differences between the two groups when adjusted for age, gender, diagnosis and time since diagnosis, indicating that children receiving HBHC (median 9 home visits) perceive better physical health (Estimated mean difference (β) 14.2, Confidence Interval (CI) 3.3–25.2 p = 0.01), less nausea (β 9.9, CI -0.2–19.5 p = 0.04) and less worry (β 10.5 CI 0.4–20.6 p = 0.04). No significant differences were found between the types of care when the psychosocial impact on the family and satisfaction with the provided health care.

The literature review (Paper III) systematically evaluates the evidence on HBHC for children with cancer. Studies included were those with a design comparable to inpatient care. The initial search of PubMed, CINAHL and EMBASE yielded 496 papers of which 466 were not relevant to the review. The remaining 30 papers, and a further three papers identified from their reference lists, were reviewed. Twenty-eight papers did not meet the inclusion criteria, thus five studies were included in the review. Despite methodological limitations in the included studies, the literature review suggests that HBHC is feasible, safe and may lead to specific improvements in the families' everyday lives and in the children's HRQOL. However, the review also revealed that children may perceive more emotional stress when receiving home chemotherapy.

In conclusion, the HBHC programme is preferred by the parents and may replace an outpatient visit or a hospital admission at equal or lower costs without decreasing the safety of the patient. The children's HRQOL may be enhanced by HBHC in specific aspects and the programme appears to support the families' and the individuals' perceived needs to maintain family functions while at the same time alleviating the perceived distress. The study highlights the importance of providing HBHC in accordance with the family members' need for the sense of safety, which can be achieved by using experienced paediatric oncology nurses, and scheduling regular hospital visits and appointments with the paediatric oncologist at the department.

DANSK RESUMÉ

Hospitalsbaseret hjemmebehandling (HBHC) til børn med kræft er i stigning, men på trods af udbredelsen af HBHC er der dog kun begrænset evidens for effekten. HBHC for børn med kræft praktiseres endnu ikke i Danmark, og det overordnede formål med denne ph.d. afhandling var at udvikle og teste gennemførligheden, samt analysere effekten af et HBHC pleje- og behandlingsprogram. Afhandlingen omfatter tre originalartikler, hvoraf to er baserede på HBHC programmet - samt en litteraturgennemgang.

Det første studie (Artikel I) beskriver familiemedlemmers erfaringer med HBHC gennem en kvalitativ indholdsanalyse af interviews med 10 familier, udvalgt med henblik på at omfatte forskellige karakteristika. Fjorten forældre blev inkluderede og fem børn deltog i hele eller dele af interviewene. Resultaterne peger på at HBHC støtter familierne gennem behandlingsforløbet ved at nedsætte belastningsniveauet hos familien og det syge barn, støtte familien i kunne opretholde et normalt hverdagsliv, samtidig med at familien oplever at deres behov for sikkerhed tilgodeses. Studiet understreger nødvendigheden af dels at benytte erfarne børnekræftsygeplejersker til HBHC, og dels at opretholde en regelmæssig kontakt med en børnekræftlæge, for at familiemedlemmerne kan opleve deres behov for tryghed tilgodeset.

Det andet studie (Artikel II) analyserede gennemførligheden af HBHC og inkluderende 51 børn, der modtog i alt 942 hjemmebesøg i perioden august 2008 – december 2009. Børnene i HBHC programmet modtog en del af deres pleje og behandling i hjemmet, for eksempel blodprøvetagning og intravenøs kemoterapi. Behandlingen blev givet af hospitalsansatte sygeplejersker som et alternativ til et ambulant besøg eller en hospitalsindlæggelse. Familierne udfyldte et evalueringsskema efter hvert hjemmebesøg, hvor de tilkendegav deres tilfredshed med HBHC samt foretrukne plejeform. Denne evaluering viste en høj grad af tilfredshed hos forældrene og at HBHC blev foretrukket frem for et hospitalsbesøg. Der var ingen utilsigtede hændelser relateret til HBHC. Sammenlignes udgifterne forbundet med HBHC med udgifterne forbundet med ambulante besøg og hospitalsindlæggelser viste en økonomisk analyse at HBHC var udgiftsneutral målt på ambulante besøg og at udgifterne var lavere sammenlignet med en indlæggelse.

Det tredje studie (også afrapporteret i Artikel II) var et non-randomiseret kontrolleret studie, der sammenlignede HBHC med standardhospitalsbehandling (SHC) ud fra børnenes selvvurderede almene og sygdomsspecifikke livskvalitet (HRQOL), forældrenes vurdering af børnenes HRHQL, den psykosocial betydning for familien, samt tilfredshed med sundhedsvæsenet vurderet ved hjælp af (PedsQL^{TM}). Otteogtyve børn (44 forældre) fra HBHC gruppen deltog og 47 børn (66 forældre)

fra SHC gruppen. SHC gruppen bestod af en historisk og en aktuel gruppe; alle børn i de to kontrol grupper modtog udelukkende pleje og behandling på hospitalet. Vi fandt signifikant højere scores i børnenes generelle HRQOL (PedsQL Generic Core) (69.2 vs. 60.9 p = 0.04) og fysiske funktion (67.8 vs. 56.3 p = 0.03) ud fra forældrenes vurderinger og børnenes selvrapporterede generelle HRQOL (75.3 vs. 61.1 p = 0.02), psykosociale velbefindende (74.6 vs. 62.4, p = 0.03) og følelsesmæssige funktion (78.1 vs. 62.2 p = 0.04). Når vi justerede for alder, køn, diagnose og tid siden diagnosen blev givet fandt vi signifikante forskelle mellem de to grupper. Forskellene indikerede at børn, som modtog HBHC oplever bedre fysisk helbred (Estimeret mean difference (β 14.2, Confidence Interval (CI) 3.3–25.2 p = 0.01), mindre kvalme (β 9.9, CI -0.2–19.5 p = 0.04) og færre bekymringer (β 10.5 CI 0.4–20.6 p = 0.04). Ingen statistisk signifikante forskelle blev fundet mellem de to typer af pleje og behandling, når vi vurderede den psykosociale betydning for familien og tilfredsheden med sundhedsvæsenet.

Et systematisk litteraturstudie (Artikel III) undersøgte evidensen på forskellige områder for HBHC for børn med kræft. Vi inkluderede studier med et design, der sammenlignede HBHC med behandling under indlæggelse. Den indledende søgning frembragte 496 artikler, hvor i blandt 466 viste sig ikke at være relevante for litteraturgennemgangen. De resterende 30 artikler, blev vurderet sammen med yderligere 3 artikler, som blev identificeret fra de øvrige artiklers referencelister. Otteogtyve artikler opfyldte ikke inklusionskriterierne og således blev fem artikler inkluderet i den endelige gennemgang. På trods af metodologiske begrænsninger i de inkluderede studier antager litteraturstudiet at HBHC er gennemførligt og sikkert, og kan føre til specifikke forbedringer i familiers hverdag og børns HRQOL. Imidlertid afslørede litteraturgennemgangen også at børn kan opleve mere emotionel stress under kemo-hjemmebehandling.

Det konkluderes, at HBHC kan erstatte et ambulantbesøg eller en hospitalsindlæggelse uden at sikkerheden forringes og med tilsvarende eller reducerede udgifter, samtidig med tilfredsheden og præferencen for hjemmebesøg blandt familierne er høj. Børnenes HRQOL kan forøges gennem HBHC på enkelte områder. Det ser desuden ud til at HBHC kan styrke individuelle behov hos familierne, således at de i højere grad kan bevare deres familieliv som vanligt og nedsætte niveauet af stress. Studiet understreger betydningen af at tilbyde HBHC i overensstemmelse med familiemedlemmernes behov for sikkerhed, hvilket kan opnås gennem brug af erfarne børnekræft-sygeplejersker i hjemmebehandlingen, og ved at tilrettelægge regelmæssige konsultationer på afdelingen ved en børnekræftlæge.

ORIGINAL PAPERS

This thesis is based on the following papers, which are referred to by their Roman numerals:

I Hansson, H., Kjærgaard, H., Schmiegelow K., Hallström I. Hospital-based home care for children with cancer; a qualitative exploration of family members' experiences in Denmark. European Journal of Cancer Care. 2012 Jan;21(1):59-66

II Hansson, H., Kjærgaard, H., Hallström I, Johansen C., Schmiegelow K. Feasibility of hospital-based home care for children with cancer and psychosocial impact on the children and their families. In manuscript.

III Hansson, H., Johansen C., Hallström I., Kjærgaard, H., Schmiegelow K. Hospital-based home care for children with cancer.
Pediatric Blood & Cancer. 2011 Sep;57(3):369-77.

ABBREVIATIONS

HBHC	Hospital-based home care
PHC	Paediatric home care
SHC	Standard hospital care
HRQOL	Health-related quality of life
PedsQL™	Pediatric quality of life inventory
CVC	Central venous catheter
ALL	Acute Lymphoblastic Leukaemia
SD	Standard deviation

INTRODUCTION

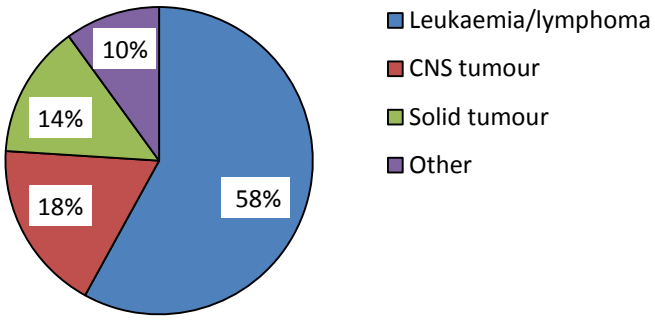
There has been a dramatic improvement in the survival rate of children with cancer since the 1970s (Craft 2000). The overall five-year survival rate for all cancers in Europe is 81% in children and 87% in adolescents (Gatta et al. 2009), although cancer remains the most frequent medical cause of death among children. The improvements in survival reflect first and foremost the intensification and prolongation of therapy (Craft 2000), though 2-4% of patients still die from treatment related complications (Lund B., Åsberg A., Heyman M. et al. 2010). This intensification has increased the frequency and duration of hospital stays and in particular the number of outpatient visits. For children with leukaemia, which is the most common childhood cancer, the treatment can last for up to two and a half year and involves hospital admissions lasting a couple of days up to several weeks, and outpatient visits up to every three days for the first six months (Nordic Society of Paediatric Haematology and Oncology (NOPHO) 2011).

In Denmark, the child is hospitalised together with one parent, relative or guardian and the diagnosis, aggressive treatment, and high frequency or long duration of hospital stays have substantial emotional and social effects on the whole family (Björk M., Wibe T., and Hallström I. 2008, Woodgate, Degner 2003). Studies show that parents caring for chronically or long-term ill children need support to be able to maintain family functions and stability (Wells, Kirk 2004). The increasing impact on the child and the family due to the child's cancer and treatment calls for alternative ways to provide care. Hospital-based home care (HBHC) is an alternative provision of care in which the patient's treatment is provided at home instead of as a hospital admission or an outpatient visit. HBHC is increasing in popularity due to the reduction of the frequency and duration of hospitalisations and outpatient visits, and the potential psychosocial benefits for the children and their families (Frierdich, Goes & Dadd 2003, Cooper et al. 2006, Parker et al. 2006). The development of better standards for chemotherapy and supportive care, a better understanding of risk factors and complications, and standardised common treatment protocols used in the Nordic countries have paved the way for new programmes as HBHC in Denmark. The HBHC programme in the present study comprises multiple services including intravenous low-toxic chemotherapy and blood samples drawn from the central venous catheter (CVC) and is provided by experienced paediatric oncology nurses, who perform 2-3 home visits per day to patients living within 50 kilometres (km) of Copenhagen University Hospital Rigshospitalet.

There are approximately 80 newly diagnosed children with cancer at the paediatric oncology department at Copenhagen University Hospital Rigshospitalet with about 2.500 inpatient

admissions and 8.000 outpatient visits per year (E-sundhed, Rigshospitalets datavarehus). A pilot study based on the hospital's patient administration system (GSOpen) and medical records, was conducted during a 2-month period in 2006 to estimate the amount of treatment services that could be provided at home according to pre-defined criteria (unpublished data). It was estimated that approximately 25% of the department's services could be provided at home; 28% of the out-patient clinic's services, 49% of the day-care unit's services and 15% of the ward's services. However, changes in criteria resulted in fewer services and patients eligible to be allocated to the HBHC programme in the present study, in which a total of 942 home visits were provided and of these 86% were outpatient visits (ambulatory or day care hospital) and 14% inpatient admissions. The distribution of patients cancer diagnoses eligible to HBHC in the pilot study was confirmed in the present study (Figure 1).

Figure 1. Distribution of the patients' diagnoses (n=57) allocated to the programme HBHC in the present study



Treatment protocols containing frequent outpatient treatments, such as leukaemia and non-Hodgkin lymphoma protocols, were more likely to be allocated to home care, while protocols requiring more inpatient treatments and potentially complex medical conditions e.g. patients with osteosarcoma needing frequent physiotherapy, as some of the solid tumour and brain tumour protocols, were less suitable for home care.

This thesis is evaluating a HBHC programme aimed at supporting children with cancer and their families, and creating flexibility in the resource allocation at the paediatric oncology department by replacing some hospital visits with home care. The thesis contributes to the understanding of the clinical requirements for and methods by which these can be delivered for a

HBHC programme that is feasible, stable and acceptable for the children, their families, and the health care providers.

BACKGROUND

Childhood cancer

The annual incidence of paediatric cancer in Denmark is approximately 150 children < 15 years of age of which 40% are diagnosed with leukaemia or lymphoma, 25% with a brain tumour, and 35% with a solid tumour (Brown et al. 1996). About 80 of these children are diagnosed and treated at the Copenhagen University Hospital Rigshospitalet. Unlike adult cancers, childhood cancer mainly originates from embryonic tissues (Scheurer, Bondy & Gurney 2011) and the treatment varies in length and intensity from a few months to two and half years depending on the diagnosis and the treatment. Leukaemia is the most common childhood cancer, of which acute lymphoblastic leukaemia (ALL) comprises about 80% with a peak in incidence in children between two and six years of age (Hjalgrim et al. 2003). The treatment consists mainly of intensive and long-lasting chemotherapy, and requires continuous hospital visits up to every three days during the first six months of the course of treatment. The lymphomas comprises Hodgkin's disease, which mainly affects adolescents, and is treated with chemotherapy combined with radiotherapy, and non-Hodgkin's lymphoma, which has an incidence peak in children between seven and 11 years of age and is treated with chemotherapy (Scheurer, Bondy & Gurney 2011). The second most common childhood cancer is brain tumour, which is most common in children up to 10 years of age (Schmidt et al. 2011). The treatment consists of surgery in combination with radiation and/or chemotherapy and the prognosis depends on the type and location of the tumour. The third group comprises solid tumours. The most common kidney tumour, Wilm's tumour, has an incidence peak in children younger than two to three years of age. Neuroblastoma (Schroeder et al. 2009) (sympathetic nervous system) is most common in children younger than two years of age, osteosarcoma and Ewing's sarcoma (bone tumour) have an incidence peak in children between 10 and 12 years of age, and rhabdomyosarcoma (muscle tumour) is most common in children between two and five years of age and during adolescence (Scheurer, Bondy & Gurney 2011). The treatment of solid tumours is generally multimodal with a combination of surgery and chemotherapy, and/or radiation (Rechnitzer, Nielsen 1999). The different types of treatment lengths and intensity play an important role in the allocation of patients to HBHC as the treatments provided in HBHC are low-toxic and non-complex. Thereby, the diagnostic groups of patients most likely to benefit from HBHC are patients with frequent out-patient treatments, like in the leukaemia and non-Hodgkin´s protocols.

Short-term treatment or protocols consisting of few hospital visits as for patients with Wilm's tumour, Hodgkin's disease, or some brain tumour protocols, are less suitable as the treatments require hospital presence. Intensive and multimodal treatment protocols like most solid tumour protocols are also less appropriate because it often implies frequent inpatient care and potentially complex medical conditions for the patient.

Treatment side effects

The intensive treatments with potentially toxic mediations have considerable physical, emotional and social effects on the child with cancer (Hedström et al. 2003, Enskär, von Essen 2008). The children suffer from physical side effects such as disease- and procedure-related pain, nausea, mouth sours, malnutrition, hair loss and fatigue that may persist for hours, days or weeks (Collins et al. 2000). Another invasive side effect is the low blood counts, which may increase the risk of infections, anaemia, and bleeding and require social and physical isolation. In addition, a number of blood transfusions, days with fever and antibiotics increase the frequency of outpatient visits and hospital admissions. Both the children and the whole family may experience these physical and emotional side effects with distress and one of the most distressing physical aspects for the children and their parents is the pain related to medical procedures and treatments (Hedström et al. 2003, Woodgate, Degner 2003, Enskär, von Essen 2008, Woodgate, Degner 2004, Enskär, von Essen 2007). Feelings of isolation and anxiety before medical procedures are aspects that are of concern in children across age groups (Enskär, von Essen 2008, Hedström et al. 2003). Cancer-related disruptions in the daily life such as hospitalisations and medical appointments may cause psychological distress, especially for adolescents (Kazak et al. 2010). Altogether, treatment side effects can have a major impact on the child's and the family's health and quality of life and HBHC may play a role in lightening this impact by supporting the child and the family to maintain a family- and daily life (Close et al. 1995, Stevens et al. 2006b).

The family in the context of childhood cancer

The diagnosis of a life-threatening illness, the intensive treatment, the high frequency and long duration of hospital stays affect the whole family (Björk M., Wibe T., and Hallström I. 2008, Woodgate, Degner 2003, Patterson, Holm & Gurney 2004). Families have described the childhood cancer trajectory as an everyday struggle in which they strive to cope with the challenges and distress they face (Björk M., Wibe T., and Hallström I. 2008, Woodgate, Degner 2004). Normal everyday family life is disrupted by hospital visits and family members have described feelings of

isolation and alienation because they cannot participate in ordinary social activities due to the child's susceptibility to infections (Björk M., Wibe T., and Hallström I. 2008). Siblings' needs may be overlooked (Enskär et al. 2011) and siblings have described feeling of being separated from the rest of the family and worrying about their ill sibling (von Essen, Enskär 2003, Nolbris, Enskär & Hellström 2007). Thus, it is imperative that the health care provided also supports the families' and individuals' perceived needs to cope with the challenges, while maintaining family functions and relieving perceived distress (McGrath 2001).

Health-related quality of life

With the enhanced survival rate for children with cancer there is an increasing interest in assessing children's health-related quality of life (HRQOL) as an important measure of outcome in clinical trials (Klassen et al. 2011, Jenney, Campbell 1997). When combined with clinical outcomes, assessment HRQOL may contribute to a more comprehensive evaluation of the risks and benefits of an intervention (Eiser, Jenney 2007). HRQOL might be greatly impaired in children with cancer, particularly immediately after diagnosis and during the course of treatment. Most research on HRQOL in children with cancer has focused on survival and long-term effects (Pickard, Topfer & Feeny 2004), whereas little is known about children's HRQOL during different phases of therapy. (Sung et al. 2011). Children's own views on HRQOL are generally underrepresented and studies with both self-report and parent proxy-reports on the basis of serial ratings are needed (Eiser, Jenney 2007). Parents' perceptions of the child's HRQOL are considered important because they often support paediatric health care decisions and programme development (Wallander, Schmitt & Koot 2001).

Hospital-based Home Care

The provision of paediatric home care for children with acute and chronic illnesses is increasing in high-income countries due to technological developments, improvements in supportive care, the costs of health care and the potential psychosocial benefit for the children and their families (Cooper et al. 2006, Parker et al. 2006). Paediatric home care refers to the provision of hospital services to patients in their own home that would otherwise necessitate a hospital admission or an outpatient visit. In general paediatric home care is either based at the hospital (HBHC), which provides an outreach service or in the community (Parker et al. 2002). The majority of paediatric home care for children with cancer is provided by community- or home-care agency based nurses

and may include the provision of intravenous chemotherapy or antibiotics (Frierdich, Goes & Dadd 2003, NACHRI 2000).

In the present thesis, the home care programme was hospital-based and provided by a designated paediatric nurses (HBHC nurse) with at least two years experience in paediatric oncology to secure the safety required for children with cancer, and to maintain a strong connection with the department and its staff. Moreover, the well-functioning road system and the population density made it possible for the HBHC nurse to reach patients living as far as 50 km from the hospital within 30-40 minutes. Children included in the HBHC programme received a minor part of their treatment and care at home. The HBHC procedures were: a) low-intensive intravenous antibiotics b) intravenous low-toxic chemotherapy c) blood samples drawn from the central venous catheter or peripheral vein d) subcutaneous injections e) nutrition treatment f) pain management (e.g. controlling an intravenous morphine pump g) supportive care e.g. changing dressings. The diagnostic groups of patients most likely to benefit from HBHC were mainly patients with leukaemia and lymphoma due their frequent out-patient treatments.

Despite the increasing provision of PHC in general, three systematic reviews of pediatric home care have found that controlled studies are rare and that the evidence base is limited (Cooper et al. 2006, Parker et al. 2006, Parker et al. 2002). The reviews did not include pediatric oncology treatment and HBHC for children with cancer involves highly potent medical treatments, which may increase the risk of adverse events and the strain on the families. Studies indicate that intravenous chemotherapy or antibiotics can be safely managed at home (Close et al. 1995, Holdsworth et al. 1997, Stevens et al. 2006). Moreover, HBHC can reduce the frequency and duration of hospitalisations and may reduce costs for the health-care system (Close et al. 1995, Holdsworth et al. 1997, Wiernikowski et al. 1991). Two controlled intervention studies have examined the impact of HBHC on children with cancer (Close et al. 1995, Stevens et al. 2006a). In the only randomized cross-over trial by Stevens et al., community-based nurses provided home chemotherapy to 23 children with ALL (Stevens et al. 2006a). They showed both improvements and decrements in parent-reported HRQOL of the children and no effect on parents' burden of care, adverse events or costs. Close et al. tested a HBHC programme with community-based nurses providing intravenous chemotherapy to 14 children with different cancer diagnoses (Close et al. 1995). The children received one treatment at home which was compared with one corresponding treatment at the hospital, and they reported that the children and their families' QOL improved, and the costs were reduced.

There are no national or regional policies or guidelines regarding HBHC for children in Denmark. HBHC for children with cancer has never been practiced in Denmark and there are no home-care agencies to provide the HBHC. Children with cancer in the Nordic countries are treated according to the same treatment protocols, but there are differences in the provision of care. In Sweden and in Norway, the children may receive chemotherapy at the local hospital in close co-operation with the paediatric oncology department. In addition, in Sweden integrated collaboration with the adult and paediatric hospital-based home care teams is possible in the areas where these exist.

As described above, paediatric health care providers have little evidence-based knowledge of the effects of HBHC when considering programme development for children with cancer. There are a number of factors that are important when considering HBHC: 1) the quality of care and safety must be maintained, 2) there must be no increase in complication- and mortality rate or strain on the child and family members, 3) there must not be a decrease in the family member's satisfaction and preference for care, and 4) the cost-effectiveness and the organisational structure within which these interventions are provided at home must be ensured (Frierdich, Goes & Dadd 2003, NACHRI 2000, Kandsberger 2007). Although, the home environment may have a positive impact on the children's recovery and well being, it must be taken into account that the shift to home care may raise concerns about parental and professional roles and responsibilities (Kirk, Glendinning 2004). Furthermore, home care may mean a loss of privacy for families by the presence of medical equipment and health care professionals in the home environment (Kirk, Glendinning 2004). When developing and evaluating such complex programmes it is important to investigate the feasibility of delivering the care, the acceptability to providers and patients, and the implementation of the programme into practice (Campbell et al. 2000). Therefore, the HBHC programme presented in this thesis aims to replace hospital admissions or outpatient visits while maintaining safety and the child's HRQOL and without increasing the costs or the psychosocial strain on the family.

AIM

The overall aim of this thesis was to evaluate the feasibility and the effects of a HBHC programme. The present thesis comprises three studies, of which two are based on the HBHC programme, and a literature review.

The primary outcomes were the family members' experiences (interview study) and the feasibility (feasibility study) of the HBHC programme. The secondary outcome was the psychosocial impact on the child and their family, and their satisfaction with the provided health care at the paediatric oncology department (controlled study).

The specific aims were:

- To describe family members' experiences with HBHC (Paper I).
- To investigate the satisfaction with HBHC, preference for care, safety and costs (presented in the thesis and Paper II).
- To evaluate the effects of HBHC on children's HRQOL, the psychosocial impact on the families (Paper II) and their satisfaction with the provided health care at the paediatric oncology department (presented in the thesis).
- To systematically review the evidence-based value of HBHC (Paper III).

METHODS

Design

The thesis consists of three study designs (Table 1 and figure 2); an interview study with a purposefully selected sample of the programme population describing family members' experiences with HBHC (interview study). Further, a descriptive study (feasibility study) assessing the feasibility of the HBHC programme, and an experimental controlled study (controlled study) in which a subsample of the programme population was compared to a standard hospital care group (SHC group). This study included a historical control group and a concurrent control group to assess the psychosocial impact on the child and their family, and the satisfaction with health care at the paediatric oncology department using a questionnaire booklet. The feasibility study and the controlled study used consecutive sampling based on geography instead of random selection due to logistical and ethical considerations.

The interviews in study 1 were performed while children and their parents were participating in or had finished the HBHC programme. The feasibility study was conducted between August 2008 and December 2009, the controlled study was conducted between December 2007 and October 2010 (last collected questionnaire) and the assessment was performed after the HBHC programme and the interviews. The HBHC programme was only available to children who lived within 50 km from the university hospital. Hospital-based nurses with at least two-year experience in paediatric oncology provided the HBHC e.g. low-toxic intravenous chemotherapy.

Figure 2. Time frame of the studies

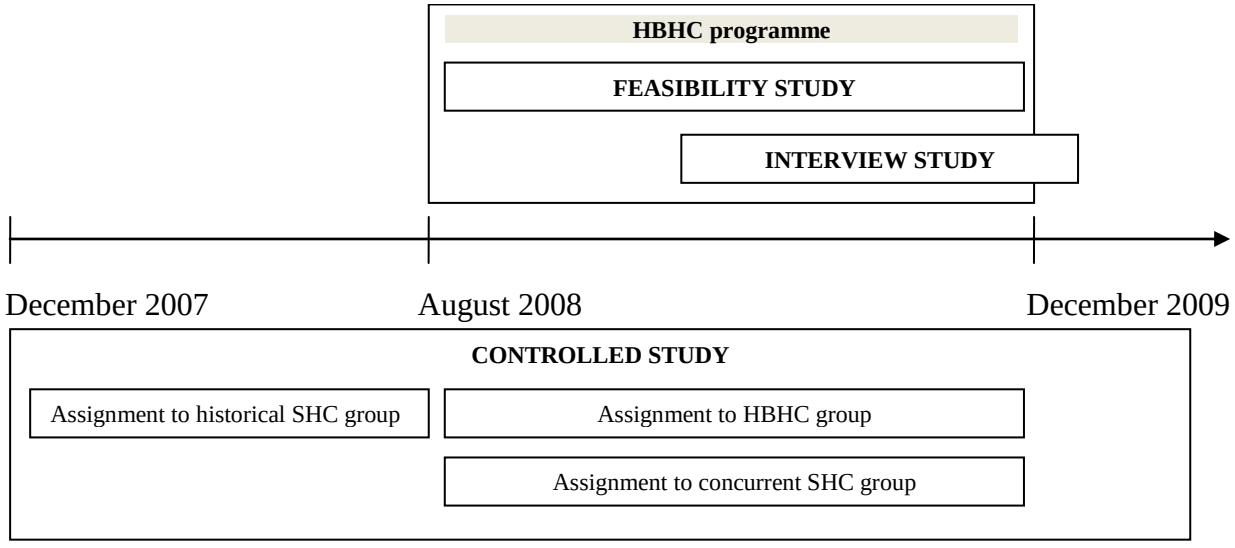


Table 1. Overview of the thesis

	Design	Participants	Time period	Methodology/ Instruments	Data analysis	Paper
Interview study	Inductive	10 families	4 months in intervention period during the programme	Interviews	Qualitative content analysis	I
Feasibility study	Prospective intervention	51 children with cancer, 6 children with other diagnoses	17 months	Evaluation form on satisfaction and preference for care, recording protocols, hospital charts, cost analysis,	Descriptive statistics	II
Controlled study	Controlled study	*HBHC group:* 28 children, 44 parents from the programme population. *Historical control group:* 35 children, 51 parents. *Concurrent control group:* 12 children, 15 parents	24 months, baseline and follow-up 3 months later	Questionnaire including demographic and clinical variables, and instruments measuring psychosocial factors	T-test, Chi square, Linear regression	II
Review	Review			Systematic	Narrative	III

Setting

Due to the complexity of paediatric oncology, the diagnostic work-up and treatment is centralised in four highly specialised departments in Denmark. All studies originated from a paediatric haematology and oncology department at a university hospital in the Eastern part of Denmark. Approximately 70-80 newly diagnosed children are admitted to the department each year, which comprises approximately 50% of the Danish children with cancer. In addition, an increasing number of adolescents (15-18 years) of age are admitted to the paediatric oncology department instead of to the adult oncology department. The university hospital's catchment area includes a total population of approximately 2.3 million people and all children with cancer in the admission area are treated at the university hospital.

The paediatric haematology and oncology department consists of a ward with 22 beds, an out-patient unit and day-care unit. In Denmark, the health care is financed through taxation and the child is hospitalised together with one parent, or guardian. Both parents are most likely to share responsibility for the day-to-day decision-making. There are no health care agencies and community-based nurses do not administer chemotherapy on a regular basis in patients' homes.

Sample

Interview study

Twelve families participating in the HBHC programme were invited for interviews about their experiences of HBHC. A purposeful sample (Patton 1990) was chosen to capture a wide range of experiences and differences, e.g. the children's diagnoses, family constellation, parents' occupation, the number of home care visits, and the duration of participation in the HBHC programme.

Feasibility study

It was estimated that a consecutive sample of approximately 50 children could be included in the HBHC programme during the inclusion period August 2008 to December 2009 based on the number of children in treatment at the paediatric oncology department per year. Eligible for inclusion were: children between 0-18 years of age, who had been diagnosed with any type of cancer at least one month prior to inclusion (median 2 months), were being treated with intravenous therapy with a curative intent, had not received stem-cell transplantation, the parent and the child were fluent in spoken and written Danish, and living within 50 km of the university hospital.

Children with thalassaemia or histiocytosis are also treated at the paediatric oncology ward and were eligible in order to assess the feasibility and provision of a cost-effective HBHC. The inclusion criteria were: children between 0-18 years of age, who had not received stem-cell transplantation, the parent and the child were fluent in spoken and written Danish, and living within 50 km of the university hospital.

The HBHC nurse identified and assigned children to the HBHC programme in collaboration with the author of this thesis and the paediatric oncologist responsible for the patient's treatment, who always could veto the assignment. The assignment was made on the basis of the inclusion criteria and the HBHC nurse also approached the families to ask about participation in the HBHC programme.

Controlled study

A total of 134 children and their parents were eligible for inclusion in the controlled study during the period from December 2007 to December 2009. Inclusion criteria were; parents and their children aged 0-18 years at diagnosis, the children had been diagnosed with any type of cancer at least two months prior to inclusion, were in treatment with intravenous therapy with a curative intent, had not received stem cell transplantation, and the parents and children were fluent in spoken and written Danish, and they had completed the questionnaire at inclusion (time point 1) and at

follow-up after three months (time point 2). In one case, the grandmother was the primary caregiver.

It was optional for the families in the HBHC programme to participate in the controlled study. A consecutive sample of patients were assigned to one of three groups according to their geographical distance from the hospital and timing of the inclusion period: (1) to the HBHC group if participating in the HBHC programme between August 2008 and December 2009; (2) to the historical SHC group between December 2007 and July 2008 (before patients were recruited to the HBHC programme) regardless of the residence distance to the hospital, and (3) to the concurrent SHC group if living more than 50 kilometres from the university hospital during the same time period as the assignment to the HBHC group.

The assignment was carried out by the author of this thesis. The children and their parents were identified through the Children's Cancer Registry Database and was confirmed by a nurse and a doctor at the paediatric oncology department. The assignment to the three different groups was made on the basis of the inclusion criteria. The historical SHC group was established to increase the sample size and sample representativeness for comparison with the HBHC group in terms of potential demographic and socioeconomic differences between the groups. The national protocols for paediatric cancer treatments did not change during the inclusion of the historical SHC group except for the Nordic ALL2008 (Acute Lymphoblastic Leukaemia) protocol that was implemented in July 2008.

Standard hospital care

The care of children in the SHC group followed routine care procedures at the paediatric oncology department. The children received all their treatments at the paediatric oncology ward, day-care unit or outpatient clinic and no home visits were provided. Standard hospital care in Denmark entails that all children with cancer are treated according to Nordic treatment protocols or European and international treatment protocols. Clinical data on all patients are registered in the Danish Childhood Cancer Registry Database (a clinical quality database), most patients participate in randomised studies and all medical care is provided at the hospital. The children and their parents in the SHC group participated in the assessment of the psychosocial impact and satisfaction with the provided health care at the paediatric oncology department in the controlled study.

Intervention: HBHC programme

Development of the HBHC programme

The HBHC programme was designed to replace outpatient visits (86% of all HBHC visits) or in-patient admissions (14%) and was administratively based in the day-care unit at the paediatric oncology department. The HBHC programme was developed by the research team, of which the author of this thesis is a member, in collaboration with a clinical supervisory group composed of two senior paediatric oncologists and two nurses who later provided the HBHC. A pilot study with 10 children with different cancer diagnoses was carried out by a nurse (later employed in the HBHC programme) from the paediatric oncology department and the author of this thesis during one week in February 2008. The nurse provided the treatments while the author of this thesis participated as an observer. The aim of the pilot study was to test the feasibility and families' perceptions of HBHC. The content and management of the HBHC programme was determined by two nurses, who were employed specifically for this task (thereafter they also provided the HBHC) and the author of the thesis during three months before the start of the HBHC programme. The content and organisation of the programme were based on the findings from the pilot study, evidence from previous studies on HBHC and a study visit to the HBHC programme at Astrid Lindgren's hospital in Stockholm, Sweden (www.sabh.nu).

Protocols

Protocols with instructions for managing e.g. medical treatments and anaphylactic shock were developed to ensure safety and compliance with the required quality regulations and approved by the hospital department of quality control (Appendix 1). There were weekly meetings between the HBHC nurses and the author of the thesis every week during the entire HBHC programme to ensure that the project guidelines were being followed and to discuss the delivery of the care. There were also regular meetings with the HBHC nurses that included the author of the thesis and the clinical supervisory group.

The children in the HBHC programme received part of their standard hospital treatment at home and the number and type of treatments varied from child to child depending on the diagnoses and treatment protocols. It was not decided beforehand how many visits they would receive during the participating period as this depended on the child's medical condition. The HBHC consisted of e.g. blood tests, intravenous chemotherapy lasting for no more than 10 minutes and antibiotics lasting for 10 – 60 minutes. The antibiotics could be provided up to three times per day/evening. All but two children with cancer had a central venous catheter (CVC) when they were included in the

HBHC. The HBHC nurse also took blood samples from a peripheral vein, e.g. patients with thalassemia who did not have a CVC, but this was an exception. For each child, the HBHC ended when the child no longer fulfilled the inclusion criteria, i.e. once the intravenous cancer treatment had been completed. Approximately 20-25 children participated continually in the HBHC programme (Table 4).

Logistics

Four HBHC nurses with long-term experience in the paediatric oncology department (two full-time and two part-time) were employed in the HBHC programme. The working hours included daytimes and evenings. For the remaining nine months only two HBHC nurses (part- and full time) were employed in the HBHC programme and it was only possible to receive home care visits in the daytime as the evening visits were too few to provide a cost-effective care. One or two HBHC nurses provided each home visit dependent on the need for an additional nurse to supervise or reflect on the home visit. The nurses used the same car, which was hired specifically for the HBHC programme at low cost thanks to the sponsorship of the rental company. The HBHC nurse uniform was different from the hospital's uniforms and the car was neutral with no identifying sign. The nurses had working shifts at the ward every fourth weekend to secure the quality of the treatment and promote the families' experience of safety. Thus, the nurses also provided treatment to the children in the SHC group although not in the patients' homes. The author of the thesis did not provide any HBHC visits and had no working shifts at the ward.

The HBHC nurse examined the patients' medical records and their treatments protocols of the included patients every day and referred them to a home visit whenever possible and with approval from a paediatric oncologist. The families could also contact the HBHC nurse or a paediatric oncologist to be referred to a HBHC visit. The parents could cancel and change the HBHC visit to a hospital visit at any time, and there was always a 24-hour open access to the ward for the HBHC nurse and the families. All preparations were made at the paediatric oncology ward and the HBHC nurse brought all equipment and medications (including an emergency kit) to the patients' homes. The waste was brought back to the hospital after the HBHC visit in order to make the care as less intrusive as possible in the family's home. The parent(s) had no additional tasks to perform under the HBHC compared to standard hospital treatment.

Instruments

Clinical and Demographic data

Clinical data e.g. diagnoses, treatment protocols and demographic background information on the children were obtained the Danish Childhood Cancer Registry Database and medical records for all three studies. A demographic form in the questionnaire booklet assessed the parent's/caregiver's marital status, number of children in the family, parents' age, employment, graduate degree, and household income.

Interview study

A descriptive inductive method with open interviews was used to describe the family members' experiences with HBHC. Each interview began with the same question: Can you describe your experiences with the HBHC programme? During the interview the participants were asked open questions from an interview guide containing four topics; 1) how did you experience the care and treatment of your child at home, 2) how did you experience home care in relation to e.g. everyday life, the ill child, and siblings, 3) the value of home care for the child according to the your perception, and 4) did you experience any benefits or difficulties. Parents were asked additional questions for clarification e.g. "Can you describe in more detail what you mean?" There were no questions specifically directed to the children in the interview guide, but additional questions such as 'What do you think about the home care?' were posed to the children by the parents or by the interviewer. The interviews were audio-recorded with the parents' permission and then transcribed verbatim including notations of non-verbal expressions such as pauses and laughter. Three interviews were transcribed by the interviewer and the remaining interviews were transcribed by a secretary.

Feasibility study

HBHC programme

A specific recording protocol for HBHC activities was developed by the author of the thesis in collaboration with the HBHC nurses. The recording protocol was based on the paediatric oncology department's mandatory standardised registration protocol of the activities for individual patients (Appendix 2). The recording protocol was approved by the university hospital's economic management and tested for content and understanding by the author of the thesis, the clinical supervisory team, the HBHC nurses and the hospital's economic management. The recording

protocol consisted of categories for type of treatments on one page. The next two pages consisted of records of nursing tasks, the duration of the visit and the HBHC nurse's perception of the child's and the parent's satisfaction and safety with the home visit, which was scored on a 5-point Likert-scale. There were also records of whether the child had the possibility to attend school/day care due to the HBHC. There was a transportation log in the car where the HBHC nurse recorded number of kilometres and gasoline consumption between home visits.

Perception of security, satisfaction with HBHC and preference for care

A one-page evaluation form to measure the parents' and children's perceptions of security, satisfaction with HBHC and preference for care was developed for the feasibility study. The evaluation form was constructed and approved by the authors of paper II and was tested for clarity and relevance by the HBHC nurses. The evaluation form was thereafter tested for face validity on five parents and was deemed simple to understand and complete. The parents rated how content they were, how secure they felt, and how satisfied they were with the HBHC on a 5-point Likert-scale ranging from *not at all* to *very much*. In addition they rated the corresponding items from their child's point of view. Finally, the parents' overall preference for SHC vs. HBHC was scored with two alternative responses (yes or no) and they were asked whether they would choose a home care visit again instead of a corresponding hospital visit if they had the opportunity.

Safety

A recording form for unintended events that is mandatory and used routinely at the paediatric oncology department was used in the HBHC programme to document of medical errors, unintended adverse events or acute allergic reactions, which were defined according the standardized hospital guidelines (Fisker, Sundhedsstyrelsen 2010), the common terminology criteria for adverse events and the Common Toxicity Criteria (National Cancer Institute, CTC version 4). The HBHC nurse also recorded vital signs and transfusion history in the children's medical records. Medication errors were defined as a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient (Aronson 2009), acute allergic reactions including drug-induced fever, injection site reaction/extravasation changes, or fatal, suspected and unexpected serious complications with life-threatening consequences caused by the HBHC. Unexpected hospital admissions due to HBHC were recorded in the patient's nursing records by the HBHC nurse. The research team and clinical supervisory group defined stopping rules for the HBHC programme s increased frequency of medical errors and unintended adverse events, or one incident of acute allergic reaction leading to hospital admission or death.

Controlled study

Questionnaire

A questionnaire booklet was developed to measure the psychosocial impact on the child and the family with established validated instruments comprising in total 50 main questions with sub-questions (Appendix 7). The questionnaire was tested for face-validity with 10 parents in a pilot study and was found to be understandable and relevant. Children's HRQOL, the psychosocial impact on the family, and the satisfaction with the health care at the paediatric oncology department were assessed by the Pediatric Quality of Life Inventory (PedsQL$^{TM)}$ instruments. The other instruments in the questionnaire booklet have not been used in the thesis. The questionnaire was not validated among a population of healthy Danish children.

PedsQL^{TM} has a high level of internal and external reliability among healthy children and children with cancer (Varni et al. 2002). PedsQL^{TM} consists of generic and disease-specific scales where the generic core scales allow comparisons across healthy children and patient groups, and the disease-specific module measures health domains relevant to chronic health conditions.

The PedsQL^{TM} 4.0 Generic Core Scales consist of four dimensions: physical health, emotional functioning, social functioning, and school functioning. Three summary scores are calculated: a physical health summary score, a psychosocial health summary score, and a total score of all dimensions. The PedsQL^{TM} 3.0 Cancer Module consists of 8 dimensions: pain and hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance and communication. Scores are calculated for each of the subscales and there is no total score. The PedsQL^{TM} 2.0 Family Impact Module measures the parent's QOL and the family function in 8 dimensions: physical functioning, emotional functioning, social functioning, cognitive functioning, communication, worry, daily activities and family relationships. A total score of all dimensions is computed as well as summary scores for the parent's HRQOL and family functioning. The PedsQL Family Impact Module has been preliminary validated as a reliable measure on families to medically fragile children (Varni et al. 2004) and on Brazilian families to children with cancer (Scarpelli et al. 2008).The PedsQL^{TM} Healthcare Satisfaction Generic Module measures the parents'/guardians' satisfaction with health care in general in six dimensions: information, inclusion of family, communication, technical skills, emotional needs, and overall satisfaction. A total score of all dimensions is computed.

PedsQL^{TM} includes age-specific versions of parent reports (ages 2-18) and child self-reports (ages 5-18 years), which are important when considering developmental changes in HRQOL across

age groups (Eiser, Jenney 2007, Savage, Riordan & Hughes 2009). It is self-administered for parents and for children aged 8-15 years and interviewer-administered for children aged 5-7 years. There is no self-report form for toddlers, aged 2-4 years, due to the developmental limitations in children younger than 5 years of age. In the controlled study, parents completed a parent-proxy report for children 0-18 years of age and children between 5-18 years of age completed a self-report. Parents and children aged 8-18 rated how much of a problem each item had been over the previous week on a Likert-scale with scores ranging from 0 (never a problem) to 4 (always a problem) and children aged 5-7 years rated the same on a 3-point scale. Responses are reverse-scored and linearly transformed to a scale ranging from 0 to 100 with higher scores indicating better HRQOL. To derive dimension- and summary scores for a given dimension, more than half of the items have to be completed. If more than 50% of the items in the scale are missing, the Scale Scores should not be computed (Varni et al. 2002).

The original versions of these PedsQL™ instruments were translated according to PedsQL™ guidelines for translations in following steps: forward translation into Danish by two professional translators individually, backward translation into English by two professional translators individually, patient-testing and finally a report to the PedsQL™ European Head Office. The translations were compared and assessed by the author of the thesis in order to examine the agreement between the Danish and English versions. The backward translation process had to be repeated three times until the Danish version was correctly written and easy to understand. The translated version was first tested for face-validity on health care professionals and then on 10 parents and their children. There were no apparent difficulties with understanding and completing the questionnaire.

Data collection

Interview study

The HBHC nurses informed the parents about the study and subsequently the author of the thesis to contact them for further information. All interviews were conducted between October 2009 and January 2010 by the author of the thesis at a time and place in accordance with the families' wishes. The parents decided whether both of the parents, the child, and the siblings would participate in the interview. In three families both parents were interviewed together, in six families one parent participated in the interview, and in one family both parents were interviewed individually. Six children (one sibling) over eight years of age participated partly in the interviews, and one child

participated in the whole interview. Efforts were made to facilitate the families' participation e.g. by performing the interviews at times and places that best suited the families. The child was not specifically addressed the child. Six families chose to be interviewed in the family's home and five families chose to be interviewed in a private room at the hospital. The interviews lasted between 20 and 75 minutes (median = 35 minutes).

Feasibility study

The HBHC nurses' recording protocols for assessing treatments and nursing tasks were collected after each home visit during the whole HBHC programme period between August 2008 and December 2009. The evaluation forms for assessing parents' perception of safety, satisfaction and preference were collected after each home visit only during the first 12 months of the programme intervention, as we estimated the acquired number of forms was sufficient to assess the effect. The HBHC nurse took the form to each home visit, the parent completed the form after the visit, which was not signed or dated and put it in an unmarked envelope. The HBHC nurse did not see the completed form and brought the sealed envelope back to the hospital. The data from the recording protocols and evaluation forms were documented in databases constructed specifically for the HBHC. The HBHC nurse recorded any medical errors, unintended adverse events or acute allergic reactions during each visit. The costs associated with HBHC were calculated at the time of evaluation in February 2011.

Controlled study

The author of thesis approached the families for participation in the controlled study. The questionnaire booklets were by mail to the mother and father individually in order to assess both caregivers' perceptions separately. The questionnaire were sent with a stamped addressed envelope with an additional letter containing written information about the study and the confidentiality with which their data would be treated in which to return the informed consent and questionnaire to the research team. Questionnaire data was collected at inclusion (time point 1) and after 3 months (time point 2) by the author of the thesis and a research assistant between December 2007 and October 2010 in order to assess the psychosocial impact over time.

Parents were given detailed written instructions about how to complete the questionnaire as well as how to administer the questionnaire to their child. It was not required that the child completed the self-report on their own and the instructions stated that, for children aged 5-7 years,

the parent should read the instructions and items aloud. Children completed the child self-report in one of the parents' questionnaire. The questionnaire was to be completed at home and the parents received a reminder after two weeks if they had not responded. Based on the pilot study, we decided to approach the families with a newly diagnosed child approximately 3 months after the cancer diagnosis to take into consideration the strained situation in the first months after the cancer diagnosis.

As the invitation to the controlled study was not sent out at the same time as the inclusion in the HBHC programme (at least 1 month post-diagnosis), 20 children in the HBHC group inadvertently received 1 - 20 home care visits prior to time point 1. Therefore, we refrained from evaluating the effect between time point 1 and time point 2 and focus on the results from time point 2.

Data analysis

Interview study

The transcribed text was analysed using qualitative content analysis following Graneheim and Lundman to describe the family member's experiences by focusing on differences and similarities in the transcribed text (Graneheim, Lundman 2004). The text was analysed with the concepts of meaning units, condensed meaning units, codes, sub-themes and themes (Graneheim, Lundman 2004). The analysis was on both the manifest and latent content and was performed in four steps, going back and forth between the four steps throughout the process, both independently and jointly by three of the authors of paper I. In the first step, three authors independently read through each interview several times to acquire an overall understanding. In the second step, the first author divided the text into meaning units, defined as exact words, sentences or paragraphs in the text where the content and context related to each other and to the aim of the study (Graneheim, Lundman 2004). In the third step, three authors categorized the condensed meaning units into codes, compared the codes for similarities or differences and then sorted them into sub-themes. In the final step, each sub-theme was compared, analysed and then grouped into a main theme. The main theme was considered to be a thread of underlying meaning (Baxter 1991) running through the condensed meaning units, codes and sub-themes on an interpretive level. Table 2 presents examples of meaning units, condensed meaning units, codes and sub-themes.

Table 2. Examples of meaning units, condensed meaning units, codes and sub-themes

Meaning units	Condensed meaning units close	Code	Sub-theme
to me, the most important issue is that home visits reduce the draining hospital visits	reducing draining hospital visits	relief for the parent	decreasing the strain on the family
it is so nice and comfortable to be able to wake up at home and walk about in pyjamas; lie down in your own bed if you feel bad after having treatment or blood samples taken	comfortable to be at home when feeling bad	relief for the child	
when at home in your own environment, you can almost forget something is wrong	forget about illness at home	remain normal	maintaining normality and an ordinary life
and when we finally came home, we could *stay* home, and did not have to get ot the hospital every second day to have chemotherpy, sometimes every day. Instead, we could just be at home, and the sibling could stay home from daycare and we could be together, and relax, all together	staying at home instead of leaving togehter with all of the family	the family being together	
when they (nurses) visit us in our homes, they have much more time for me as a person and I feel more safe and secure at home	more time creates feelings of more security at home for the ill child	feelings of more security for the child	fulfilling the need for safety and security
the nurses know what they are talking about and I can ask them about a lot of things, well, we have felt completely safe wtih them being here and if we wonder about something, they can explain it to us, well, they have seen so much over the years	the nurses' knowledge and explanations create a safe environment	the nurses experience ensures the perception of safety	

The primary investigator and interviewer (the author of this thesis) is a nurse who has worked at the paediatric haematology and oncology ward for several years. The author of this thesis was responsible for the assessment of the HBHC. None of the authors were involved in the care of the children and their families and had no previous professional or personal interactions with the interviewees. The authors discussed and reflected on their pre-understandings throughout the study to ensure they were unambiguous and thereby decreased the risk of subjectively influencing the study and the interpretation of the family member's experiences.

Feasibility study

Descriptive statistics were used for analysis of the recording protocols and evaluation forms. The responses *not at all* and *almost not at all* in the evaluation form were interpreted as indicating that HBHC was perceived as less satisfying, whereas the remaining response alternatives indicating that HBHC was perceived as satisfying. The economic evaluation was made by an employee at the department of finance at the university hospital in accordance with their guidelines for evaluating health care costs. Medical charges for the health care service associated with HBHC were evaluated

by comparing operational and overhead costs of the HBHC with the charges of an outpatient or inpatient admission at the hospital.

The costs were evaluated by comparing the HBHC related actual costs with an outpatient visit or an inpatient admission. As childhood cancer treatment is a highly specialised service, the university hospital applies a daily hospital charge, so called Land-landsdelscharge (LL) when calculating the costs of an outpatient visit or inpatient admission at the university hospital according to the Activity- Based Cost Model (Kaplan, Cooper 1998). The LL-charge includes costs for medication but not special medication such as oral chemotherapy. Costs for these medications were estimated.

The costs of the HBHC were calculated using the database of the recording protocols, the HBHC hospital accounts comprising expenses related to HBHC and the hospital IT-based administration system. There were additional operational costs related to HBHC including the nurses' wages, car hire, fuel and parking, new uniforms for the HBHC nurses, nursing bags, equipment and safe storage of medications and blood samples. Payroll costs for the HBHC nurses included the actual costs during the whole period excluding weekend working shifts at the ward, which the paediatric oncology department paid for. Wages of the author of this thesis and the clinical supervisory group were not included. Overhead costs comprised 31.5% of the total operating cost and covered rental costs and hospital administration.

Controlled study

Statistical analysis

Baseline data were compared between HBHC and SHC groups with *t* tests and χ^2 tests. PedsQL^{TM} means and standard deviations were calculated for descriptive purposes at time points 1 and 2. We assessed the differences in PedsQL^{TM} scores between the HBHC and SHC groups from time point 1 to time point 2. For continuous variables, Student's t-test was used to compare the mean in the two groups, and χ^2-test were used for categorical variables. Multivariable linear regression analysis was used to explore the relationship between a set of independent values and HRQOL-scores as the dependent variable. The dependent variable was tested for normal distribution and we found no deviations. In the adjusted models, we adjust for child's diagnosis, age at diagnosis, gender, and time since diagnosis, and we include these variables because they could have an effect on the family impact and HRQOL-scores. The historical and concurrent SHC groups were combined for statistical analysis. The potential inconsistencies between child self-reported and parent reported

scores may be critical, but was not included in the study and will be analysed subsequently. All tests of significance were two-sided, and statistical significance was defined as $p < 0.05$.

ETHICAL CONSIDERATIONS

In all three studies, the parents were given written and verbal information about the study's aim, design and procedure and they gave their written consent to take part in the study. The parents gave individual written consent and the children were given verbal age-appropriate information and gave verbal assent when appropriate (Kirk 2007, Gibson et al. 2007). Participation was voluntary, and the parents were informed that they could withdraw from the study at any time without affecting the child's cancer treatment in any way. All family members were assured confidentiality and all data was kept safe and separately from each other in a secure location. The overall study (including the three studies) was approved by the Danish Data Protection Agency (jr.nr.2005-415380) and was registered at ClinicalTrials.gov (ID:NCT01538706). We applied to the Copenhagen and Frederiksberg's Committee on Biomedical Research Ethics for permission to conduct the studies in the present thesis even though, according to Danish law, it was not necessary to obtain ethical approval for this type of studies. The studies were conducted in accordance with the Declaration of Helsinki II (World Medical Association 2002). The studies were conducted according to ethical principles and guidelines for conducting research with children (Gill, Ethics Working Group of the Confederation of European Specialists in Paediatrics 2004, Joffe, Kesselheim & Shurin 2011).

LITERATURE REVIEW

The aim of the literature review (Paper III) was to systematically evaluate the evidence on HBHC for children with cancer. We searched the databases PubMed, CINAHL, and EMBASE to identify studies of health care programmes with home care nursing services using medical subject headings and text words relating to HBHC services in combination with terms for children and cancer. We did not use specific terms for study design or outcome in order to cover the widest possible range of papers. No language restrictions were used in the initial search. We did not search for unpublished data, ongoing studies, or conference abstracts. Additional papers were identified through the reference lists of the studies obtained from the database search.

The initial search yielded 496 papers of which 466 were not relevant to the review. The remaining 30 papers, and a further three papers identified from their reference lists, were reviewed and 28 papers did not meet the inclusion criteria. We identified five controlled studies (Close et al. 1995, Stevens et al. 2006, Lange et al. 1988, Miano et al. 2002) of which only one was a randomized controlled cross-over trial (Stevens et al. 2006). We systematically included, extracted data and preformed quality assessment according to the guidelines in Centre for Reviews and Dissemination (Centre for Reviews and Dissemination 2009) and PRISMA statement (Moher et al. 2009) as far as was practically possible (detailed description in paper III). The author of this thesis (HH) performed the initial screening of titles and abstracts of all papers to identify HBHC for children with cancer, and the last author of paper III (KS) conducted a random rescreening of 20% of the initially identified papers. In the second step, potentially relevant papers identified in the pre-selection process were obtained as full text and screened by two reviewers (HH, KS) for inclusion criteria according to a standardized checklist. One reviewer extracted the data (HH) into a standardized data collection form that included information about study design, sample size, participant, home care intervention, and outcome variables. The second reviewer (KS) checked the data extraction forms for correctness. The methodological quality of the included studies was independently assessed according to predetermined criteria, the quality of the studies was not scored but individual aspects of methodological quality were considered. The two reviewers (HH, KS) resolved any disagreement in the screening, extraction, and assessment process by consensus. A narrative summary was provided because sensitivity analysis, statistical assessment, subgroup analysis, and meta-analysis were inappropriate due the small number of studies, diversity of interventions, and lack of common outcome measures.

The review showed that there is limited data on the effect of HBHC for children with cancer and that it is difficult to draw clear conclusions from the published studies given the disparity in the interventions, the methodological limitations, and the differences in health care systems. Despite this, the studies suggests that HBHC for children with cancer is feasible, is not associated with any crucial negative effects and may lead to specific improvements and impairments in children's quality of life. These findings are consistent with three systematic reviews (Cooper et al. 2006, Parker et al. 2006, Parker et al. 2002) of HBHC for acute and chronically ill children that did not include childhood cancer. They found limited data on the frequency of hospital admissions, length of hospital stays, children's health outcomes and HRQOL, and cost effectiveness but indicate that HBHC is feasible and may lead to greater parent and child satisfaction with the medical care.

We systematically reviewed the studies according to standardized guidelines (Centre for Reviews and Dissemination 2009, Moher et al. 2009). We chose the databases PubMed, CINAHL, and EMBASE as they cover a wide range of health care programmes, and nursing care. However, the search strategy did not include meeting reports, ongoing studies, or publications in languages other than English. Therefore, the review might be subject to language and publication bias even though most studies are published in English. The study selection process could have been improved if the two authors had independently performed the search and the whole screening process. However, two reviewers checked the data extraction forms, independently assessed the methodological quality of the included studies, and resolved any disagreement in the review process by consensus.

There are some important issues of bias in the studies in the included review that are not addressed in detail in our review e.g. issues of methods for assessment in the included studies and the potential effect of missed reports/studies on our conclusions. Despite these limitations, we believe that the review identifies and provides reliable information about the current status of research and is thus valuable for planning HBHC programs and future research.

RESULTS

Interview study

Table 3. Background characteristics of study participants

Charateristic	N
Parents	**14**
Female	5
Male	9
Ethnicity	14
Danish	
Partner relations	
Cohabiting with partner	13
Divorced	3
Single-parent	1
Age (years)	
31-40	5
41-50	9
Employment	
Employed	13
Unemployed	1
Sick leave due to child's cancer illness full time	5
Sick leave due to child's cancer illness part time	6
Distance to hospital	
0-15 km	6
16-30 km	1
31-45 km	4
Time to hospital, minutes	
0-30	
31-60	
Children with cancer	
Gender	
Boys	5
Girls	5
Age (years)	
0-4	3
5-7	2
8-12	4
13-15	1
Diagnosis	
ALL	6
Lymphoma	3
Brain tumour	1
Siblings living at home	
0	3
1	5
2	2

Two of the 12 invited families declined to participate due to the burden of the disease and treatment on their family, leaving 10 included families. The demographic characteristics of the participating families are given in Table 3. The number of home care visits in the included families ranged from 9 to 66 and the duration of participation in HBHC ranged from 3 to 16 months. Two families had completed their participation in the HBHC at the time of the interview (1 and 3 months after completion).

The main theme of experiences with HBHC was identified as *supporting the family throughout the childhood cancer trajectory* since it decreased the strain on the family and their ill child and supported their ability to maintain an ordinary life. The main theme was composed of the three identified sub-themes, *maintaining normality and an ordinary life*, and *fulfilling the need for safety and security* (Paper I).

The parents described how the HBHC *decreased the strain on the family and the ill child* that they experienced during the child's cancer treatment by reducing the number of hospital visits as the hospital visits were experienced as physically and emotionally draining for both the parent and the child, and especially for school-age children. Their experience was that HBHC supported them by decreasing practical problems such as fetching siblings from the day care and thereby they could invest their energy and strength in more important matters. There were no descriptions of HBHC as increasing the strain or burden on the family.

The parents described HBHC as way of *maintaining normality and an ordinary life* because it did not interrupt the families' everyday life in the same way the hospital visits did. The lack of a normal everyday life due to the hospital visits was described as draining and it was important to the parents and children to continue their daily routines and family life as usual. The children participating in the interviews described how they felt less ill and more normal in their own home e.g. they could go to school or receive home schooling. Parents also emphasised the value of the child sleeping more and eating better at home. In addition, the siblings and the family were able to be together and meant that the siblings did not experience being left alone or left out.

Overall, family members described the HBHC as *fulfilling the need for safety and security* and well-functioning. Some parents described that they felt less insecure at home because they could avoid the risk of the child getting an infection at the hospital. The parents and children emphasised the importance of the HBHC nurses' experience in paediatric oncology as an essential aspect for their sense of safety and security. Thus, the HBHC nurses were able to support them as they were familiar with the treatment, course of illness and the effects on the whole family. Parents and children described the increased familiarity with the HBHC nurses due to the home visits as enhancing the experience of security both at home and at the hospital.

They did not perceive HBHC as interference in their private sphere and expressed pleasure with meeting the HBHC nurses both at home, at the ward and in the day care unit. However, some parents experienced that they were less often in direct contact with the paediatric oncologist due to the HBHC and this created some insecurity. Some parents wanted potentially harmful treatments to be provided at the hospital so that the home remained associated with a safe and pleasant place for the child. Other parents experienced that their child coped better with potential harmful procedures at home e.g. receiving a feeding tube through the nose.

Feasibility study (Thesis and Paper II)

A total of 155 children were assessed for eligibility during the inclusion period in August 2008 and December 2009 and 51 children with cancer were included. Five children with the diagnoses thalassaemia or histiocytosis were included (Table 4). Three families declined to participate in the HBHC programme. One family did not want health care in their home and the two other families because they preferred the treatment to be provided at the hospital as only a few hospitals visits were necessary according to the treatment protocol. Figure 3 illustrates the inclusion. The three

families that declined to participate in the HBHC programme did not differ from the participating families in clinical or demographic characteristics.

Table 4. Participants and HBHC programme activities

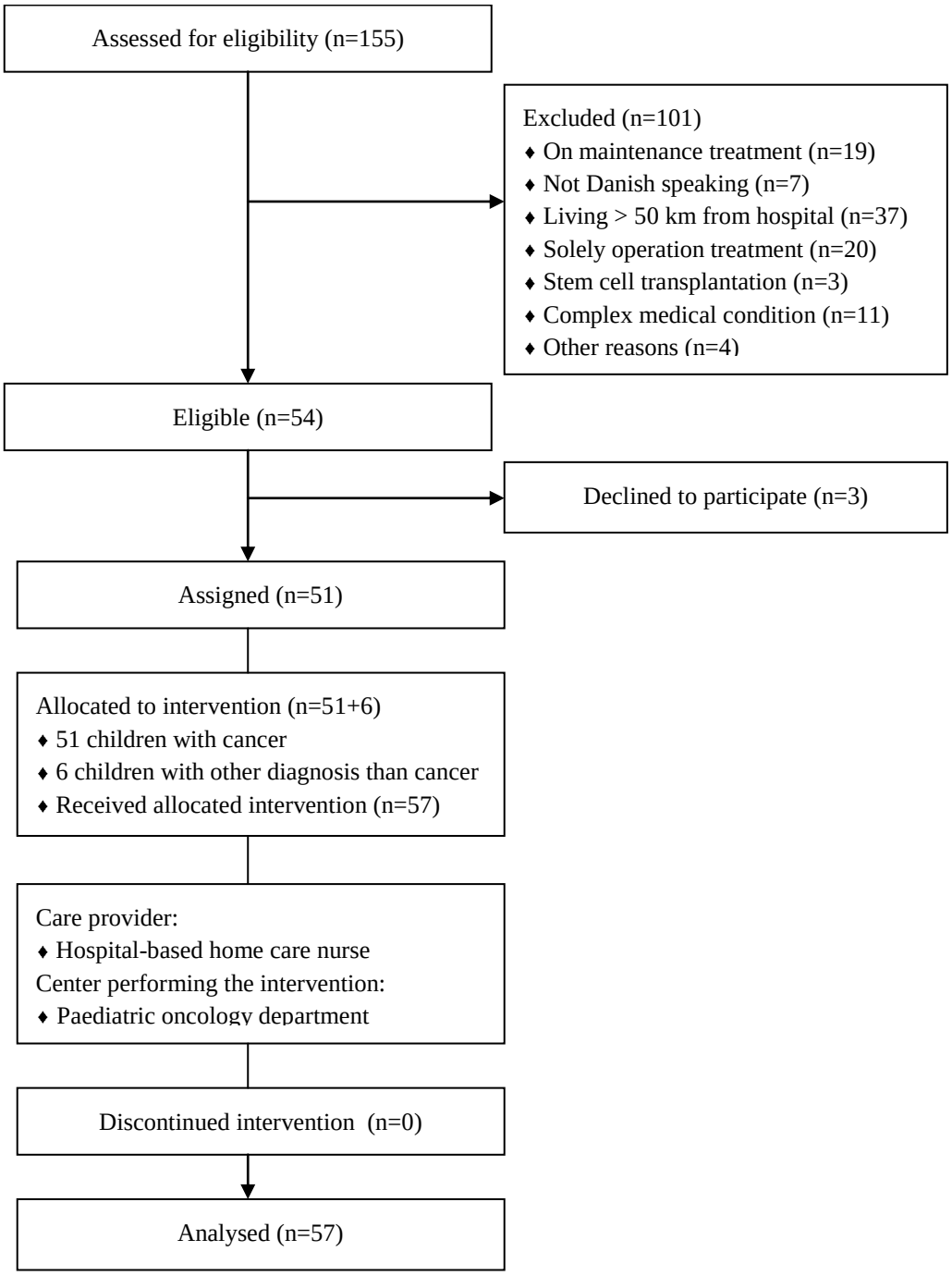
		HBHC programme (Feasibility study)		HBHC group (Controlled study)
	N	**Range (median)**	**N**	**Range (median)**
Children	57		28	
Male	28		15	
Female	29		13	
Age		0-17 (8)		0-13 (5)
0-4	17		10	
5-7	10		6	
8-12	15		8	
13-17	15		12	
Diagnosis				
ALL/AML/ Lymphoma	33		20	
CNS tumor	10		3	
Solid tumor	8		5	
Thalassaemia	5			
Histiocytosis	1			
Home care visits	942	1 – 75 (10)	478	1 – 75 (9)
Duration home care visit (minutes) [1]	784	10-200 (20)	474	10-200 (20)
Nurse transport time (minutes) [1]	786	3-150 (30)	476	5-150 (30)
Length in the HBHC intervention (months)[2]		0 – 17 (5)		0-17 (4)
Treatments				
Infusion of antibiotics Carbapenem and Ciproflaxine	117		69	
Infusion of chemotherapy Vincristine and Dactinomycin	317		211	
Other intraveneous medications	82		57	
Blood sample central venous catheter (CVC)	619		379	
Blood sample peripheral vein	128		37	
CVC occlusion	14		5	
Other care procedures e.g. cleansing CVC	63		20	

[1]Numbers differ due to missing registration
[2]From first to final visit

There were 942 HBHC visits distributed over 337 working-days with a mean of 2.8 visits per day (maximum 6) during the whole HBHC programme. The number and type of treatments of the individual child varied depending on the diagnosis, treatment protocol and on the remaining duration of the cancer treatment at the time the child was included in the HBHC programme. One child stopped participation in the HBHC programme after the first visit because the HBHC nurse

could not take blood samples from the peripheral vein of the child. The families cancelled less than 3% of the referred HBHC visits and the HBHC nurse cancelled less than 10%.

Figure 3. Flowchart HBHC programme



Perception of security, satisfaction with HBHC and preference for care

A total of 657 parent-reported evaluation forms (70% of the 942 HBHC visits) were collected. The number of missing items was less than 3%. In all evaluation forms except one, parents reported that they would prefer to receive a home visit instead of a hospital visit. All parents felt secure with the HBHC, 94% were very satisfied with the HBHC and none scored lower than 'satisfied' (Table 5). The parents' responses and their evaluation of the children's perceptions with the home visit were consistent.

Table 5. Participants' perceptions based on the HBHC programme

	Evaluation form n= 657 (%)
How do you feel about the child receiving home treatment	
Badly	
Uncomfortable	
Good	
Very good	
Extremely good	
How satisfied were you with the home care visit?	644
Very unsatisfied	0
Unsatisfied	0
Neither satisfied or unsatisfied	0
Satisfied	39 (6)
Very satisfied	605 (94)
How safe did you feel about receiving treatment at home?	642
Not at all	0
A little	0
Quite safe	0
Safe	61 (10)
Very safe	581 (90)
How did the child feel about receiving home treatment?	
Badly	
Uncomfortable	
Good	
Very good	
Extremely good	
How satisfied was the child with the home care visit?	644
Very unsatisfied	0
Unsatisfied	0
Neither satisfied or unsatisfied	2 (0,3)
Satisfied	67 (10
Very satisfied	573 (89
How safe did the child feel about receiving treatment at home?	637
Not at all	0
A little	0
Quite safe	1 (0,3)
Safe	63 (10)
Very safe	573 (89)
If you had the opportunity to choose home treatment for the child again, would choose it?	652
Yes	651
No	1

Safety

There were no reports of medical errors, acutely affected general conditions, unscheduled hospital visits or acute anaphylactic reactions related to HBHC. On two occasions, the HBHC nurse forgot to bring the medication. Failed attempts at taking blood samples from a peripheral vein were reported and 14 occasions with CVC occlusions but none of these lead to hospital admissions.

Costs

The cost analysis (Paper II) showed that HBHC was provided at equal costs compared to a corresponding outpatient visit and at lower costs than a corresponding inpatient admission. The daily hospital charge for a HBHC visit was 3.443 Danish Kroner (DK), the charge for an outpatient visit was 3.457 DK and the charge for an in-patient admission was 3.895 DK. Pay roll costs accounts for the largest cost of HBHC. The total costs of HBHC would decrease assuming that two HBHC nurses provide at least three visits per day, even though the costs of fuel, parking and medications would increase (Tables 6 and 7).

Table 6. HBHC costs in Danish Kroner (DK)

Costs	**2008**	**2009**	**Total***
Wages	738.515	1.047.278	1.823.383
Fuel	4.232	6.227	10.586
Uniforms and working clothes	6.102	4.641	10.926
Nursing-bags	2.442	64	2.579
Parking	1.400	2.420	3.862
Car	2.925	1.217	4.229
Mobile phone	60	747	809
Various expenses	1.008	152	1.191
Leasing of car**			51.408
Operating costs in total			**1.908.972**
Overheadcosts			**601.326**
Operating costs in total incl. leasing of car			**2.510.299**

*Wages 5.08% and operating costs 3.00%

**Leasing of car costs 3.024 kr per month

Table 7. Charge per HBHC visit in DK

Costs HBHC	2.510.299
Medications costs*	44.520
Costs in total	2.554.819
Number of visits	942
Number of working days	337
Costs per visits in total	**3.443**
Costs per working-day in total	7.581

*60 kr per visit

Controlled study

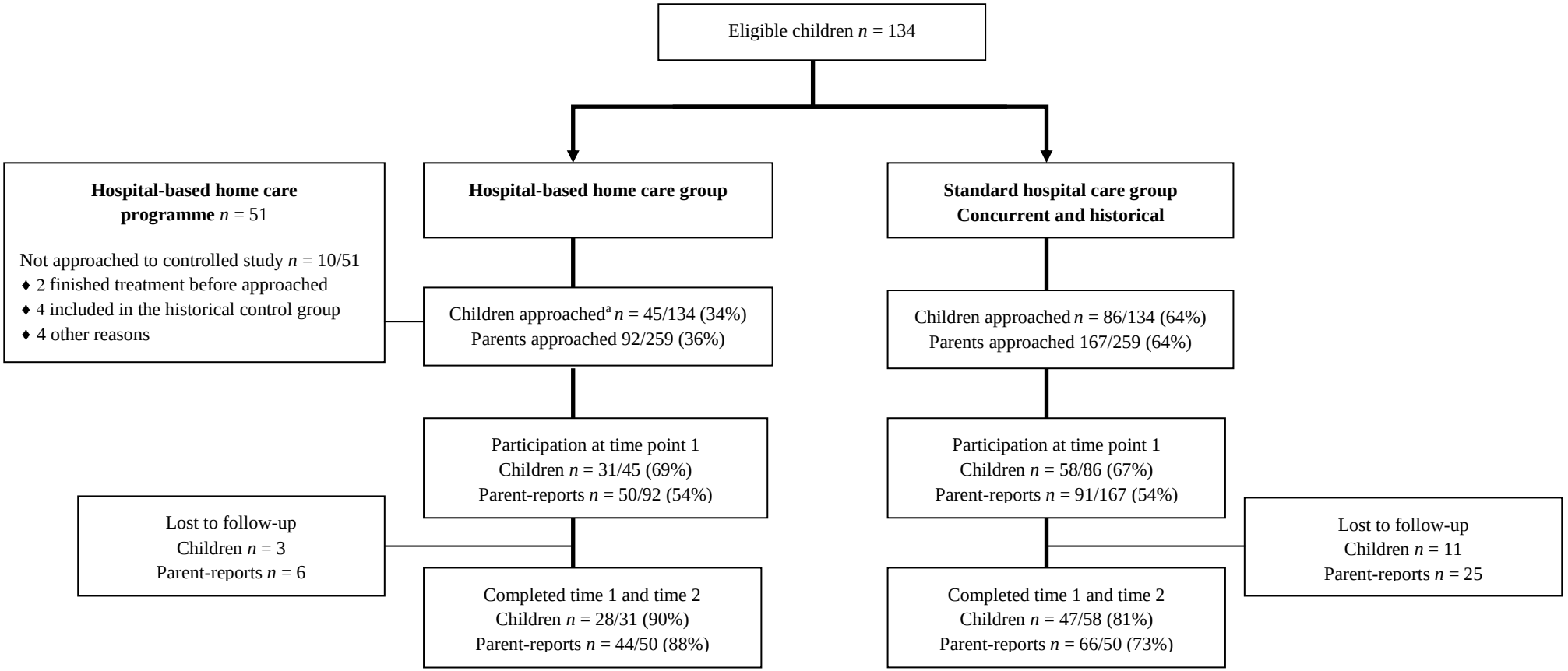
A total of 134 children and their parents were eligible for inclusion in the controlled study during the inclusion period from December 2007 to December 2009. The families in the controlled study were included in three groups: (1) the HBHC group, which was a subsample of 28 children and 44 parents from the 51 families in the HBHC programme (median: 10 kilometres from the hospital), (2) the historical SHC group of 35 children and 51 parents (median: 40 kilometres from the hospital) and, (3) the concurrent SHC group of 12 children and 15 parents (median: 89 kilometres from the hospital). Figure 4 illustrates the inclusion and table 8 presents the participants.

The response rate among families was 60% in the HBHC group and 54% in the SHC group. Comparison between participants and non-participants (n=45 children) in the HBHC and SHC groups showed no differences according to child's gender and age, though there were more children with solid tumours (31%) in the non-participant group. Seventy-five% of the non-participants were between one and three months since diagnosis when they were approached and 76% resided within 50 kilometres of the university hospital. Thirty-eight of the non-participant parents (of 28 children) agreed to a short telephone interview by an HBHC nurse (conducted in December 2008) about the reasons why they declined to participate according to a predefined form (Table 9). Seventy-four% of the parents responded that the questionnaire was too large to complete.

Table 9. Parents' responses in the non-participant forms.

	Non-participants in the controlled study n= 38 (%)
I could not cope with it.	9 (24%)
I did not have the strength to read it.	7 (18%)
I did not have more time.	4 (11%)
The questionnaire was too large.	28 (74%)
The questions were too difficult to understand.	0
The language was too difficult to understand.	0
I forgot to read it and then time passed.	2 (5%)
My child has completed the anticancer treatment.	1 (3%)
I wanted to move on and not think about the treatment trajectory.	1 (3%)
I do not have much contact with the child.	0
I completed the questionnaire with my partner.	0
I cannot see that it is (the questionnaire) important to us.	0

Figure 4. Flowchart of the controlled study



[a] From HBHC programme *n* = 4 and four children approached December 2009 and HBHC in 2010

Table 8. Characteristics of the participants in the HBHC group and SHC group

	No. (%)				
	HBHC group	**SHC group**	**P-value**	**Historical SHC group**	**Concurrent SHC group**
Parents	***44 (100)***	***66 (100)***		***51 (100)***	***15 (100)***
Parents/Guardian			.47		
Female	25 (57)	42 (63)		33 (65)	9 (60)
Male	19 (43)	24 (37)		18 (35)	6 (40)
Age (years)			.32		
21-30	2 (5)	8 (12)		5 (10)	3 (20)
31-40	21 ()	26 (39)		24 (47)	2 (13)
41-50	19 (43)	25 (38)		16 (31)	9 (60)
≥ 50	2()	7 (10)		6 (12)	1 (7)
No data	0	3 (3)		0	0
Marital status			.62		
Married or cohabiting	40 (90)	58 (88)		46 (90)	12 (80)
Living alone	4 (10)	8 (12)		5 (10)	3 (20)
Education			.009		
Basic (ISCED 1-2)	0 (0)	0 (0)		0 (0)	0
Secondary (ISCED 3)	9 (20)	30 (45)		21 (41)	9 (60)
Higher (ISCED 4-6)	33 (75)	30 (45)		25 (49)	5 (34)
Unknown	2 (5)	6 (10)		5 (10)	1 (6)
Employment			.96		
Employed	35(80)	53 (80)		41(80)	12 (80)
Sick leave or unemployed	2 (5)	4 (6)		3 (6)	1 (6)
Retired or other	5 (10)	6 (10)		5 (10)	1 (6)
Unknown	2 (5)	3 (4)		2 (4)	1 (6)
Number of children			.96		
1	6 (14)	9 (14)		8 (16)	1 (6)
2	25 (56)	36 (54)		29 (57)	7 (47)
3 or more	13 (30)	21 (32)		14 (27)	7 (47)
Annual household income			.40		
Low (0-249 000)	1 (2)	1 (2)		0	1 (7)
Medium (250 000–549 000)	6 (14)	9 (14)		6 (12)	3 (20)
High (≥ 550 000)	33 (75)	42 (64)		34 (66)	8 (53)
Do not wish to answer	4 (9)	14 (21)		11 (22)	3 (20)
Children	***28 (100)***	***47 (100)***		***35 (100)***	***12 (100)***
Gender			.70		
Male	15 (54)	23 (49)		15 (43)	8 (67)
Female	13 (46)	24 (51)		20 (57)	4 (33)
Age (years)			.33		
0-1	5 (18)	3 (6)		1 (3)	2 (17)
2-4	7 (25)	16 (3)		13 (37)	3 (25)
5-7	6 (21)	8 (17)		7 (20)	1 (8)
8-12	7 (25)	9 (19)		7 (20)	2 (16)
13-18	3 (10)	11 (23)		7 (20)	4 (33)
Diagnosis			.94		
ALL/AML/ Lymphoma	20 (71)	32 (68)		25 (71)	7 (59)
CNS tumour	3 (11)	5 (10)		4 (11)	1 (8)
Solid tumour	5 (18)	10 (22)		6 (17)	4 (33)
Time since diagnosis (months)			.0003		
1-3	18 (64)	10 (22)		5 (14)	5 (42)
4-6	7 (25)	12 (26)		5 (14)	7 (59)
7-11	3 (11)	7 (14)		7 (20)	2 (17)
≥ 12	0	18 (38)		18(52)	0 (0)
Distance to hospital			<0.0001		
≤ 50 km	27 (96)	23 (49)		23 (66)	0 (0)
> 50 km	1 (4)	24 (51)		12 (34)	12 (100)

The participating families in the HBHC and SHC groups were comparable with regards demographic and medical characteristics except for the parents' education level, which was higher in the HBHC group. In addition, more time had passed since diagnosis for the children in the SHC group when the questionnaire was completed at time point 1. The average time period since diagnosis was three months in the HBHC group and seven months in the SHC group at time point 1, due to the inclusion of the historical SHC group, and seven months and 11 months, respectively, at time point 2.

HRQOL – PedsQL™ Generic Core Scales and Cancer Module

The mean PedsQL™-Generic Core and Cancer Module scores in self- and parent-reports are presented in table 10. In PedsQL™-Generic Core, we found higher self- and parent reported scores in all dimensions at time point 2 in the HBHC group (Paper II). The scores were significantly higher for the self-reported total score, psychosocial health and emotional functioning at time point 2. In the parent-reports, the scores were significantly higher for the total score, physical health and school functioning. Several of the children did not attend school, which affected the mean score in the school dimension. The proposed cut-off point for impaired HRQOL is determined as 68.9 in self-reported total scores and as 67.0 for parent-reports (Varni et al. 2002, Varni, Limbers & Burwinkle 2007)(Cooper et al. 2006, Parker et al. 2006, Varni, Limbers & Burwinkle 2007, Hansson et al. 2011a). We found self-reported mean values higher than 68.9 only in the HBHC group at both time points. The parent-reported mean values were lower at time point 1, but close to 70.0 in the HBHC group at time point 2.

We found no significant differences between the groups at time point 2 in the PedsQL™ Cancer Module, but there were higher scores in cognitive problems in both parent-reports and self-reports in the HBHC group (Paper III). Self-reported and parent-reported mean scores for procedural anxiety were lower in the HBHC group and decreased between the time points. Pain scores improved between time points in both groups. Results from time point 1 are shown in appendix 3.

Table 10. Comparison of Generic Core and Cancer Module scores

	Time point 2				
			Mean (SD)		
PedsQL™ Scales	**N**	**HBHC group**	**N**	**SHC group**	**p-value**
Generic Core					
Child self-report					
Total score	13	75.3 (19.11)	25	61.1 (16.68)	.02
Physical functioning/ physical health	13	76.3 (25.14)	25	59.0 (25.96)	.06
Psychosocial health*	13	74.6 (17.30)	25	62.4 (14.50)	.03
Emotional functioning	13	78.1 (16.65)	25	62.2 (25.59)	.04
Social functioning	13	82.3 (20.27)	25	71.7 (18.83)	.12
School functioning	12	51.1 (19.78)	23	49.8 (46.83)	.91
Parent proxy					
Total score	41	69.2 (16.15)	66	60.9 (19.75)	.04
Physical health/ physical functioning	41	67.8 (20.09)	66	56.3 (26.89)	.03
Psychosocial health	42	70.6 (15.11)	63	64.6 (19.04)	.11
Emotional functioning	43	69.0 (17.29)	66	62.0 (20.27)	.08
Social functioning	42	77.9 (16.57)	63	72.4 (20.79)	.18
School functioning	27	57.9 (22.12)	30	44.8 (21.23)	.03
Cancer Module					
Child self-report					
Pain and hurt	13	73.1 (25.94)	25	62.5 (27.24)	.26
Nausea	13	71.2 (11.93)	25	66.4 (23.78)	.42
Procedural anxiety	12	52.8 (33.58)	25	65.0 (32.63)	.30
Treatment anxiety	13	87.8 (21.95)	25	77.7 (28.23)	.16
Worry	12	76.4 (28.17)	25	67.2 (22.38)	.29
Cognitive problems	13	74.9 (19.47)	25	62.2 (18.92)	.06
Perceived physical appearance	13	72.4 (22.41)	25	67.3 (27.10)	.56
Communication	13	79.5 (29.58)	25	63.7 (26.45)	.10
Parent proxy					
Pain and hurt	39	73.4 (19.91)	65	64.4 (28.49)	.05
Nausea	40	71.8 (19.14)	63	70.1 (26.39)	.68
Procedural anxiety	40	60.8 (33.93)	63	71.0 (32.75)	.11
Treatment anxiety	40	79.6 (20.32)	64	85.4 (22.03)	.15
Worry	39	86.3 (20.19)	63	77.8 (26.73)	.08
Cognitive problems	39	77.8 (16.53)	62	70.5 (24.11)	.06
Perceived physical appearance	40	73.4 (25.97)	61	74.2 (25.94)	.99
Communication	38	67.3 (27.43)	60	63.7 (33.61)	.77

*Psychosocial health is a summary score of emotional, social and school dimensions
Scale ranging from 0 to 100 with higher scores indicating better HRQOL
1-2 parent proxy-reports per child in the treatment groups because both parents were invited

When the results were adjusted for the potential effects of diagnosis, age, gender and time since diagnosis, the large differences between the groups in parent-reported and self-reported PedsQL™-Generic Core Scales suggest a trend towards higher scores at time point 2 in all dimensions except for school functioning (Table 11). However, only parent-reported physical health reached statistical significance (p=.01). In the PedsQL™-Cancer Module, there were significant differences between treatment groups in parent-reported nausea (p=.04) and worry (p=.04) at time point 2. Importantly,

parent-reported scores in procedural and treatment anxiety appeared to be higher in the SCH group than the HBHC group. Results from time point 1 are shown in appendix 4.

Table 11. Linear regression for Generic Core and Cancer Module

PedsQL™ Scales	Time point 2			
	Crude β 95% CI	p-value	Adjusted β 95% CI	p-value
Generic Core				
Child self-report				
Total score	14.2 (2.0–26.3)	.02	14.8 (-0.4–30.1)	.06
Physical Health Summary	17.3 (-0.5– 35.2)	.06	20.3 (-2.2–42.7)	.07
Psychosocial Health Summary	12.3 (1.5–23.0)	.03	11.7 (-1.8–25.3)	.09
Emotional functioning	15.9 (0.9–31.0)	.04	13.6 (-7.6–33.9)	.20
Social functioning	10.7 (-2.7–24.0)	.12	15.5 (0.0–31.1)	.05
School functioning	1.3 (-27.6–30.1)	.93	-6.1 (-45.4–33.1)	.75
Parent proxy				
Total score	7.7 (0.4–14.9)	.04	7.7 (0.6–16.1)	.07
Physical Health Summary	10.5 (0.8–20.2)	.03	14.2 (3.3–25.2)	.01
Psychosocial Health Summary	5.7 (-1.2–12.5)	.11	3.6 (-4.1–11.2)	.35
Emotional functioning	6.7 (-0.7–14.0)	.08	5.2 (-3.3–13.7)	.23
Social functioning	5.2 (-2.3–12.7)	.17	3.8 (-5.2–12.8)	.40
School functioning	13.1 (1.6–24.6)	.03	9.4 (-7.5–26.4)	.27
Cancer Module				
Child self-report				
Pain and hurt	10.6 (-8.0–29.2)	.26	2.7 (-21.0–26.4)	.82
Nausea	4.8 (-9.5–19.0)	.50	7.3 (-11.5–26.1)	.43
Procedural anxiety	-12.2 (-35.7–11.3)	.30	-2.6 (-32.5–27.5)	.86
Treatment anxiety	10.2 (-8.1–28.4)	.27	12.0 (-11.9–35.0)	.29
Worry	9.2 (-8.1–26.6)	.29	6.9 (-15.3–29.1)	.53
Cognitive problems	12.7 (-0.5–26.0)	.06	7.0 (-10.2–24.1)	.41
Perceived physical appearance	5.1 (-12.7–22.9)	.56	7.3 (-15.2–30.0)	.51
Communication	15.8 (-3-3–34.9)	.10	21.3 (3.9–46.6)	.09
Parent proxy				
Pain and hurt	9.6 (-0.6–19.9)	.06	9.9 (-2.0–21.8)	.10
Nausea	1.8 (-7.6–11.3)	.70	9.9 (-0.2–19.5)	.04
Procedural anxiety	-10.9 (-24.1–2.3)	.11	-5.0 (-20.3–10.3)	.52
Treatment anxiety	-6.1 (-14.6–2.3)	.15	-6.3 (-16.5–4.0)	.23
Worry	8.8 (-0.9–18.6)	.08	10.5 (-0.4–20.6)	.04
Cognitive problems	7.8 (-0.8–16.5)	.08	1.7 (-7.8–11.2)	.72
Perceived physical appearance	0.1 (-10.5–10.3)	1.0	-1.7 (-12.6–9.2)	.76
Communication	1.9 (-11.1–15.0)	.80	0.6 (-14.0–15.3)	.93

β is the estimated mean difference and positive differences imply a higher score in the HBHC group
CI: Confidence Interval
Scores are adjusted for diagnosis, time since diagnosis, age at inclusion, and gender

Family Impact Module and Healthcare Satisfaction Module

The scores in the Family Impact Module were not significantly higher at time point 2 but there were higher scores in social functioning in the SHC group (55.8 *vs.* 63.7 p=0.08). In the Healthcare Satisfaction Module, the scores were overall higher in the SHC group at time point 2 and significant

higher in emotional needs (55.8 *vs.* 63.7 *p*=0.02) (Table 12). Results from time point 1 are shown in appendix 5.

Table 12. Comparison of Family Impact and Satisfaction with Health Care Generic Module scores

	Time point 2				
	Mean (SD)				
PedsQL™ Scales	**N**	**HBHC group**	**N**	**SHC group**	**p-value**
Family Impact Module					
Total score	41	62.8 (16.02)	65	65.6 (17.36)	.35
Parent HRQOL summary score	41	63.8 (16.22)	65	67.6 (17.76)	.25
Family functioning summary score	41	61.1 (21.08)	64	65.4 (22.41)	.27
Physical functioning	41	61.9 (16.84)	65	64.3 (18.45)	.57
Emotional functioning	41	69.2 (18.60)	65	71.8 (20.40)	.45
Social functioning	41	55.8 (23.40)	65	63.7 (24.97)	.08
Cognitive functioning	41	67.1 (20.28)	64	70.4 (19.32)	.36
Communication	41	69.3 (15.42)	65	71.6 (21.13)	.41
Worry	41	57.7 (21.77)	65	54.0 (20.05)	.45
Daily activities	41	56.9 (24.15)	64	59.5 (28.59)	.49
Family relationships	41	63.6 (23.17)	64	69.0 (23.32)	.24
Healthcare Satisfaction Module					
Total score	41	65.2 (17.22)	65	70.2 (11.29)	.08
Overall satisfaction	41	82.5 (21.79)	65	83.7 (12.45)	.79
Information	41	63.7 (20.59)	65	70.5 (15.67)	.05
Inclusion of family	41	68.8 (22.53)	65	76.1 (14.94)	.05
Communication	41	66.1 (19.59)	64	72.4 (14.17)	.05
Technical skills	41	75.4 (18.54)	64	76.2 (16.19)	.73
Emotional needs	39	45.0 (14.72)	62	50.7 (11.64)	.02

When adjusted for the same confounding factors as in the PedsQL™-Generic and Cancer Modules, we found similar or small differences overall in scores between groups in the PedsQL™-Family Impact Module. In the Health Care Satisfaction Module, the differences seemed to be larger, indicating higher scores in the SHC group in total score, inclusion of family, communication, and emotional needs (Table 13). Results from time point 1 are shown in appendix 6.

Table 13. Linear regression for Family Impact and Satisfaction with Health Care Generic Module

PedsQL™ Scales	Time point 2			
	Crude β 95% CI	p-value	Adj β 95% CI	p-value
Family Impact Module				
Total score	-3.1 (-9.7–3.5)	.35	0.8 (-7.1–8.6)	.85
Parent HRQOL summary score	-3.9 (-10.7–2.8)	.25	0.8 (-8.7–7.2)	.84
Family functioning summary score	-4.8 (-13.4–3.8)	.27	2.8 (-7.2–12.9)	.58
Physical functioning	-2.0 (-9.0–5.0)	.57	0.6 (-7.6–8.7)	.89
Emotional functioning	-2.9 (-10.6–4.8)	.46	0.6 (-8.5–9.7)	.89
Social functioning	-8.6 (-18.2–1.0)	.08	-4.5 (-15.7–6.8)	.43
Cognitive functioning	-3.6 (-11.3–4.1)	.36	-1.2 (-10.6–8.2)	.80
Communication	-3.0 (-10.5–4.6)	.44	-1.1 (-10.1–7.8)	.80
Worry	3.1 (-5.0–11.3)	.45	5.8 (-4.2–18.8)	.25
Daily activities	-3.8 (-14.5–7.0)	.49	5.0 (-7.7–17.7)	.44
Family relationships	-5.5 (-14.6–3.6)	.24	1.6 (-9.2–12.3)	.77
Healthcare Satisfaction Module				
Total score	- 5.4 (-10.8–0.1)	.05	-3.7 (-9.5–2.2)	.22
Overall satisfaction	- 1.0 (-7.5–5.5)	.77	2.2 (-4.7–9.1)	.53
Information	- 6.8 (-13.8–0.1)	.05	-4.1 (-12.1–4-0)	.32
Inclusion of family	- 7.9 (-15.0– -0.7)	.03	-5.8 (-13.4–1.8)	.14
Communication	- 7.1 (-13.7– -0.5)	.03	-6.3 (-13.5–0-8)	.08
Technical skills	- 1.2 (-7.9–5.6)	.73	0.8 (-8.4–6.9)	.84
Emotional needs	- 6.1 (-11.3– -0.9)	.02	-4.9 (10.5–0.8)	.09

β is the estimated mean difference and positive differences imply a higher score in the HBHC group
CI: Confidence Interval
Scores are adjusted for diagnosis, time since diagnosis, age at inclusion, and gender

DISCUSSION

Discussion of findings

This thesis adds to the knowledge of the feasibility of implementing a HBHC programme that is safe, cost effective and satisfactory to the families. In addition, families may experience HBHC as a psychosocial support throughout the course of treatment and some specific aspects of the child's perceived HRQOL may even be enhanced. The findings from the studies are discussed below followed by a separate discussion of the methodological considerations related to the findings.

Interview study

The family members described HBHC as being a psychosocial support throughout their child's cancer treatment because it reduced the number of hospitals visits. The findings indicated that the experiences with HBHC did not differ among diagnostic groups, social classes, family sizes or configurations, distance from hospital, number of visits or type of HBHC treatments. Thus, our findings are consistent with Stevens et al.'s findings when they interviewed the participants in their home chemotherapy programme provided by community nurses to children with ALL (Stevens et al. 2006b). In previous studies families have described the everyday struggle with the challenges and distress they experience during the child's cancer treatment (Björk M., Wibe T., and Hallström I. 2008, Woodgate, Degner 2003) and it seems that HBHC may relieve the families of some of the challenges they face.

The parents described that HBHC supported them in continuing their daily routines and family life as usual. Previous studies have shown how the child's cancer affects the whole family (Patterson, Holm & Gurney 2004) and that sibling's needs may be overlooked (Enskär et al. 2011). Furthermore, Björk et al. found that family members experienced feelings of isolation and alienation by not participating in ordinary social activities and in school (Björk M., Wibe T., and Hallström I. 2008). This indicates that the HBHC may provide more opportunities for the family to be united and to meet the individuals' perceived needs.

The families experienced that their need for safety was fulfilled by the HBHC nurses' paediatric oncology experience and by meeting them both at home and the hospital. However, the families' need for safety was not always fulfilled, as some parents described that the appointments with the paediatric oncologist were sometimes lacking. This concern was related to children with many hospital visits according to the treatment protocol and indicates that the need for safety can be fulfilled by having regular appointments with the paediatric oncologist. Moreover, some parents in

had concerns about the potential occurrence of treatment-related harm of the child at home. This concern was addressed by making the HBHC visits optional and the families themselves were able to decide where a given treatment should be provided. In contrast, some families described that the children coped better with potentially harmful procedures at home.

In Stevens et al.'s study, some families felt safer at the hospital as they were close to the health professionals with all the necessary facilities, and some families experienced the inconsistencies in care by the community nurses and laboratories as emotionally stressful (Stevens et al. 2006b). Our HBHC was based at the paediatric oncology day-care unit and the HBHC nurses had working shifts at the ward to ensure quality of care. This indicates that there are benefits of home care being based at a hospital rather than in the community.

Overall, the findings indicate that school-age children may experience additional psychosocial benefits of the HBHC. The study highlights the importance of providing HBHC tailored to the family members' need for the sense of security, which can be achieved by using experienced paediatric oncology nurses and scheduling regular appointments with the paediatric oncologist. Moreover, it seems that the HBHC provides care that supports the families' and the individuals' perceived needs to maintain family functions as well as relieving the perceived distress.

Feasibility study

This descriptive part of the study (Paper II and Thesis) was exploratory in nature, and showed that HBHC visits can safely replace hospital visits with a high patient satisfaction and preference for HBHC care at equal or lower cost. Our findings are similar to other studies of HBHC as a safe (Close et al. 1995, Stevens et al. 2006a, Lange et al. 1988, Miano et al. 2002) and cost-effective provision of care (Close et al. 1995, Holdsworth et al. 1997, Lange et al. 1988, Miano et al. 2002). Although none of the studies evaluated satisfaction or preference for care as a separate outcome, Close et al. reported that the families preferred home chemotherapy (Close et al. 1995).

When comparing the feasibility and advantages of HBHC among other studies, it is important to include whether the health care and the organisation of HBHC are public or insurance-based. In insurance-based health care systems, such as in the United States, the provision of HBHC is extensive, as are the potential cost savings. In Denmark, the health care is financed through taxation and we compared actual costs associated with HBHC with the charges of an outpatient or inpatient admission at the hospital. However, it may give a misleading impression of the costs when only actual costs are included in the calculations since indirect costs for the families and the society may

balance the overall costs. The only study evaluating both actual and indirect costs in HBHC from a societal perspective in Canada reported no difference in costs (Stevens et al. 2006a).

HBHC is usually provided by health-care agencies or community-based nurses (Frierdich, Goes & Dadd 2003, NACHRI 2000). The principles of the provision of HBHC are important as it may affect the safety and the family member's perceptions of the benefits of receiving HBHC. Challenges may arise when the provision is based in a home-care agency or in the community through e.g. poor communication with the primary treatment centre and the lack of qualified nurses with experience in providing intravenous therapies (Frierdich, Goes & Dadd 2003, Kandsberger 2007). Stevens et al. reported difficulties related to the process of organising home chemotherapy with community-based nurses and clinics (Stevens et al. 2006a). These challenges may have contributed to greater emotional distress in the children as reported by the parents in their questionnaire study (Stevens et al. 2006a) and described in their interview study (Stevens et al. 2006b).

These concerns were taken into account in our study by basing the HBHC at the paediatric oncology department and applying rigorous safety controls and well-prepared communication systems. All of the organisation and medical preparations were performed at the day-care unit at the paediatric oncology department and provided in the home by the HBHC nurses who were experienced in paediatric oncology. In Denmark, community-based nurses rarely provide intravenous therapy and administrating chemotherapy requires an additional competence. Moreover, it may be difficult to maintain a high quality of care in the community-based system due to the low prevalence of childhood cancer.

Two families declined to participate in the HBHC programme because the treatment protocol included only few hospitals visits and they preferred the treatments to be provided at the hospital. This may indicate the need for regular hospital visits and that HBHC might be more beneficial for patients with treatment protocols that prescribe frequent hospital visits. Interestingly, parents of children with frequent hospital visits described in the interview study that the appointments with the paediatric oncologist were sometimes lacking. This suggests that the children need regular appointments with the paediatric oncologist regardless of whether their treatment protocols prescribe frequent or few hospital visits.

One family declined to participate because they did not want the feeling of the hospital invading their home. We had expected the families to be concerned about this aspect but the family members in study 1 did not perceive HBHC as being intrusive in their home. Though, they

emphasised the importance of the fact that the HBHC nurse was not wearing a hospital uniform, the car was unmarked and that there were no medical equipment was left in the home. This indicates that our set-up had the intended effect of being as little intrusive as possible.

Controlled study

The findings indicate that specific dimensions in children's HRQOL may improve when they receive HBHC. The significant adjusted estimated differences in the PedsQL^{TM}-Generic and Cancer Module for parent-reporting indicate that Children in the HBHC group perceived better physical health and less nausea and worry. This is in line with the findings from the interviews (Paper 1), where some parents described that the children were less nauseous and less emotionally preoccupied with the illness at home. The trend towards significantly higher child self-reported and parent-reported PedsQL^{TM}-Generic scores in the HBHC group indicates that HBHC may enhance the children's HRQOL in all these dimensions. However, according to the lower parent-reported scores in the HBHC group in PedsQL^{TM} Cancer Module, it seems that the children in the SHC group experienced less treatment anxiety than the HBHC group, although the difference was not significant. This may reflect the concern about the potential occurrence of treatment-related harm of the child at home that the parents described in study 1. It might also indicate that the beneficial impact on specific dimensions in the child's HRQOL may balance the perceived shortcomings with HBHC because, according the findings in the evaluation forms in the feasibility study, the families still prefer HBHC.

Our findings are consistent with Stevens et al.'s randomised crossover trial of home chemotherapy (n=23 children with leukaemia) (Stevens et al. 2006a). Stevens et al. used the disease-specific parent proxy instrument POQOLS with repeated measures over one year. They found significant improvements in the children's physical and social functioning during the first three months of home chemotherapy but not after six months. They also found that the children appeared to experience more emotional distress after receiving home chemotherapy over six months (Stevens et al. 2006a). The children in our study had received HBHC for a median of 5 months when they completed the questionnaire at time-point 2. The families still preferred home chemotherapy, partly due to the social benefits reported in their interview study (Stevens et al. 2006b); this is supported by our findings from the interviews (paper I) and the evaluation forms (paper II).

Close et al. used a parent-reported self-developed instrument in their controlled study (n = 14 with different cancer diagnoses comparing one chemotherapy treatment at home with a corresponding treatment at the hospital (Close et al. 1995). They found that the patients had significantly greater well being and better appetite, felt more independent, were more satisfied, and had greater ability to keep up with their school work when they received chemotherapy at home. Additionally, the parents were significantly better at keeping up with household tasks, maintaining their jobs, and spending time with one another and with their other children during HBHC. Their findings may indicate that their instrument may be more sensitive to the effect of HBHC on the family.

Razzouk et al. is one of the few randomized controlled studies that use PedsQL^{TM} Generic Core and Cancer Modules (Razzouk et al. 2006). They assessed the effect of the medication Epoetin Alfa in children with ALL or Lymphoma and found no significant differences in PedsQL^{TM} scores between treatment groups. The PedsQL^{TM} Cancer Module mean scores in their study were overall higher than in our study, while the PedsQL^{TM} Generic Core scores were generally similar to the HBHC group at time point 2.

We found no significant differences between treatment groups in the PedsQL^{TM} Family Impact Module or PedsQL^{TM} Satisfaction with Health Care at time point 2 after adjustments for confounding factors. Still, there was an indication of higher scores in the SHC group in the PedsQL^{TM} Satisfaction with Health Care in the total, inclusion of family, communication and emotional needs scores indicating that these needs may be better fulfilled at the hospital. On the contrary, families in the interview study described that they were particularly satisfied with the communication and the fulfilment of emotional needs when receiving HBHC. These findings indicate that there may be perceived dimensions in the child's HRQOL, the psychosocial impact on the family, and satisfaction with health care at the paediatric oncology department that remain the same regardless of the place of treatment delivery. It may also indicate that the effect of HBHC was not large enough (median 9 HBHC visits per child) to be reflected in the parents' scores in these modules.

Methodological considerations

The primary strengths of the present studies include the reflection of clinical practice, the broad sample of children with cancer and their families, the use of both qualitative and quantitative methods in the evaluation of a complex programme and the detailed information on the feasibility and acceptability of the HBHC programme. A further strength is the high recruitment of children admitted to the pediatric oncology department into the HBHC programme and the maintenance of safety and quality of care. In this study, we used repeated measures and assessed the child's HRQOL and the psychosocial impact on the family at two time points with both parent-proxy and self-reports, although it would also have been useful to assess the effect over a longer period of time. However, to our knowledge, this thesis comprises the largest controlled study with HBHC provided by hospital-based nurses for children with cancer to date.

We used a non-randomised design and acknowledge that this design is more susceptible to bias than a randomised design. Moreover, the clinical diversity and the measurement methods used entail certain limitations, which also may affect the validity of the results. These considerations are discussed below.

Trustworthiness

Qualitative research is advantageous for evaluating complex programmes to show how the participants experience the programme in depth and for assessing the process of implementation, which can further validate the findings (Campbell et al. 2000). A qualitative content analysis described by Graneheim & Lundman (Graneheim, Lundman 2004) was chosen for describing the phenomenon in the study. This approach was chosen because content analysis provides a method for attaining a condensed and broad description of the phenomenon (Elo, Kyngas 2008). The analysis process and the findings should be described in detail in order to show the strengths and limitations and thereby the trustworthiness of the findings (Elo, Kyngas 2008).

The credibility of a study refers to whether the analysis process and data address the intended aim of the research (Graneheim, Lundman 2004) and whether the findings and interpretations are trustworthy. To establish the credibility of the data collection, a sample of 10-12 families with various backgrounds and different children's cancer diagnoses was chosen, although no children with solid tumours were included. The participants lived in both rural and urban areas. The sample was deemed adequate to describe the families' experiences in depth and to answer the research question (Patton 1990).

To establish the credibility of the analysis process, three members of the research team first performed the analyses independently and then jointly. A coding scheme was used by all three members to systematically distil the transcribed text to limited and controllable concepts and to enhance the consistency in coding (Potter, Levine-Donnerstein 1999). The three research members discussed and interpreted the findings in order to analyse how well codes, sub-themes and themes covered data, and to prevent relevant data from being systematically excluded or irrelevant data included. To verify the robustness of the findings, similarities and differences between the condensed meaning units, codes, sub-themes and themes were discussed and reflected upon throughout the analysis process until the authors reached agreement (Graneheim, Lundman 2004, Potter, Levine-Donnerstein 1999). To further strengthen the credibility of the study, the context, participants and analysis process are described in detail in text and tables to facilitate the judging of the findings.

Confirmability refers to whether the findings are grounded in data (Lincoln, Guba 1985) and whether preliminary interpretations and themes were discussed in peer discussions, seminars, or presentations with health care professionals and researchers. Descriptions of the analysis process and quotations from the interviews were also presented to represent the findings, which further strengthens the confirmability.

Dependability refers to the stability of the findings over time and changes made in the researcher's decisions during the analysis process (Graneheim, Lundman 2004, Lincoln, Guba 1985). To establish dependability, the interviewer had an open dialogue with the research team about the new insights that evolved from interviews as these new insights might narrow or diffuse the aim of the interview. The three research members judged to what extent similarities and differences of content were consistent over time by discussing and considering them throughout the analysis process. A fourth researcher with long-time experience in paediatric oncology took part in the final analysis to verify the plausibility of the findings.

'Transferability' refers to whether the findings could be transferred to other settings or groups. A detailed description of context and participants, data collection, analysis process and findings were presented in the thesis and Paper 1 to facilitate the transferability of the findings (Graneheim, Lundman 2004). The findings may be applicable to other settings for HBHC of childhood cancer, although individuals and their experiences are unique.

The interviewer responsible for the assessment of the HBHC has experience as a paediatric oncology nurse. On the one hand, this involves a risk of restricting the families' stories or jumping

to conclusions too quickly. It may also influence the family members' descriptions as they may withhold negative perceptions of the HBHC. However, the interviewer did not disclose to the families that the interviewer had also initiated the HBHC programme. On the other hand, the interviewer's knowledge about the course of illness and the HBHC may make the families feel more confident and facilitate the interviews. Therefore, the interviewer considered any presumptions together with the research team in order to make them explicit.

Internal validity

Bias

Non-randomised design

The choice of a non-randomised design with group stratification based on geography reflects logistic and ethical considerations. The aim of the thesis was to test both feasibility including costs, overall satisfaction with HBHC, and focused analyses of specific QOL domains. A randomised design might reduce the willingness to participate. In addition, randomisation would prevent half of the potential recipients to receive HBHC. Furthermore, due to the geographical distribution of our families, only 2/3rd of all patients would live within the geographical distance feasible for home visits. As an alternative and since we regarded HBHC to be safe we chose the geographical stratification to increase the participation rate. The compliance of >95% in the HBHC programme not only demonstrates that the families perceived HBHC as a "safe" alternative but in addition and even more important, due to the high participation rate the included families in the HBHC programme are truly representative of the childhood cancer families. Furthermore, it would have been difficult to avoid interactions between families in the two groups and the health care professionals, which would further impair randomization since the groups might be unbalanced.

Power

The confidence intervals in the adjusted scores indicate that the PedsQL^{TM}-Generic scores might have reached significance with a larger sample size. Even though we did not reach statistical significance in PedsQL^{TM} scores the consistency in the observed tendencies should be noted as these findings may have clinical relevance.

Inconsistencies in inclusion into HBHC programme and controlled study

It is a methodological weakness that children in the HBHC group received home visits before completing the first questionnaire, as we cannot determine whether the HBHC group and SHC group would have had similar mean value scores in the PedsQL^{TM} instruments at time point 1. Furthermore, the parent-reported mean values in the PedsQL^{TM} Generic Core were significantly higher for total score, psychosocial health and social functioning in the HBHC group at time-point 1, which could reflect either the 20 children that already received home visits before responding to the time point 1 questionnaire, or other less obvious causes. Due to both logistical and ethical considerations, we did not regard mandatory completion of the questionnaire baseline before any HBHC visit would be offered for these psychosocially burdened families as being justifiable. Further analyses will be done to adjust for the time-lag and other potential confounders.

Historical control group

In the controlled study (Paper II), the historical control group was a precondition for obtaining a sufficient number of participants in the SHC group for comparison with the HBHC group. A systematic bias can be induced by using a historical control group as the participants may not experience the same underlying secular trends or changes over time (Eccles et al. 2003). This may lead to overestimates of effectiveness of the intervention and to a control group, which is not truly comparable with the intervention group (Deeks et al. 2003). In the present study, the average time period since diagnosis at time point 1 was three months in the HBHC group and 12 months in the historical SHC group. Studies suggest that HRQOL decreases the months following a cancer diagnosis and improves over time (Meeske et al. 2004, Hinds et al. 2009, Klaassen et al. 2010, Penn et al. 2008). Furthermore, the inclusion to the historical control group was initiated nine months before the HBHC programme began and all protocols except for the treatment protocol of ALL were unchanged during the inclusion period. Thus, the variation over time it is not likely to be considerable. These things considered, diminishes the probability of an overestimation of the results.

Measurement methods

In the feasibility study (Paper II), all families handed in the evaluation form after each home care visit and less than 5% of the items were missing over all the forms indicating that the families had no difficulty in responding to the items. However, even though the form was anonymous and the HBHC nurse did not see the answers because they were put in a sealed envelope, the families

completed the form while the HBHC nurse was present in the home. This may have influenced the reporting, as we do not know if the nurse's presence influenced the parents' response and this may be reflected in the high safety and satisfaction rate and the preference for care.

The questionnaire booklet in the controlled study was time- and energy consuming to complete. The questionnaire was posted by mail to the parents as we assumed that it would be more convenient for the families to complete the questionnaire at home whenever it fit in with their daily routine and we wished to take into consideration the families' need for time. The response rate is probably affected by the extent of the questionnaire. A shorter questionnaire, a telephone interview, or completion at an appointed outpatient visit might have achieved a higher response rate (Nathan, Furlong & Barr 2004, Jenney 1998). Families in the HBHC group may not be representative of all the families in the HBHC programme. The questionnaire booklet was time-consuming to complete suggesting that parents in the HBHC group may have more mental energy than non-participants and adherence thus may reflect both capabilities and motivations. However, it is unlikely that non-participating families would answer differently, considering the high satisfaction and preference for HBHC combined with the findings in the interview study.

We chose to include families with children younger than two years of age in study 3 as this patient group was included in the HBHC programme. However, the PedsQL™ is not validated for children younger than two years of age and this may cause imprecise PedsQL™ scores. The parents could comment on the questionnaire booklet in free text at the end of the questionnaire and some parents stated that it was difficult to complete the PedsQL™ Generic Core and Cancer Modules for children younger than 4 years of age. Moreover, the children did not receive individual PedsQL™ instruments and the parents read the items out loud for children aged five to seven years and maybe to children older than seven years of age. This methodology implies both advantages and disadvantages. Children may have difficulties completing questions that have multiple responses and limited understanding of negatively worded items (Nathan, Furlong & Barr 2004) as found in the PedsQL™ instruments and the parents could then facilitate the understanding of the questions. However, the children's responses may also be influenced by the parents' presence as children have a tendency to agree with the interviewer (Nathan, Furlong & Barr 2004). The shortcomings of the measurement methods may have attenuated the results as mentioned above but we do not consider this to have biased the results in any specific direction.

Number and type of HBHC visits

In the statistical analyses in the controlled study, we did not differentiate between the number of HBHC visits and the type of treatments the children received and this may have biased our results. An explorative sub-group analysis showed that children (n=4) who received more than 9 visits scored higher in the PedsQL^{TM}-Generic total score compared to other children in the HBHC group but there were no differences in parent-reports (n=17). This subset result must be interpreted with caution. It is possible that the effect of HBHC is more apparent in children e.g. with ALL or lymphomas who generally received more home care visits than children with other diagnoses. However, the trend towards higher scores indicates that HBHC may have an effect regardless of treatment type and number of HBHC visits; this is supported by the findings in the interview study.

Selection bias

In the feasibility study (Paper II and Thesis), we included 94% of the 54 eligible families. The three families who declined to participate did not differ from the participating families in clinical and demographic characteristics. Two families declined participation because the treatment protocol included only few hospitals visits. They preferred the treatments to be provided during more visits at the hospital. Furthermore, the HBHC programme was not suitable for patients with complex medical conditions necessitating hospital visits and these children are likely to be underrepresented in the HBHC programme.

The controlled study (Paper II) included 55% of the families participating in the HBHC programme. However, the HBHC group may not be representative of the all parents participating in the HBHC programme. Those who benefited the most or the least from the HBHC may not be among the included families. The non-participant group was comparable to the participant group in clinical and demographic characteristics. We thus consider potential bias from these characteristics to be reduced. The SHC group may include more patients with complex medical conditions necessitating hospital visits, as the HBHC programme was not suitable for this patient group. The probability that this difference would be large enough to statistically affect the PedsQL^{TM} scores is low. However, it is a clinically important aspect when considering the implementation of a HBHC programme.

Classification of diagnosis in three groups

We classified the diagnoses into three diagnostic groups. However, the treatment intensity varies greatly within a given group e.g. the classification of solid tumours do not take into account the

treatment differences between Ewing's sarcoma and Wilms' tumour. The treatment intensity and the related side effects may affect the perceived burden of illness in the child and the family. However, the distribution of diagnoses was similar in the HBHC and SHC groups. Thus, the classification of diagnoses is not likely to bias the effect in a specific direction.

Potential conflict of interest

The author of the thesis prepared the HBHC programme together with two nurses and subsequently undertook the evaluation of the programme, which implies a possibility of bias. In non-randomised studies, the assigning of patients and outcome of treatment may be influenced by the investigator (Deeks et al. 2003, McKee et al. 1999). In the present study, this was taken into account as the inclusion criteria were established a priori and all eligible patients that fulfilled the criteria were invited to participate in the HBHC programme. Only three eligible families declined to participate. The HBHC nurse assigned children to the HBHC programme after consulting the author of the thesis and a paediatric oncologist, who always could veto the inclusion. The influence of the author of the thesis was thereby diminished in the assignment process. Furthermore, the effect of the researcher should be assessed during all steps of the research process in order to account for potential bias (Malterud 2001). This effect was reflected upon throughout the study and data were discussed in the research group, peer discussions, and with the health care professionals at the paediatric oncology department to decrease the risk of subjectively influencing the interpretation of the results. Thus, it is unlikely that the potential conflict of interest have caused a considerable over- or underestimation of the treatment effect.

Confounding factors

Heterogeneity of the groups

The assignment distance and the inclusion of the broad sample of children with different diagnoses and ages were a precondition for implementing a feasible HBHC and for detecting the average effect of the HBHC intervention across this diverse group. To minimize bias due to these conditions, we adjusted for diagnosis, time since diagnosis, age, and gender when comparing PedsQL^{TM} scores between the HBHC group and the SHC group. Most of the estimates in PedsQL^{TM} Generic Core, Cancer Module and Health Care Satisfaction Module that were significant in the unadjusted analyses became insignificant after adjustment. The adjustment indicates that the effects of diagnosis, time since diagnosis, age, and gender may constitute a major cause of the differences between the groups than the HBHC. However, the significant differences in the adjusted PedsQL^{TM}

Generic Core and Cancer Modules and the trends towards higher scores in the HBHC group in PedsQL^{TM} Generic Core indicate that HBHC has a measurable effect.

The HBHC and SHC groups were comparable except for and time since diagnosis and distance from the hospital, which were both greater in the SHC group. We did not adjust for the parents' education level however, household income did not differ between the groups, indicating that a considerable overestimate of the effect of HBHC is unlikely.

Assignment distance from the university hospital

Families in the HBHC programme and HBHC group resided within the assignment area of 50 km from the university hospital. Parents' education level was higher in the HBHC group, which may reflect an effect of location as families living close to the hospital might in general be better educated and economically advantaged. This may be reflected in the higher PedsQL^{TM} Generic and Cancer Module scores in the HBHC group. When education was included in the statistical model, it was found to overall accentuate the significance in mean scores indicating that education has no considerable confounding effect. There are potential socioeconomic and cultural differences associated with living in urban or rural areas in Denmark, which may have an effect on the HRQOL scores. Studies from Canada suggest that socioeconomic factors may influence the HRQOL (assessed by PedsQL^{TM}) in childhood cancer e.g. children with ALL with lower household incomes had worse HRQOL (Sung et al. 2009) Though, they did not find the association with parents' education level. Thus, household income, rather than the parents' education level may predict HRQOL and household income did not differ between groups in our study. When distance was included in our statistical model, it was found to overall accentuate the significant differences in mean scores indicating that distance has no considerable confounding effect.

However, the socioeconomic differences between the HBHC and SHC groups are not likely to be considerable. Forty-five% of Denmark's population live within the paediatric oncology department's catchment area. Moreover, the childhood cancer population do not probably differ from the Danish population background as there is no indication that socioeconomic factors influence the psychosocial effects on childhood cancer survivors in Denmark (Koch et al. 2004, Koch et al. 2006). Thus, it is unlikely that the effect of HBHC is overestimated due to the distance of the patients from the hospital.

Despite the methodological limitations discussed above, we believe that the results are reliable but must be viewed with caution and further studies are necessary for strengthening the evidence.

External validity

Representativeness

The selected population is assumed to be representative for the childhood cancer population to which the programme is likely to be offered when implemented. The treatment protocols are the same at all hospitals treating childhood cancer in Denmark indicating that our results may be extrapolated to other settings of childhood cancer in Denmark. The HBHC programme may be applicable to a selected population in countries with similar health care systems.

Qualitative and quantitative methods

The work in this thesis was based on the different interacting phases of a complex programme, which entail an evaluation with both qualitative and quantitative evidence (Campbell et al. 2000). The interviews were conducted while the interviewees were still participating in or had finished the HBHC programme. The analyses and interpretation of results of the questionnaires in the controlled study were conducted after the programme and the interviews had ended. Thus, we avoided being influenced by the results from the questionnaire study when we conducted the interviews according to our aim in the interview study. The findings from the interview study and the controlled study were analysed and discussed separately but comparisons were made between the results when attempting to explain the findings from the controlled study. The interview findings increased our opinion that HBHC could have a psychosocial benefit for the children and their families even though we could not detect all the aspects of the psychosocial impact by statistical means.

CONCLUSIONS AND RELEVANCE TO CLINICAL PRACTICE

Paediatric health care providers currently have little evidence of the effects of HBHC when considering programme development for children with cancer. This thesis adds to the knowledge base by showing that HBHC may safely replace hospital visits at equal or lower costs and with high parent satisfaction and preference for HBHC. Moreover, the children's quality of life may be enhanced in specific aspects and the family member's experiences showed that HBHC may support the families throughout the course of treatment. In addition, it seems that the HBHC provides care that supports the families' and the individuals' perceived needs to maintain family functions as well as alleviating perceived distress. The study highlights the importance of providing HBHC in accordance with the family members' needs for a sense of safety, and that this can be achieved by using experienced paediatric oncology nurses and regular hospital visits as well as scheduling regular appointments with the paediatric oncologist.

Due to the preliminary findings from the HBHC programme, HBHC was implemented as routine care at the paediatric oncology department in February 2010.

FUTURE RESEARCH

Future studies should address the following issues to complement the research presented in this thesis:

- Exploratory sub-group analyses to identify specific subgroups of patients for whom HBHC may be more effective.
- Assessment of the incidence of infections and unexpected hospital admissions related to HBHC.
- HRQOL assessments during different phases of therapy on the basis of serial ratings.
- Individual interviews with the children participating in the HBHC including children with solid tumours and siblings.
- Focus-group interviews with the nurses to explore their experience of providing treatment and care in the patients' homes.
- Economic evaluations that include both actual and indirect costs.
- Future reviews on HBHC for children with cancer including relevant qualitative studies and data from a broader range of study designs to improve the synthesis and interpretation of the programmes.

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APPENDIX 1

Content list for protocols with instructions for managing HBHC	
1. Chemotherapy	**14. Bloodtransfusion**
✓ Vincristine	✓ Sag-m
✓ Cytarabine	✓ TK
✓ Velbe	**15. Nasogastric tube**
✓ Dactinomycin	✓ Application
✓ Preparations of chemotherapy	✓ Care
✓ Storage	✓ Nuitrition
2. Antibiotics	**16. Percutaneous Endosopic Gastromy**
✓ Meropenem	✓ Care
✓ Hexamycin	✓ Precautions
✓ Vancomycin-plug	**17. Car**
✓ Metronidazol	**18. Parking**
✓ Aciclovir	**19. Petrol**
✓ Bactrim	**20. Mobile phone**
✓ Cancidas	**21. Adverse events**
✓ Ciproxin	**22. Waste**
✓ Diclocil	✓ Chemotherapy
✓ Vfend	✓ Needles, other sharp objects
✓ Diflucan	✓ Various waste
✓ Preparations of antibiotics	**23. Plan of the day**
✓ Storage	✓ Tasks
3. Granocyte	✓ Division of labour in the shifts
4. Innohep	✓ Time per. patient/Tasks
5. CVK/PAC	✓ Various meetings
✓ Care	**24. Content of the car/ Store**
✓ Precautions	✓ Checklist
6. Hygiene	✓ Best before date
7. Bloodsamples	**25. Content of the Nursing bag**
✓ Peripheral	✓ Checklist
✓ CVK	**26. Content of the Emergency bag**
✓ PAC	✓ Checklist
8. Analgesia	**25. Mileage records**
9. Patient Controlled Analgesic pump	**27. Telephone list**
10. Stomatitis care	**28. Prewritten prescriptions**
11. Nausea treatment	
12. Anaphylactic treatment	
13. Febrile	

APPENDIX 2

Færdigregistrering af patienter.

Behandling i den udgående funktion. Procedurekode AAF6 5051-AE 3782

Navn og CPR. nr.	Dato:	Udfyldt af: Klokkeslæt:

Grunddiagnose:		Ambulant
		Indlagt på inf. 5051 (cytosar)
		Indlagt på sengeafd. (AB)

REGISTRERING AF YDELSER/KODER.

	Kode	Procedurer
Cytostatika		
	BWHA1	Cytostatisk behandling, basis, ambulant uden hydrering, samt pr. os cytostatika
	BWHA2	Cytostatisk behandling under indlæggelse, en serie der bliver givet flere dage i træk
		Vincristin
		Bleomycin
		Cytosar
		Dactinomycin
		Velbe / Vinblastin
Antibiotika		
	BPHB2	Beta-lactam (meropenem)
	BPHY4	Quinoloner (ciproxin)
	BPHY5	Behandling med metronidazol
		Vfend
		Gentamycin
Anden medicinsk behandling		
	BWAA60	Medicingivning ved intravenøs injektion
	BWAA31	Medicingivning ved subkutan injektion
	BWAA30	Medicingivning ved intramuskulær injektion
	BOHE20	Vækstfaktor: G-CSF (Neupogen og Granocyte)
	BAHY0	Stærkt analgeticum (opioder / PCA pumpe)
	BIHA81	Behandling med laksantium
	BWDB01	Udlevering af medicin som led i speciel behandling
	WEHKBXX	Synacten test
Ernæring		
	BIAZ00	Anlæggelse af nasogastrisk sonde
		Fjernelse af nasogastrisk sonde
	BILF1	Pleje af gastrostomi sonde
	BIBG0	Behandling med gastrisk sonde (Ernæring og/ eller medicin)

Diverse opgaver				
	BMBD01	Anvendelse af tunneleret CVK		CVK-stop
	BMBZ01A	Anlæggelse af gripper i port		Dyrkning / Venyler
	BMBZ21A	Fjernelse af gripper i port		Stomatitpleje
	BNPA0	Rensning af sår /pleje af CVK indstiksted		Drænagepleje
	BNPA80	Suturfjernelse		Temperaturmåling
		Blodprøver perifert		
		Blodprøver CVK/Port		Stuegang

Telefonsamtale						
	BVAA33A	Telefonsamtale				
		Hvem ringer op:			Pårørende	Sygeplejerske
		Årsag:				Varighed:

Tidsforbrug

Sygeplejerske:

Tidsforbrug transport:	Tidsforbrug besøg:

Forældre:

Hvor lang tid i alt vil I have brugt, hvis I skulle have været	
på hospitalet i stedet for i hjemmet (inkl. transport)?	Tidsforbrug:

Pårørende

Pårørende 1.

Hvor **tryg** var pårørende ved at barnet fik		Mor		Far
behandling hjemme?		Anden, hvem:		

slet ikke | en smule | i nogen grad | ret meget | i meget høj grad

Hvor **tilfreds** var pårørende med hjemmebesøget?

meget utilfreds | utilfreds | hverken tilfreds eller utilfreds | tilfreds | meget tilfreds

Pårørende 2.

Hvor **tryg** var pårørende ved at barnet fik		Mor		Far
behandling hjemme.		Anden, hvem:		

slet ikke | en smule | i nogen grad | ret meget | i meget høj grad

Hvor **tilfreds** var pårørende med hjemmebesøget?

meget utilfreds | utilfreds | hverken tilfreds eller utilfreds | tilfreds | meget tilfreds

		Mor		Far
Spørgsmål fra pårørende.		Anden, hvem:		
Samtale med pårørende, mere end 10 min.		Mor		Far
		Anden, hvem:		
Oplæring af pårørende.		Mor		Far
		Anden, hvem:		

Barn

Hvor **tryg** var barnet ved at få behandling i hjemmet.

slet ikke | en smule | i nogen grad | ret meget | i meget høj grad

Hvor **tilfreds** var barnet med hjemmebesøget?

meget utilfreds | utilfreds | hverken tilfreds eller utilfreds | tilfreds | meget tilfreds

Var hjemmebesøget medvirkende til at barnet:

		Ja		Nej
Kunne komme i skole?		Ja		Nej
Kunne komme i børnehaveklasse?		Ja		Nej
Kunne komme i daginstitution?		Ja		Nej
Kunne komme i SIV-huset?		Ja		Nej
Kunne komme til fritidsaktiviteter?		Ja		Nej
Kunne komme til hjemmeundervisning?		Ja		Nej
Andet:		Ja		Nej

Spørgsmål fra barn.

Samtale med barnet, mere end 10 min.

Årsager til at hjemmebesøget ikke kunne gennemføres	
	Familien var ikke hjemme
	Samarbejdsvanskligheder
	Trafik/bilproblemer
	Barnet er indlagt på afdelingen eller er indkaldt til ambulant kontrol. Udfyldes kun hvis BUS ikke er blevet oplyst herom og er kørt til hjemadresse.
	Anden årsag
	Hvilken:

Noter

APPENDIX 3

Table 10 extended version. Comparison of Generic Core and Cancer Module mean scores at time point 1

	Time point 1				
		Mean (SD)			
PedsQL™ Scales	**N**	**HBHC group**	**N**	**SHC group**	**p-value**
Generic Core					
Child self-report					
Total score	13	70.0 (18.60)	26	58.6 (14.84)	.05
Physical functioning/ physical health	13	66.7 (29.16)	26	50.6 (25.62)	.09
Psychosocial health	12	72.3 (18.66)	26	63.7 (13.96)	.12
Emotional functioning	13	75.4 (17.97)	26	64.4 (19.92)	.10
Social functioning	12	81.7 (20.15)	26	71.8 (17.51)	.13
School functioning	8	59.1 (30.09)	21	44.3 (17.51)	.11
Parent proxy					
Total score	40	66.8 (16.39)	62	58.8 (16.92)	.03
Physical health/ physical functioning	39	59.5 (26.25)	62	51.5 (26.36)	.15
Psychosocial health	40	72.5 (13.45)	59	64.2 (16.28)	.01
Emotional functioning	41	65.8 (15.33)	63	63.0 (17.71)	.48
Social functioning	39	82.4 (14.72)	59	72.5 (19.37)	.01
School functioning	16	57.9 (22.36)	34	46.7 (17.97)	.06
Cancer Module					
Child self-report					
Pain and hurt	13	65.4 (33.13)	26	59.6 (28.35)	.57
Nausea	13	61.5 (22.49)	26	62.7 (25.27)	.89
Procedural anxiety	13	62.8 (24.68)	26	61.2 (33.66)	.88
Treatment anxiety	13	84.6 (20.65)	26	86.9 (23.82)	.77
Worry	13	71.2 (33.44)	26	63.0 (24.90)	.40
Cognitive problems	12	70.3 (29.17)	24	65.4 (19.19)	.55
Perceived physical appearance	13	89.1 (22.41)	26	65.7 (26.18)	.009
Communication	13	69.2 (27.09)	26	65.0 (34.16)	.70
Parent proxy					
Pain and hurt	40	67.2 (23.63)	63	57.5 (28.00)	.06
Nausea	41	65.2 (21.55)	63	59.0 (25.31)	.16
Procedural anxiety	41	63.6 (33.16)	60	63.3 (33.76)	.95
Treatment anxiety	41	79.7 (19.55)	61	82.4 (22.16)	.51
Worry	40	83.5 (21.31)	58	77.0 (24.84)	.15
Cognitive problems	38	77.7 (17.98)	56	70.5 (20.59)	.07
Perceived physical appearance	38	80.4 (21.64)	58	72.7 (23.61)	.09
Communication	36	65.1 (32.42)	56	62.9 (32.01)	.96

APPENDIX 4

Table 11 extended version. Linear regression for Generic Core and Cancer Module at time point 1

PedsQL™ Scales	Time point 1			
	Crude β (95% CI)	p-value	Adjusted β 95% CI	p-value
Generic Core				
Child self-report				
Total score	11.4 (0.2–22.5)	.05	11.2 (-2.9–25.3)	.12
Physical Health Summary	16.0 (-2.4–34.5)	.09	21.5 (-1.5–44.5)	.07
Psychosocial Health Summary	8.6 (-2.4–19.6)	.12	5.1 (-8.5–18.8)	.45
Emotional functioning	11.0 (-2.3–24.2)	.10	9.3 (-7.4–26.0)	.27
Social functioning	9.9 (-3.1–22.9)	.13	6.3 (-9.0–21.6)	.41
School functioning	14.8 (-3.5–33.1)	.11	18.7 (-5.0–42.4)	.12
Parent proxy				
Total score	7.6 (0.9–14.3)	.03	9.9 (2.2–17.6)	.01
Physical Health Summary	7.7 (-2.9–18.2)	.15	17.4 (5.7–29.0)	.004
Psychosocial Health Summary	7.8 (1.6–14.0)	.01	2.4 (-4.4–9.1)	.49
Emotional functioning	2.4 (-4.3–9.0)	.48	0.7 (-6.9–8.3)	.86
Social functioning	9.3 (2.1–16.5)	.01	5.9 (-2.5–14.2)	.17
School functioning	11.1 (-0.7–23.0)	.06	2.4 (-11.7–16.5)	.74
Cancer Module				
Child self-report				
Pain and hurt	5.8 (-14.9–26.4)	.57	10.9 (-14.6–36.3)	.39
Nausea	-1.2 (17.9–15.6)	.89	4.0 (-14.7–22.8)	.66
Procedural anxiety	1.6 (19.8–23.0)	.88	17.1 (-8.3–42.5)	.18
Treatment anxiety	-2.2 (-18.0–13.5)	.77	3.0 (-14.7–20.7)	.73
Worry	8.2 (-11.1–27.4)	.40	4.5 (-18.1–27.2)	.69
Cognitive problems	4.9 (-11.6–21.3)	.55	-5.7 (-26.3–14.9)	.58
Perceived physical appearance	23.4 (6.2–40.6)	.009	30.6 (10.9–50.3)	.003
Communication	4.2 (-17.9–26.2)	.70	11.5 (-12.8–35.8)	.34
Parent proxy				
Pain and hurt	10.1 (-03.–20.6)	.06	13.7 (2.1–25.3)	.02
Nausea	6.7 (-2.8–16.1)	.16	12.1 (2.0–22.1)	.02
Procedural anxiety	-0.4 (-13.8–12.9)	.95	-1.7 (-16.6–13.3)	.83
Treatment anxiety	-2.8 (-11.2–5.6)	.51	1.9 (-8.1–11.9)	.71
Worry	6.9 (-2.5–16.4)	.15	4.8 (-5.3–14.8)	.35
Cognitive problems	7.4 (-0.7–15.4)	.07	-1.0 (-10.0–8.0)	.82
Perceived physical appearance	8.2 (-1.2–17.6)	.09	6.9 (-3.6–17.5)	.20
Communication	0.3 (-13.4–14.1)	.96	2.0 (-13.5–17.4)	.80

APPENDIX 5

Table 12 extended version. Comparison of Family Impact and Satisfaction with Health Care mean scores at time point 1

	Time point 1				
	Mean (SD)				
PedsQL™ Scales	**N**	**HBHC group**	**N**	**SHC group**	**p-value**
Family Impact Module					
Total score	43	58.7 (16.15)	64	59.9 (14.31)	.52
Parent HRQOL summary	43	60.2 (16.03)	64	61.6 (14.70)	.49
Family functioning summary	42	57.1 (23.04)	64	60.0 (18.91)	.33
Physical functioning	43	60.7 (17.35)	64	59.6 (18.53)	.87
Emotional functioning	43	62.3 (17.54)	64	62.7 (20.67)	.75
Social functioning	43	50.9 (22.64)	64	54.6 (22.64)	.32
Cognitive functioning	43	64.8 (21.38)	64	68.5 (15.42)	.24
Communication	42	72.6 (21.09)	64	69.8 (18.87)	.59
Worry	42	48.6 (20.46)	64	46.4 (21.26)	.68
Daily activities	42	51.2 (25.42)	63	46.7 (20.32)	.47
Family relationships	42	60.2 (25.70)	64	67.7 (22.48)	.07
Healthcare Satisfaction Module					
Total score	43	70.5 (13.76)	66	69.9 (12.38)	.92
Overall satisfaction	43	89.3 (14.47)	66	82.1 (15.21	.03
Information	43	69.7 (17.64)	66	72.0 (13.88)	.34
Inclusion of family	43	76.7 (18.72)	66	75.3 (15.52)	.94
Communication	43	69.0 (16.60)	66	71.5 (14.99)	.35
Technical skills	43	81.1 (13.31)	66	76.6 (16.49)	.28
Emotional needs	42	48.1 (12.44)	63	47.4 (13.92)	.98

APPENDIX 6

Table 13 extended version. Linear regression for Family Impact and Satisfaction with Health Care at time point 1

PedsQL™ Scales	Time point 1			
	Crude β 95% CI	p-value	Adjusted β 95% CI	p-value
Family Impact Module				
Total score	-2.0 (-7.9–4.0)	.52	0.2 (-6.9–7.2)	.96
Parent HRQOL summary	-2.1 (-8.1–3.9)	.48	0.5 (-7.6–6.7)	.90
Family functioning summary	-4.0 (-12.3–4.2)	.33	1.0 (-8.3–10.4)	.83
Physical functioning	0.6 (-6.4–7.6)	.87	4.2 (-3.9–12.4)	.30
Emotional functioning	-1.2 (-8.1–6.4)	.75	1.5 (-7.7–10.4)	.75
Social functioning	-4.4 (-13.3–4.4)	.32	-3.1 (-13.4–7.2)	.55
Cognitive functioning	-4.5 (-11.6–2.6)	.21	-6.1 (-14.6–2.3)	.15
Communication	2.1 (-5.7–9.9)	.59	0.5 (-8.6–9.6)	.92
Worry	1.7 (-6.5–9.9)	.68	2.4 (-7.2–12.1)	.62
Daily activities	3.3 (-5.7–12.3)	.47	12.0 (2.0–22.1)	.02
Family relationships	-8.6 (-18.0–0.8)	.07	-5.1 (-16.0–5.8)	.36
Healthcare Satisfaction Module				
Total score	0.5 (-4.4–5.5)	.83	0.5 (-5.3–6.2)	.88
Overall satisfaction	7.3 (1.6–13.1)	.01	5.9 (-0.8–12.5)	.09
Information	-2.1 (-8.1–3.8)	.48	-1.4 (-8.2–5.4)	.68
Inclusion of family	1.6 (-4.9–8.0)	.63	-2.3 (S:S.3–9.9)	.54
Communication	-3.0 (-9.1–3.0)	.32	-3.1 (-10.1–3.9)	.39
Technical skills	4.3 (-1.6–10.2)	.15	2.8 (-4.0–9.6)	.42
Emotional needs	0.5 (-4.7–5.8)	.84	2.3 (-4.0–8.5)	.47

APPENDIX 7

Extracted from the questionnaire booklet:

- PedsQL™ Generic Core parent-proxy report for children 5 – 7 years of age
- PedsQL™ Cancer Module parent-proxy report for children 5 – 7 years of age
- PedsQL™ Generic Core child self-report for children 5 – 7 years of age
- PedsQL™Cancer Module child self-report for children 5 – 7 years of age
- PedsQL™ Family Impact Module
- PedsQL™ Healthcare Satisfaction Generic Module

DE NÆSTE SPØRGSMÅL HANDLER OM DIN VURDERING AF DIT BARNS GENERELLE LIVSKVALITET

43. På følgende side finder du en liste over mulige problemer for dit barn. Angiv hvor store problemerne har været for dit barn inden for den sidste måned ved at sætte en ring omkring det tal som passer bedst.

Indenfor den sidste måned, hvor store problemer har dit barn haft med:

		Aldrig	Næsten aldrig	Nogle gange	Ofte	Næsten altid
	Fysisk sundhed og aktiviteter					
1.	Problemer med at gå mere end 100 meter……..	0	1	2	3	4
2.	Problemer med at løbe……	0	1	2	3	4
3.	Problemer med at dyrke sport eller motion..…….……	0	1	2	3	4
4.	Problemer med at løfte tungt..……	0	1	2	3	4
5.	Problemer for ham/hende at tage et bad...……..	0	1	2	3	4
6.	Problemer med at udføre pligter i hjemmet, som at samle sit legetøj op...	0	1	2	3	4
7.	Problemer med at have ondt eller have smerter…….....	0	1	2	3	4
8.	Problemer med mangel på energi……	0	1	2	3	4
	Følelser					
1.	Han/hun er bange……..……	0	1	2	3	4
2.	Han/hun er ked af det eller i dårligt humør…..……	0	1	2	3	4
3.	Han/hun er vred…...……	0	1	2	3	4
4.	Han/hun har problemer med at sove….	0	1	2	3	4
5.	Han/hun er bekymret for hvad der vil ske med ham/hende……	0	1	2	3	4
	Sociale aktiviteter					
1.	Problemer med at være sammen med andre børn……	0	1	2	3	4
2.	De andre børn vil ikke lege med ham/hende……..……	0	1	2	3	4
3.	De andre børn driller ham/hende..……	0	1	2	3	4
4.	Problemer med at gøre de ting, som andre børn på hans/hendes alder kan...	0	1	2	3	4
5.	Problemer med at følge med når han/hun leger med de andre børn...……	0	1	2	3	4

		Aldrig	Næsten aldrig	Nogle gange	Ofte	Næsten altid
	Skoleaktiviteter					
1.	Problemer med at koncentrere sig eller høre efter i timen…..……..	0	1	2	3	4
2.	Han/hun har problemer med at huske ting…….……..	0	1	2	3	4
3.	Han/hun har problemer med at lave alle sine lektier…….……..	0	1	2	3	4
4.	Bliver hjemme fra skole, når han/hun er syg...……..	0	1	2	3	4
5.	Går ikke i skole, når han/hun skal til lægen eller på sygehuset…..……...	0	1	2	3	4

DE NÆSTE SPØRGSMÅL HANDLER OM DIN VURDERING AF DIT BARNS LIVSKVALITET I FORHOLD TIL CANCERSYGDOMMEN

44. Indenfor den sidste måned, hvor store problemer har dit barn haft med:

		Aldrig	Næsten aldrig	Nogle gange	Ofte	Næsten altid
	Smerte og svie					
1.	Smerter i led og/eller muskler…….	0	1	2	3	4
2.	Har mange smerter……	0	1	2	3	4
	Kvalme					
1.	At få kvalme under medicinske behandlinger……..	0	1	2	3	4
2.	At mad ikke smager ham/hende særlig godt…….	0	1	2	3	4
3.	At få kvalme, når han/hun tænker på medicinske behandlinger…….	0	1	2	3	4
4.	At have for meget kvalme til at kunne spise……	0	1	2	3	4
5.	At nogle retter og dufte giver ham/hende kvalme……	0	1	2	3	4
	Procedureangst					
1.	At nålestik (f.eks. injektioner, drop) gør ondt på ham/hende.……	0	1	2	3	4
2.	Angst i forbindelse med at få taget blodprøver……	0	1	2	3	4
3.	Angst i forbindelse med nålestik (f.eks. Injektioner, drop)…..……..	0	1	2	3	4

		Aldrig	Næsten aldrig	Nogle gange	Ofte	Næsten altid
	Behandlingsangst					
1.	Bliver ængstelig når han/hun venter på at skulle ind til læge……	0	1	2	3	4
2.	Bliver ængstelig når han/hun skal til læge……	0	1	2	3	4
3.	Bliver ængstelig når han/hun skal på hospitalet……..	0	1	2	3	4
	Bekymring					
1.	Bekymring for bivirkninger ved medicinske behandlinger…….	0	1	2	3	4
2.	Bekymring for om hans/hendes medicinske behandlinger virker eller ej…….	0	1	2	3	4
3.	Bekymring for om cancersygdommen vender tilbage og vedkommende får tilbagefald……	0	1	2	3	4
	Kognitive problemer					
1.	Svært ved at finde ud af, hvad han/hun skal gøre, når noget er svært for ham/hende…….	0	1	2	3	4
2.	Svært ved tal og at løse matematik-opgaver……	0	1	2	3	4
3.	Svært ved at koncentrere sig……..	0	1	2	3	4
4.	Svært ved at huske hvad der bliver læst op for ham /hende……	0	1	2	3	4
	Opfattelsen af sit fysiske udseende					
1.	Føler at han/hun ikke ser godt ud……..	0	1	2	3	4
2.	Bryder sig om, at andre ser hans/hendes ar……	0	1	2	3	4
3.	Bliver genert, når andre ser hans/hendes krop…….	0	1	2	3	4
	Kommunikation					
1.	Svært ved at fortælle lægerne og sygeplejerskerne, hvordan han/hun har det…….	0	1	2	3	4
2.	Svært ved at stille spørgsmål til lægerne og sygeplejerskerne……..	0	1	2	3	4
3.	Svært ved at forklare andre mennesker om hans/hendes sygdom……	0	1	2	3	4

DE NÆSTE SPØRGSMÅL SKAL DIT BARN SELV SVARE PÅ.
DE HANDLER OM HANS/HENDES GENERELLE LIVSKVALITET

45. **Vejledning til forælder eller interviewer - sådan udfylder du og dit barn skemaet sammen:**

Sig f.eks.: "Jeg vil stille dig nogle spørgsmål om ting, der nogle gange er et problem for børn. Jeg vil gerne have dig til at fortælle mig, hvor stort et problem de ting er for dig."

Vis barnet skabelonen og peg på svarmulighederne imens du læser højt.

"Hvis det aldrig er et problem for dig, peger du på det glade ansigt

Hvis det nogle gange er et problem for dig, peger du på det midterste ansigt

Hvis det næsten altid er et problem for dig, peger du på det sure ansigt"

"Jeg vil læse hvert spørgsmål højt. Peg på ansigterne for at vise mig, hvor stort et problem det er for dig. Lad os prøve en gang."

	Aldrig	Nogle gange	Næsten altid
Er det svært for dig at knipse med fingrene?	☺	😐	☹

Bed barnet om at knipse med fingrene for at se om spørgsmålet blev besvaret korrekt. Gentag spørgsmålet hvis barnet viser en svarmulighed, der er forskellig fra hans/hendes demonstration.

"Tænk på hvordan du har haft det inden for de sidste par uger. Lyt omhyggeligt til hvert af spørgsmålene og fortæl mig, hvor stort et problem dette er for dig."

Spørgsmålet læses højt. Herefter peges på skabelonen. Hvis barnet tøver eller ikke ser ud til at forstå hvordan det skal besvare spørgsmålet, skal svarmulighederne gennemgåes igen, mens der peges på ansigterne.

		Aldrig	Nogle gange	Næsten altid
	Fysiske aktiviteter			
1.	Er det svært for dig at gå…….……	0	2	4
2.	Er det svært for dig at løbe……...……	0	2	4
3.	Er det svært for dig at dyrke sport eller motion….	0	2	4
4.	Er det svært for dig at løfte store ting…….……..	0	2	4
5.	Er det svært for dig at tage bad……...……...	0	2	4
6.	Er det svært for dig at udføre pligter (som at samle legetøj op)…….…….	0	2	4
7.	Har du ondt eller smerter (Hvor_____)…	0	2	4
8.	Er du for træt til at lege……...…….	0	2	4
	Følelser			
1.	Føler du dig bange…….……	0	2	4
2.	Føler du dig ked af det……..	0	2	4
3.	Føler du dig vred…….	0	2	4
4.	Har du svært ved at sove……..	0	2	4
5.	Tænker du på hvad der vi ske med dig……	0	2	4
	Sociale aktiviteter			
1.	Er det svært for dig at være sammen med andre børn……	0	2	4
2.	Siger de andre børn, at de ikke vil lege med dig…	0	2	4
3.	Driller de andre børn dig…….	0	2	4
4.	Kan de andre børn gøre ting du ikke kan……	0	2	4
5.	Er det svært for dig at følge med, når du leger med andre børn……	0	2	4
	Skoleaktiviteter			
1.	Er det svært for dig at koncentrere dig eller høre efter i timen…….	0	2	4
2.	Har du problemer med at huske ting……..	0	2	4
3.	Har du svært ved at lave lektier……	0	2	4
4.	Bliver du hjemme fra skolen, når du er syg……	0	2	4
5.	Går du ikke i skole, når du skal til lægen eller på sygehuset……..	0	2	4

DE NÆSTE SPØRGSMÅL HANDLER OM DIT BARNS EGEN VURDERING AF SIN LIVSKVALITET I FORHOLD TIL CANCERSYGDOMMEN

46. ***"Tænk på hvordan du har haft det inden for de sidste par uger. Lyt omhyggeligt til hvert af spørgsmålene og fortæl mig, hvor stort et problem dette er for dig."***

		Aldrig	Nogle gange	Næsten altid
	Smerte og svie			
1.	Smerter eller gør det ondt i dine knogler og/eller muskler……..	0	2	4
2.	Har du mange smerter……	0	2	4
	Kvalme			
1.	Får du kvalme af din medicin……	0	2	4
2.	Smager mad dig dårligt…..…….	0	2	4
3.	Får du kvalme, når du tænker på din medicin……	0	2	4
4.	Har du så meget kvalme, at du ikke kan spise….	0	2	4
5.	Er der nogle madretter og lugte, der giver dig kvalme……..	0	2	4
	Procedureangst			
1.	Gør nålestik ondt (f.eks. injektioner, drop)…….	0	2	4
2.	Bliver du bange når du skal have taget blodprøver…….	0	2	4
3.	Bliver du bange når du skal stikkes med nåle (f.eks. injektioner, drop)…….	0	2	4
	Behandlingsangst			
1.	Bliver du bange, når du venter på at skulle til lægen……	0	2	4
2.	Bliver du bange, når du skal til lægen…….	0	2	4
3.	Bliver du bange, når du skal på sygehuset…….	0	2	4
	Bekymring			
1.	Er du bekymret for hvordan du får det, når du har fået medicin……..	0	2	4
2.	Er du bekymret for om medicinen virker eller ej....	0	2	4
3.	Er du bekymret for om kræftsygdommen kommer igen……	0	2	4

		Aldrig	Nogle gange	Næsten altid
	Kognitive problemer			
1.	Ved du hvad du skal gøre, når der er noget der er svært for dig…….	0	2	4
2.	Er det svært for dig at arbejde med tal eller lave matematik……	0	2	4
3.	Er det svært for dig at koncentrere dig……	0	2	4
4.	Er det svært for dig at huske, hvad der bliver læst op for dig……..	0	2	4

"Tænk på hvordan du har haft det inden for de sidste par uger. Lyt omhyggeligt til hvert af spørgsmålene og fortæl mig, hvor stort et problem dette er for dig."

	Opfattelsen af det fysiske udseende			
1.	Føler du, at du ikke ser godt ud……..	0	2	4
2.	Generer det dig, at andre mennesker ser dine ar….....	0	2	4
3.	Bliver du flov, når andre ser din krop……	0	2	4
	Kommunikation			
1.	Er det svært for dig at fortælle lægerne og sygeplejerskerne, hvordan du har det…….	0	2	4
2.	Er det svært for dig at stille spørgsmål til lægerne og sygeplejerskerne……	0	2	4
3.	Er det svært for dig at fortælle andre, at du er syg……	0	2	4

DE NÆSTE SPØRGSMÅL HANDLER OM HVILKEN INDVIRKNING BARNETS CANCERSYGDOM HAR PÅ FAMILIEN

47. Børnefamilier har nogle gange særlige bekymringer eller vanskeligheder på grund af barnets helbred. Angiv hvor stort et problem, det har været for dig inden for den sidste måned ved at sætte en ring omkring det tal som passer bedst.

Indenfor den sidste måned, hvor store problemer har du, som følge dit barns helbred, haft med:

		Aldrig	Næsten aldrig	Nogle gange	Ofte	Næsten altid
	Fysiske funktioner					
1.	Jeg føler mig træt i løbet af dagen……..	0	1	2	3	4
2.	Jeg føler mig træt, når jeg vågner om morgenen…….	0	1	2	3	4
3.	Jeg føler mig for træt til at gøre de ting, som jeg kan lide……	0	1	2	3	4
4.	Jeg får hovedpine……..	0	1	2	3	4
5.	Jeg føler mig fysisk svag……..	0	1	2	3	4
6.	Jeg har kvalme……..	0	1	2	3	4
	Følelsesmæssige funktioner					
1.	Jeg føler mig ængstelig……	0	1	2	3	4
2.	Jeg føler mig ked af det……	0	1	2	3	4
3.	Jeg føler mig vred……..	0	1	2	3	4
4.	Jeg føler mig frustreret…….	0	1	2	3	4
5.	Jeg føler mig hjælpeløs eller håbløs.....	0	1	2	3	4
	Sociale funktioner					
1.	Jeg føler mig isoleret fra andre……	0	1	2	3	4
2.	Jeg har svært ved at støtte fra andre…..	0	1	2	3	4
3.	Det er svært at finde tid til sociale aktiviteter……	0	1	2	3	4
4.	Jeg har ikke energi nok til sociale aktiviteter……	0	1	2	3	4
	Kognitive funktioner					
1.	Det er svært for mig at holde opmærksomheden på ting……..	0	1	2	3	4
2.	Det er svært for mig at huske, hvad folk fortæller mig……	0	1	2	3	4
3.	Det er svært for mig at huske, hvad jeg lige har hørt……	0	1	2	3	4
4.	Det er svært for mig at tænke hurtigt….	0	1	2	3	4
5.	Det er svært for mig at huske, hvad jeg lige har tænkt på……..	0	1	2	3	4

		Aldrig	Næsten aldrig	Nogle gange	Ofte	Næsten altid
	Kommunikation					
1.	Jeg føler, at andre ikke forstår min families situation……	0	1	2	3	4
2.	Det er svært for mig at tale med andre om mit barns helbred……	0	1	2	3	4
3.	Det er svært for mig at fortælle læger og sygeplejersker, hvordan jeg har det..	0	1	2	3	4
	Bekymring					
1.	Jeg er bekymret for, om mit barns medicinske behandlinger virker eller ej..	0	1	2	3	4
2.	Jeg er bekymret for, de bivirkninger der er ved de medicinske behandlinger, som mit barn får…….	0	1	2	3	4
3.	Jeg er bekymret for, hvordan andre vil reagere på mit barns tilstand……..	0	1	2	3	4
4.	Jeg er bekymret for, hvordan mit barns sygdom indvirker på andre familie-medlemmer……..	0	1	2	3	4
5.	Jeg er bekymret for mit barns fremtid…	0	1	2	3	4

Nedenfor er der en liste over emner, som kan være et problem for din familie.
Angiv hvor stort et problem hvert af disse emner har været for din familie i den sidste måned.

Indenfor den sidste måned, hvor store problemer har din familie, som følge dit barns helbred, haft med:

	Daglige aktiviteter					
1.	Familieaktiviteter tager mere tid og indsats……	0	1	2	3	4
2.	Svært at finde tid til at blive færdig med de huslige gøremål……	0	1	2	3	4
3.,	At føle sig for træt til at blive færdig med de huslige gøremål……..	0	1	2	3	4
	Familieforhold					
1.	Manglende kommunikation blandt familiemedlemmer…….	0	1	2	3	4
2.	Konflikter mellem familiemedlemmer….	0	1	2	3	4
3.	Svært ved at tage beslutninger sammen som en familie……..	0	1	2	3	4
4.	Svært ved at løse familieproblemer sammen…….	0	1	2	3	4
5.	Stress eller spændning mellem familiemedlemmer…….	0	1	2	3	4

DE NÆSTE SPØRGSMÅL HANDLER OM DIN TILFREDSHED MED SUNDHEDSVÆSENET

49.	Hvor tilfreds er du med:	Meget utilfreds	Utilfreds	Hverken tilfreds eller utilfreds	Tilfreds	Meget tilfreds
	Generel tilfredshed					
1.	Den overordnede pleje, som dit barn får.....	1	2	3	4	5
2.	Hvor venligt og hjælpsomt personalet er.....	1	2	3	4	5
3.	Måden dit barn bliver behandlet på på hospitalet.....	1	2	3	4	5
	Information					
1.	Hvor meget information du fik om dit barns diagnose.....	1	2	3	4	5
2.	Hvor meget information du fik om dit barns behandling og sygdomsforløb…..	1	2	3	4	5
3.	Hvor meget information du fik om bivirkningerne ved dit barns behandling.....	1	2	3	4	5
4.	Hvor hurtigt du fik information om resultaterne af dit barns prøver…….…	1	2	3	4	5
5.	Hvor ofte du bliver opdateret om dit barns sygdom og helbred…..……....	1	2	3	4	5
	Inddragelse af familien					
1.	Den følsomhed, der blev vist din familie under dit barns behandling….....	1	2	3	4	5
2.	Villigheden til at besvare spørgsmål, som du og din familie måtte have……..	1	2	3	4	5
3.	Indsatsen for at inddrage din familie i diskussionen om dit barns pleje, og anden information om dit barns sygdom…….	1	2	3	4	5
4.	Hvor meget tid personalet gav dig til at stille spørgsmål, som du måske har haft om dit barns sygdom og behandling…..…….	1	2	3	4	5

	Hvor tilfreds er du med:	Meget utilfreds	Utilfreds	Hverken tilfreds eller utilfreds	Tilfreds	Meget tilfreds
	Kommunikation					
1.	Hvor godt personalet forklarede dit barns sygdom og behandling til **dit barn** på en måde, som han/hun kunne forstå..……..	1	2	3	4	5
2.	Den tid, der blev afsat til at forklare dit barns sygdom og behandling til **dig** på en måde, som du kunne forstå..……	1	2	3	4	5
3.	Hvor godt personalet lytter til dig og dine bekymringer...……	1	2	3	4	5
4.	Den forberedelse, som **du** modtog i forbindelse med, hvad man kunne forvente under prøver og procedurer.....	1	2	3	4	5
5.	Den forberedelse, som **dit barn** modtog i forbindelse med, hvad man kunne forvente under prøver og procedurer..……	1	2	3	4	5
	Tekniske færdigheder					
1.	Hvor godt personalet reagerer på dit barns behov..……	1	2	3	4	5
2.	De indsatser, der gøres for at sørge for, at deres barn er så tilpas og så smerterfri, som muligt…..……..	1	2	3	4	5
3.	Hvor hurtigt personalet reagerer på dit barns kvalme..…..……	1	2	3	4	5
4.	Hvor meget tid personalet brugte på at hjælpe dig når du og dit barn skulle hjem…..……..	1	2	3	4	5
	Følelsesmæssige behov					
1.	Det tidsrum, der blev afsat til dit barn at lege i, tale om hans/hendes følelser og stille spørgsmål, som han/hun måttte have...……..	1	2	3	4	5
2.	Det tidsrum, der blev brugt til at hjælpe dit barn med at komme tilbage til skolen...……	1	2	3	4	5
3.	Det tidsrum, der blev brugt til at tage sig af **dit barns** følelsesmæssige behov……..…….	1	2	3	4	5
4.	Det tidsrum, der blev brugt til at tage sig af **dine** følelsesmæssige behov..……	1	2	3	4	5

Paper I

European Journal of Cancer Care

Original article

Hospital-based home care for children with cancer: a qualitative exploration of family members' experiences in Denmark

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Hospital-based home care for children with cancer: a qualitative exploration of family members' experiences in Denmark

The study aims to describe the experiences of a hospital-based home care programme in the families of children with cancer. Fourteen parents, representing 10 families, were interviewed about their experiences of a hospitalbased home care programme during a 4-month period in 2009 at a university hospital in Denmark. Five children participated in all or part of the interview. The interviews were transcribed verbatim and analysed using qualitative content analysis. The findings indicate that hospital-based home care enabled the families to remain intact throughout the course of treatment, as it decreased the strain on the family and the ill child, maintained normality and an ordinary everyday life and fulfilled the need for safety and security. According to family members of children with cancer, hospital-based home care support enhanced their quality of life during the child's cancer trajectory. Our study highlights the importance of providing hospital-based home care with consideration for the family members' need for the sense of security achieved by home care by experienced paediatric oncology nurses and regular contact with the doctor. In future studies, interviews with children and siblings could be an important source of information for planning and delivering care suited to the families' perceived needs.

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INTRODUCTION

The provision of hospital-based home care for children with acute illnesses and with complex medical conditions is rising in several countries due to technological developments, increased understanding of factors for complications, the costs of hospital-based health care, changing policies and the potential psychosocial advantages (Frierdich *et al*. 2003; Cooper *et al*. 2006; Parker *et al*. 2006; Kandsberger 2007). Hospital-based home care is defined as the delivery of hospital care to patients at home; in general, it is either based at the hospital, which provides an outreach service where hospital professionals visit the homes, or based in the community (Parker *et al*. 2002). Three systematic reviews of paediatric home care conclude that the evidence base is limited, not only with regard to the effect of hospital-based home care on the children's and their parents' quality of life, but also with regard to the frequency of hospital admissions, the length of hospital stays, the outcome of the children's health and the general cost-effectiveness of hospital-based home care (Parker *et al*. 2002; Cooper *et al*. 2006; Parker *et al*. 2006). To date, most studies on hospital-based home care have primarily investigated the clinical and economic impact and the impacts on quality of life have mainly been assessed using quantifiable methods (Parker *et al*. 2002; Cooper *et al*. 2006; Parker *et al*. 2006).

The home environment may have a positive influence on children's recovery and well-being, but the shift to home care raises questions concerning parental and professional roles and responsibilities, which must also be taken into account (Kirk & Glendinning 2004). Considerable social, emotional and financial impacts on parents caring for chronically or long-term ill children have been documented as having the parents' need for support to maintain family functions and stability (McGrath 2001; James *et al*. 2002; Kirk & Glendinning 2004). Children with cancer and their families may have specific needs that differ from those of children with chronic disabilities or acute illnesses due to their complex intensive treatment and their potentially fragile somatic and psychosocial condition. The diagnosis and the aggressive treatment, as well as the high frequency and long duration of hospital stays, have considerable emotional and social effects on the whole family (James *et al*. 2002; Björk *et al*. 2005; Nolbris *et al*. 2007; Björk *et al*. 2009). In Denmark, the child is hospitalised together with one parent, relative or guardian; the treatment involves continuous hospital admissions or outpatient visits up to every 3 days for the first 6 months of the course of treatment for the cancer and its side effects. The treatment for children with cancer can last for up to 2.5 years, for example, for children with leukaemia, which is the most common childhood cancer diagnosis.

Hospital-based home care for this patient group often involves highly potent medical treatments which may increase the risk of adverse events and the strain on the families (Close *et al*. 1995; National Association of Children's Hospitals and Related Institutions (NACHRI) Patient Care Oncology FOCUS Group 2000; Goldsmith *et al*. 2002; Frierdich *et al*. 2003; Stevens *et al*. 2006a). Stevens *et al*. found that a home chemotherapy programme for children with leukaemia provided by community nurses had specific improvements and decrements in the children's and the parents' quality of life, and the majority of the families preferred home chemotherapy (Stevens *et al*. 2006a,b). Thus, research focused on the family as a whole is important and remains an area in which we lack a deeper understanding of the family members' own experiences of hospital-based home care. Such knowledge is valuable for planning and delivering care to meet the families' needs. Consequently, the aim of this study is to describe family members' experiences of a hospital-based home care programme provided by hospital nurses for children with cancer.

METHODS

Design

A descriptive inductive method with open interviews was used.

Setting

The study took place at a paediatric oncology ward at a university hospital in Denmark. On average, 75 children are newly diagnosed with cancer each year, of which 40% are diagnosed with leukaemia and lymphomas, 25% with brain tumours and 35% with solid tumours. This study complimented an experimental study comparing hospitalbased home care and standard hospital care for children with cancer. Between August 2008 and December 2009, the hospital-based home care programme included children between 0 and 15 years of age, who had received the diagnosis of cancer at least 1 month previously, were treated according to a standard treatment protocol, were in medically stable condition and lived within 50 km of the university hospital.

Fifty-three children with different cancer diagnoses received part of their standard hospital treatment at home, for example, blood tests, intravenous chemotherapy

lasting for 10 min and treatment with antibiotics lasting for 10–60 min. Two nurses who were employed specifically for hospital-based home care at the paediatric oncology ward provided the care. Home care visits lasted 15–90 min and, depending on the task performed, included one or both nurses. The number and type of treatments performed during hospital-based home care varied according to the children's diagnoses and treatment protocols. No adverse events such as fatal or unexpected serious complications occurred during the hospital-based home care programme.

Participants

A purposeful sample was selected to capture a wide range of experiences and differences among families, for example, the children's diagnosis, family constellation, parents' occupation, number of home care visits and the duration of the home care programme (Patton 1990). Fourteen parents representing 12 families were invited for interviews about their experiences. Two of the 12 families declined to participate because they felt overwhelmed by the burden the disease put on their family, thus 10 families were interviewed. Demographic characteristics of the participating families are shown in Table 1. The number of home care visits ranged from 9 to 66 visits and the duration of participation in hospital-based home care ranged from 3 to 16 months. For two families, the hospital-based home care was completed at the time of the interview (1 and 3 months after completion).

Procedure

The nurses in the hospital-based home care programme gave the parents written information about the study and the parents gave verbal consent for the first author (H. H.) to contact them for further information. All interviews were conducted between October 2009 and January 2010 by the first author (H. H.) at a time and place in accordance with the families' wishes. The parents decided whether both parents, the child or the siblings would participate in the interview. A total of 11 interviews were conducted. In three families both parents were interviewed together, in six families one parent participated in the interview, in one family both parents were interviewed individually and in five families the child and its sibling (one) participated in the interview. One child (14 years of age) participated actively throughout the whole interview. Six families chose to be interviewed in the family's home and five families wanted to be interviewed in a separate room at the hospital.

Table 1. Background characteristics of study participants

Characteristic	*n*
Parents	14
Father	5
Mother	9
Ethnicity	
Danish	14
Partner relations	
Cohabiting with partner	13
Divorced	3
Single parent	1
Parent age (years)	
31–40	5
41–50	9
Employment	
Employed	13
Unemployed	1
Sick leave due to child's cancer full-time	5
Sick leave due to child's cancer part-time	6
Distance to hospital (km)	
0–15	6
16–30	1
31–45	4
Time to hospital (min)	
0–30	7
31–60	4
Children with cancer	10
Gender	
Boys	5
Girls	5
Child age (years)	
0–4	3
5–7	2
8–10	4
13–15	1
Diagnosis	
ALL	6
Lymphoma	3
Brain tumour	1
Siblings living at home	
0	3
1	5
2	2

ALL, acute lymphoblastic leukaemia.

Each interview began with the same question: Can you describe your experiences with the hospital-based home care programme? During the interview the participants were asked open questions from four topics such as how they experienced home care in relation to everyday life, the value of home care for the child according to the parents' perceptions and if they had experienced benefits or difficulties. Parents were asked additional questions for clarification, for example, 'Can you describe in more detail what you mean?' There were no questions specifically directed to the children in the interview guide, but additional questions such as 'What do you think about the home care?' were posed to the children by the parents or by the interviewer. The interviews were audio-recorded

with the parents' permission and were transcribed verbatim including notations of non-verbal expressions such as pauses and laughter. The interviews lasted between 20 and 75 min (median = 35 min).

Data analysis

The transcribed text was analysed using qualitative content analysis following Graneheim and Lundman, who argue that content analysis is an interpretative process to analyse written communication in a systematic way to describe a person's experiences by focusing on differences and similarities in the text (Graneheim & Lundman 2004). The text was analysed with the concepts of meaning units, condensed meaning units, codes, subthemes and themes based on Graneheim and Lundman (2004). The analysis was performed in four steps, switching back and forth between the four steps throughout the process. In the first step, all three authors independently read through each interview several times to get an overall understanding. In the second step, the text was divided into meaning units by the first author. Meaning units were defined as exact words, sentences or paragraphs in the text where the content and context related to each other and to the aim of the study (Graneheim & Lundman 2004). Text that was not relevant to the aim of the study, for example, the parent's experiences with the social security system, was excluded. Each meaning unit was then condensed into a description, which adhered closely to the core meaning of the text. In the third step, the condensed meaning units were labelled with codes, which were abstracted and compared for similarities and differences and then sorted into subthemes by all three authors. In the final step, each subtheme was critically read, compared and analysed; the subthemes were then unified and a main theme was formulated. The main theme was considered to be a thread of underlying meaning running through the condensed meaning units, codes and subthemes on an interpretive level in accordance with Graneheim and Lundman (2004). To strengthen trustworthiness, the condensed meaning units, codes, subthemes and themes were discussed and reflected upon by all three authors throughout the analysis process until the authors reached agreement. External checks to enhance credibility were also made by considering preliminary interpretations and themes in peer discussions, seminars and presentations with healthcare professionals and researchers.

Pre-understanding

The first author (H. H.) is a nurse and has worked at the paediatric haematology and oncology ward for several years. H. H. was responsible for the assessment of the hospital-based home care programme. The second (H. K.) and fourth (I. H.) authors both have experience in carrying out qualitative research. None of the authors were involved in the care of the children and their families and had no previous professional or personal interactions with the interviewees. The authors discussed and reflected on their pre-understandings throughout the study to ensure they were unambiguous and thereby decreased the risk of subjectively influencing the study and the interpretation of the family member's experiences.

Ethical considerations

The parents were given written and verbal information about the study's aim, design and procedure and they gave their written consent to take part in the study. If the children wanted to participate, they were given verbal age-appropriate information and gave verbal assent with close attention paid to ethical issues as awareness of the child's cognitive and language ability (Gibson & Twycross 2007; Kirk 2007). Participation was voluntary; the parents were informed that they could withdraw from the study at any time and that this would not affect the child's cancer treatment in any way. All family members were assured confidentiality. The interviews were coded and code lists and transcripts were kept separately in a secure location. The Danish National Committee on Biomedical Research Ethics was applied to for permission to conduct the study. To preserve the participants' confidentiality, the family members are referred to as 'mother' and 'father', the children with cancer and their siblings are referred to as 'he' or 'she'.

RESULTS

We identified three subthemes, 'Decreasing the strain on the family and the ill child', 'Maintaining normality and an ordinary life' and 'Fulfilling the need for safety and security', which described the family members' experiences of hospital-based home care as a support in their disrupted, uncertain and strained lives. The subthemes were bound together in a main theme, which reflected the families' core experience of hospital-based home care: 'Supporting the family to remain intact throughout the childhood cancer trajectory'.

Decreasing the strain on the family and the ill child

When the parents reflected upon how they experienced hospital-based home care, they often drew on the negative

impact the hospital visits had on the family. They described how the hospital-based home care relieved the strain and stress that they experienced as a consequence of having a child with cancer by reducing the number of hospital visits. The parents illustrated it as if a great burden had been lifted from their shoulders in a period when they did not have much energy due to their child's life-threatening disease and their lack of a normal everyday life. One father said:

> Home care diminishes the invasion in one's life that the illness represents. It simply makes that invasion smaller: you don't feel that affected by the illness as a family, when it means 20 minutes in your own home compared to when it means 6 hours at the hospital. (Father 104)

Practical problems in their everyday life were something the parents experienced as being very difficult to cope with during the child's treatment. They felt that hospital-based home care enhanced their lives by decreasing practical problems and thereby conserving their energy and strength.

Family members described the hospital visits as strenuous, both physically and mentally. It was exhausting for the parents and the child to get up in the morning and go to the hospital and they experienced it as stressful to leave the home with a child who was plagued by nausea and vomiting. In contrast, with hospital-based home care the children could sleep as much as they needed and in that way conserve their energy. In addition, they did not have to leave home when the child was fatigued or feeling ill. Parents and children alike felt exhausted after a hospital visit and some of them spent a lot of energy speculating on the visit several days in advance. Some parents expressed how taxing the confrontation with other ill children and parents at the ward was and they described it as a relief not to have to relate to other families. Parents and children alike felt a physical and mental support from being able to stay at home, since they were strongly affected by the hospital visits or even by just thinking about going to the hospital.

> It was just that those thoughts of hospital, they made me feel physically unwell. I felt like vomiting, had headaches and dizziness and things like that, without it being necessary. (Child 106)

Maintaining normality and an ordinary life

Parents strived to maintain their everyday life as close to normal and ordinary as possible for the whole family, despite their disrupted family life. They described how hospital-based home care did not interrupt the families' everyday life in the same way as the hospital visits did. Several parents expressed that they and their child wanted to avoid being pulled into a world of illness at the hospital as much as possible, and at home they could almost forget what was wrong with the child. The children described how they felt less ill and more normal in their own home. It was important to the parents and children to continue their daily routines and family life as usual, for example, the child could go to school or receive home teaching; the parent could plan the routine of the day, go to work and fetch siblings from day care. One father explained how his child did not like changes, and that the maintenance of normality and everyday life had made her experience of the cancer easier, which was crucial in her disrupted life. His child said:

> I don't think it would be that nice if I could not go to school. Because then I would just sit at home and not having that, then I would just think about the illness. (Child 103)

Parents expressed how much it meant for their children to be able to attend school and thereby avoid lagging behind both socially and educationally.

> There was something very symbolic to be on that class photo. If it had not been for the home care, he would have had to go to the hospital, and he would not have had his happy face on that class photo. (Mother 101)

Being at the hospital was described as tearing the family apart. The opportunity for the family to be at home meant that the siblings did not experience being left alone or left out. The parents emphasised that the siblings felt worried if the parent and the ill child were not at home, as they then became anxious about the ill child's condition and if and when the parent and child would return home. They also expressed great contentment from being able to relax and eat together as a family, to support and bring the siblings to their leisure-time activities and thereby maintain their ordinary family existence.

Fulfilling the need for safety and security

Overall, family members felt safe and secure when the child received hospital-based home care and found that it worked well. Some parents described that they felt less insecure at home as they could avoid the risk of the child contracting an infection from others. The nurses always called back as agreed and were punctual, which enhanced the parents' experience of being in control of the emotionally demanding situation they were in.

The parents and children described it as crucial for their sense of safety and security that the home care nurses had experience in paediatric oncology, as they were familiar with the course of illness, the treatment and its consequences. Consequently, the nurses were able to support, guide and comfort the families.

The parents did not perceive hospital-based home care as interfering with their private sphere and they explained how pleased the children were to meet the nurses both at home and at the hospital and how they enjoyed showing them their home. Some parents described how the relationship with the home care nurses had an extra familiar and intimate dimension.

> They get to know us in another way when they come to us at home and see how we live, and they see us with morning hair, and everything in a mess and when we sit at the table eating breakfast .... (Mother 108)

The increased familiarity with the nurses facilitated talking with the home care nurse about difficult issues relating to the illness and the family's well-being, which enhanced the experience of security.

> The nurses in the ward are just so very busy. When they visit us in our homes, they have much more time for me and I feel more secure. (Child 103)

However, some parents did not experience any difference in the relationship and one couple felt that the home care nurse had less time for questions and talking than the nurses at the ward. For some parents home care even challenged their sense of security and safety at home, since they were less often in direct contact with the doctor at the ward. This could make them unnecessarily worried, especially in the beginning of the course of treatment when they were especially vulnerable and scared. However, it appears that they overcame this by calling the ward if they needed to ask something. Some parents were pleased with visiting the ward regularly to maintain a steady contact with the other families at the clinic, while others perceived it to be sufficient if they met other families at social events outside the hospital environment, or they felt no need to see them at all.

Some parents wanted potentially harmful treatments to be provided at the hospital so that the home remained associated with a safe and pleasant place for the child. One family described that the first time their child had to have a blood sample taken from the vein the home care nurse failed at first but kept trying several times. The child and parents had experienced this as a violation and it made the child frightened to have blood samples taken from the vein for a long time. However, the child in this family preferred having blood samples taken at home as long as the nurse was competent to take the blood sample. Other parents described how their children were actually more relaxed in the home environment even when they experienced potentially harmful treatments. Parents also explained how the children and their siblings became more familiar with treatments at home, which resulted in reducing their fear of them when at the hospital. One father said:

> I think it's good that the brother knows how it works and that it does not hurt. So yes, in that way I think it has helped, and of course it is easier to have him here at home to see it. So in that way he is more involved than he would have been if it had taken place at the hospital. (Father 107)

DISCUSSION

Interviews with family members were carried out to increase our understanding of their perspectives on the impact of hospital-based home care. Previous studies have described the distress arising from hospital treatments for children with cancer and how the family members experienced the cancer treatment to be a struggle and emotionally demanding (Svavarsdottir 2005; Björk *et al*. 2009). We found that hospital-based home care was a support for the family to remain intact throughout the childhood cancer trajectory by decreasing the strain on the family and the ill child, maintaining normality and an ordinary lifestyle, and fulfilling the need for safety and security. The family members in our study experienced the hospital-based home care as safe and secure even if some parents had concerns about the lack of regular contact with the child's doctor and the potential occurrence of treatment-related harm of the child at home. However, the nurses' experience in paediatric oncology and the positive impact of hospital-based home care on several aspects of life outweighed these concerns.

Stevens *et al*. showed similar findings when they interviewed 24 parents and 14 children with leukaemia who were included in a home chemotherapy programme provided by community nurses in Canada (Stevens *et al*. 2006b). The parents experienced less disruption of everyday life and work and the children reported more time to go to school and engage in normal activities. But some parents described that they felt safer and more secure at the hospital, as they were close to the health professionals with all the necessary facilities and some children experienced the inconsistency with the community nurses and

laboratory as emotionally stressful (Stevens *et al*. 2006b). The family members in our study did not describe any emotional distress but they emphasised the importance of the home care nurses familiarity with the treatment as an essential aspect for their sense of safety and security. This is in line with previous findings that the staff play an important role in supporting both the individual and the family as a whole when a child has cancer (Björk *et al*. 2009).

During hospitalisation, a strong need for being in control of the situation is central to parents and children (Hallström *et al*. 2002; Björk *et al*. 2006). This is also applicable to the family members in the present study as they described how home treatment provided the ability for them to control their own time and space, whereas at the hospital they were subjected to the health professionals' schedules and control. Being at home enhanced the parents and children's sense of control, which may influence the children's sense of autonomy and ability to master even the most difficult treatment situations.

Methodological considerations

To meet the demand of trustworthiness in this qualitative study, the authors conducted the analytical process both independently and jointly, and the results were compared and discussed throughout the process to strengthen the credibility and dependability of the data (Graneheim & Lundman 2004). Our sample included children with leukaemia, lymphoma and brain tumours. No children with solid tumours were included as the aggressive treatment for those children often made hospital-based home care impossible. Thus, our findings are only applicable to similar groups in similar settings. The purposeful sample of 12 families was considered to be sufficient as most interviews were rich in variation and contained detailed information to achieve abundance and variation of the data. The analytical process, the context and the participants are described in detail in both the text and the tables and representative quotations are used to show how the findings are based on the data. In this way, we sought to meet the objective of our interpretations being in line with the families' narratives of their experiences.

The interviewer (H. H.) has experience as a paediatric oncology nurse and was responsible for the assessment of the hospital-based home care. On one hand, this involves a risk of restricting the families' stories or of drawing hurried conclusions. On the other hand, the interviewer's knowledge about the course of illness and the home care made the families feel confident and facilitated the interview of the experiences.

The families were in a vulnerable and strained situation and therefore efforts were made to facilitate their participation, for example, by performing the interviews at times and places that best suited the families, and not specifically addressing the child. This diversity of the interview situation may have influenced the content of the interviews.

The reason for purposeful sampling was to select information-rich cases to capture an open range of experiences and variations of the impact of hospital-based home care on the family members (Patton 1990). We expected that a sample of 10–12 families would cover a variety of participants with various experiences. Our findings demonstrated that the experiences with hospitalbased home care did not differ among social classes, family sizes or configurations, distance from hospital, number of visits or other forms of treatments, as it was still shown to have a positive impact on the families. However, the experiences of the families in the hospitalbased home care programme who declined to participate in this study, as well as the families who were not included, may differ from those of the participants. Our findings appear to support the provision of hospital-based home care to children with cancer but our understanding and interpretation of the results must be considered with caution.

Implications for practice and research

The present study shows that hospital-based home care has an important positive social and psychological impact on children with cancer and their families' experiences of the childhood cancer trajectory. For these families, hospital-based home care provided the opportunity to reduce the frequency and duration of hospitalisation and allowed the families to continue their usual everyday life. Family members experience hospital-based home care as a support to the family as a whole in a strained situation by reducing hospital visits and this should be an essential priority for healthcare providers. Our study highlights the importance of providing hospital-based home care with consideration for the family members' need for the sense of security achieved by home care by experienced paediatric oncology nurses and regular contact with the doctor. Finally, in future studies, interviews with children and siblings separately from families with children in end-of-life care about their experience of hospital-based home care could be an important source of information of the families' needs. Such information is valuable for planning and delivering care suited to the families' perceived needs.

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Paper II

Feasibility of hospital-based home care for children with cancer and psychosocial impact on the children and their families

Short running title: Hospital-based home care for children with cancer

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Abstract

Objective: To assess the feasibility and the psychosocial impact of a hospital-based home care (HBHC) programme for children with cancer.

Methods: An HBHC programme was carried out with 51 children (0-18 years) with cancer to assess the feasibility in terms of preference for care, safety and costs. A subsample comprising 28 children and 43 parents (HBHC group) was assigned to a controlled trial and 47 children and 66 parents were assigned to receive standard hospital care (SHC group). The children's health-related quality of life (HRQOL) was measured by parent-reported and self-reported (5-18 years) PedsQL Generic Core Scale, PedsQL Cancer Module, and the psychosocial impact on the family by PedsQL Family Impact Module.

Results: All parents included in the HBCH preferred the home care. There were no serious adverse events directly associated with HBHC, and costs did not increase. In PedsQL Generic Core, there were significantly higher mean values in the HBHC group for the parent-reported total score (p = 0.04) and physical functioning (p = 0.03) as well as for the self-reported total score (p = 0.02), psychosocial health (p = 0.03), and emotional functioning (p = 0.04). When adjusted for age, gender, diagnosis and time since diagnosis, there were significant differences between the HBHC group and the SHC group in parent-reported physical health and worry indicating higher HRQOL in these dimensions in the HBHC group. No significant difference was found in the Family Impact Module.

Conclusion: This study indicates that HBHC is a feasible and acceptable alternative to hospital care for children with cancer. Specific dimensions in children's HRQOL may be improved and the psychosocial impact on the family does not increase.

Keywords: Paediatric Oncology, Home Care, Quality of Life, Chemotherapy

1. Introduction

The highly complex and intensive treatment of children with cancer has considerable health, emotional and social effects on both the child and the whole family[1,2]. Hospital-based home care (HBHC), which refers to the delivery of hospital care to patients at home that would otherwise necessitate a hospital admission, is increasingly provided due to technological developments, the costs of health care, and improvements in supportive care[3,4]. It includes the delivery of intravenous therapy and complex nursing in the child's home provided by either community-based or home care agency-based nurses or, more rarely, by hospital-based nurses[5]. Although HBHC may have potential psychosocial benefits for the children and their families by reducing hospital visits[6,7], there is, despite the increasing provision of HBHC world-wide, a lack of knowledge about the impact on clinical outcomes, cost effectiveness and the children's health-related quality of life (HRQOL)[8-10]. Some studies on home care programmes for children with cancer suggest that HBHC is safe[6,11-13] and may reduce costs[6,14], but the only randomized trial showed that children may also experience more emotional stress with home chemotherapy when provided by community-based nurses[13].

HBHC for children with cancer has never been practiced in Denmark. There are no home-care agencies and there is no established collaboration with community-based nurses. This allowed us to explore whether or not an HBHC programme could replace hospital visits and be acceptable for the children and their families. The aim of the present study was to assess the feasibility in terms of safety, satisfaction, preference for care, costs and the psychosocial impact of an HBHC programme for children with cancer and their families.

. Patients and methods

2.1. Study design

This study integrates two parallel designs: a descriptive study assessing the feasibility of the HBHC programme and an experimental controlled trial assessing the psychosocial impact of the HBHC programme on the child and the family including historical and concurrent control groups that receive standard hospital care (SHC). A consecutive sampling was used based on geography instead of random selection due to ethical and practical considerations. The study was conducted at the paediatric haematology and oncology department at a university hospital in Copenhagen that covers approximately half of the Danish childhood cancer patients. The Copenhagen and Frederiksberg's Committee on Biomedical Research Ethics and the Danish Data Protection Agency (jr.nr.2005-

415380) approved the study. The parents or the legal guardian provided written informed consent for participation and the children, of an appropriate age, gave oral assent.

2.2. Study population

Children, below the age of 18 at diagnosis, who had been diagnosed with any type of cancer at least one month prior to inclusion, were in first-line treatment with intravenous therapy with a curative intent, had not received a haematopoietic stem cell transplantation, and who, like their parent(s), spoke and read Danish, were included.

Between August 2008 and December 2009, 51 children were included (median 2 months from diagnosis) in the HBHC programme if they lived within a radius of 50 kilometres from the hospital. The sample in the controlled trial consisted of three groups: (1) a subsample of 28 children from the HBHC programme was included in the HBHC group (median 10 kilometres from the hospital), (2) 12 children were included in the concurrent SHC group if they lived beyond a radius of 50 kilometres from the hospital (median 89 kilometres from the hospital), and (3) 35 children were included in the historical SHC group for an eight-month period before the HBHC programme started regardless of their radius from the hospital (median 40 kilometres from the hospital). Figure 1 illustrates the inclusion. The historical SHC group was included to increase sample size and sample representativeness for comparison with the HBHC group in terms of potential demographic and socioeconomic confounders. The national protocols for paediatric cancer treatments did not change during the inclusion of the historical SHC group except for the Nordic ALL2008 (Acute Lymphoblastic Leukaemia) protocol that was implemented in July 2008. The concurrent and historical SHC groups were subsequently combined for statistical analysis.

Children were included regardless of the time passed since diagnosis when establishing the groups and thereafter newly diagnosed children were included approximately 3 months after diagnosis.

2.3. HBHC programme

The HBHC programme was designed to replace an out-patient visit or an in-patient admission (86% and 14% of all HBHC visits, respectively). An allocated HBHC nurse with extensive experience from the paediatric oncology department referred the patients to a home visit based on the condition of the patient and the planned medical treatment followed by approval from a senior paediatric oncologist. Less than 5% of these referrals were refused by the paediatric oncologist. The HBHC nurse provided HBHC treatments and did all practical medical preparations at the ward. Patients discontinued participation in the HBHC programme when the inclusion criteria were no longer

fulfilled. At each visit, the HBHC nurse recorded vital signs, transfusion history, acute deteriorations of the general condition, acute anaphylactic reactions, and any medical errors according to the mandatory hospital guidelines for registering treatment errors (reference region H).

2.4. Outcome measures

Every family completed a one-page evaluation form, specifically developed for the HBHC programme, after each HBHC visit during the first 12 months of the HBHC programme (n=652). This evaluation form assessed the child's and the parent's perceptions of security and satisfaction with HBHC using a 5-point scale ranging from *not at all* to *very much*. Finally, the parents' overall preference for SHC vs. HBHC was scored. Furthermore, we evaluated safety and type and number of HBHC visits per day using the nurse's registration records. Costs associated with HBHC for the health care service were evaluated by comparing operational and overhead costs of the HBHC with the expenses of an outpatient or inpatient admission at the hospital.

Data regarding psychosocial impact were assessed with a questionnaire booklet including demographic information and validated instruments measuring psychosocial factors comprising, in total, 50 main questions with sub-questions. The PedsQL^{TM} instruments were used to measure the child's general and disease-specific HRQOL. These instruments are established validated multidimensional instruments for measuring HRQOL in children with cancer[15-17]. They include age specific versions for parent proxy-reporting (ages 2-18) and self-reporting (ages 5-18 years) where they rate the perceived burden of each item over the past week ranging from 0 (never a problem) to 4 (always a problem) except for children aged 5-7 years who rate on a 3-point scale. Responses are reversely scored and linearly transformed to a scale ranging from 0 to 100 with higher scores indicating better HRQOL. The PedsQL-Generic Core Scale (PedsQL-Generic) consists of four dimensions, and a total score of all dimensions is computed together with a physical and psychosocial summary score. The PedsQL^{TM} 3.0 Cancer Module (PedsQL-Cancer) consists of seven dimensions without a total score. The PedsQL^{TM} 2.0 Family Impact Module (PedsQL-Family Impact) consists of 8 dimensions with a total score as well as the parent's HRQOL and family functioning as summary scores.

Psychosocial outcome data were to be collected at inclusion (T1) and 3 months later (T2). The questionnaire booklet was to be completed at home and was mailed to the parents individually along with a return-addressed stamped envelope. Children completed the self-report in one of the parents' questionnaires. The parents received a reminder after two weeks if they had not responded. Based on 10 parents' experiences in a pilot study validating the booklet, we did not approach

families with newly diagnosed children until approximately three months after the cancer diagnosis due to their strained situation during the first months. It was non-compulsory for the families in the HBHC programme to participate in the controlled trial. The inclusion time points of the HBHC programme and the controlled trial were not consistent due to practical and ethical considerations. Thereby, 20 of 28 children in the HBHC group received HBHC visits (median=7 visits) between the time of assignment to the HBHC group and the first questionnaire data collection (data baseline) at T1. Thus, we assessed the differences between treatment groups at T2, and not the effect between T1 and T2.

2.6. Statistical analysis

Means and standard deviations were calculated for descriptive purposes. The primary end-point was the PedsQL-Generic total score. For continuous variables Student's t-tests were used to compare the mean between groups, and χ^2-tests were used for categorical variables. Multivariate, linear regression analysis was used to explore the relationship between a set of independent values and HRQOL-scores as a dependent variable. The dependent variable was tested for normal distribution with no significant deflections found. In the adjusted models we adjusted for cancer diagnoses, age at diagnosis, gender, and time since diagnosis since these variables could confound the outcome scores. All tests of significance were two-sided, and statistical significance was defined as $p < 0.05$. All statistical analyses were performed using the SAS statistical program (version 9.2; SAS Institute, Cary, NC).

3. Results

3.1. Participants

Participants and non-participants in the controlled study did not differ significantly with respect to child's gender, age, diagnosis and time since diagnosis. The 45 non-participating families responded in a short telephone interview that it was too time and energy consuming to complete the questionnaire required for study participation. The HBHC and SHC groups did not differ significantly with respect to demographic and medical characteristics except for the parents' educational level and the children's time since diagnosis at T1 (Table 1). The average time period since diagnosis at T1 was 3 months in the HBHC group and 8 months in the SHC group due to the historical SHC group, and 7 months and 12 months, respectively, at T2.

3.2. Feasibility

During August 2008 – December 2009, the HBHC nurses provided 942 visits with a mean of 3 visits per day. The number and type of treatments varied depending on the children's diagnoses and treatment protocols or on the remaining duration of their cancer treatment when included in the HBHC programme (Table 2). No medical errors, acute deteriorating general condition, or acute anaphylactic reactions related to HBHC were reported. The cost analysis showed that HBHC was provided to equal costs to an outpatient visit, and lower costs than an inpatient admission (data not shown). A total of 657 parent-reported evaluation forms (70% of the total number of HBHC visits) were collected. The response rate was > 95%, and the number of missing answered items was less than 3%. In all evaluation forms except one, parents reported that they would prefer to receive a home visit instead of a hospital visit. All parents felt secure with the HBHC, 94% were very satisfied (score 5) with the HBHC, and none scored less than satisfied (score 4).

3.4. Psychosocial impact

At T2, all self and parent-reported mean scores in PedsQL Generic Core were higher in the HBHC group with significantly higher self-reported mean scores in the total score of psychosocial health and emotional functioning. Similarly, parent-reported total scores were significantly higher as well as those of physical health (Table 3). Several of the children did not attend school which affects the mean score in the school dimension. The proposed cut-off point for impaired HRQOL has previously been proposed to be 68.9 in the self-reported total score, and 67.0 for parent reports[15,18]. We found more self-reported mean scores above 68.9 only in the HBHC group. Parent-reported mean scores were close to 70.0 in both groups.

In the PedsQL-Cancer Module, self-reported mean scores were overall higher in the HBHC group, but not statistically significant. Parent-reported mean scores were higher in pain, worry, and cognitive problems in the HBHC group while procedural and treatment anxiety were lower in the HBHC group. The mean scores in the PedsQL-Family Impact Module were overall similar between the groups (data not shown).

When controlling for the effects of diagnosis, age, gender and time since diagnosis, the large differences between the groups in parent-reported and self-reported PedsQL-Generic Core suggest a trend towards higher scores, but only parent-reported physical health ($p = 0.01$) reached statistical significance (Table 4). There were significant differences in parent-reported nausea ($p = 0.04$) and worry ($p = 0.04$) with higher scores in the HBHC group, but no statistically significant differences between treatment groups were found in self-reports. However, there were lower scores in the self-

reported procedural anxiety as well as parent-reported procedural and treatment anxiety in the HBHC group. There were no differences between groups in the PedsQL-Family Impact Module.

5. Discussion

This study showed that an HBHC visit can safely replace hospital visits with a high patient satisfaction and preference for HBHC care to equal or lower costs. Hence, the HBHC programme is feasible and widely accepted among the families and due to these findings the HBHC programme was implemented as the routine care procedure at the paediatric oncology department in February 2010. Although findings from the few controlled trials of HBHC for children with cancer and other patient groups in general are disparate, they are, on the whole, consistent with our findings[8-10].

We found that the children's HRQOL may be enhanced when receiving HBHC since there was a trend of higher scores in PedsQL Generic Core in the HBHC group after adjusting for age, gender, diagnosis and time since diagnosis. The differences between groups varied more in the PedsQL Cancer Module as there were indications of less nausea and worry at the same time as there was a higher level of treatment anxiety for children receiving HBHC when reported by parents. These indications are in line with the findings in an interview study with a sample of families participating in the HBHC programme[19]. We did not find differences in scores between the HBHC and SHC groups in the PedsQL Family Impact Module, and we had expected to find as beneficial a psychosocial impact on the child and family as we found in the interview study[19].

The findings indicate that on the one hand, there may be perceived dimensions in the child's HRQOL and the psychosocial impact on the family that remain the same regardless of the place of treatment delivery. On the other hand, there may be important dimensions which the PedsQL instruments do not cover that may have a great influence on the individuals and the whole family such as the practical and social consequences of pro-longed and frequent hospital visits. The parents were highly satisfied and preferred HBHC, in spite of the fact that they scored the child's treatment-related anxiety as higher at home, indicating that there may be a beneficial impact of HBHC that balances the shortcomings. Stevens et al. showed, using the disease-specific parent proxy instrument POQOLS (n=23 children with leukaemia), that children appeared to experience more emotional distress with home chemotherapy[13]. In accordance with our findings, the families in Stevens et al.'s home chemotherapy programme preferred home chemotherapy partly due to the social benefits for the families reported in their interview study[7].

There may be other challenges in measuring HRQOL in children with cancer[21,22,23,24]. Previous studies on childhood cancer have showed that differing diagnoses and treatments most likely have different impacts on the HRQOL[16,23,25,26]. Age and time since diagnosis[17,27,28] may also have different impacts on the HRQOL. Furthermore, the clinical status and symptoms often fluctuate in children receiving active cancer treatment relative to when the specific treatments are administered[23,29]. Thereby it may be difficult to show that any changes in the patient's HRQOL are due to the true change[23].

The clinical nature of the studies implies certain limitations. Ninety-three per cent of the approached families participated in the HBHC programme while 58% of those families participated in the controlled trial possibly due to the fact that participation was voluntary and to the extent of the questionnaire. This meant that families in the HBHC group may not be representative for all of the families in the HBHC programme. The questionnaire booklet was time consuming to complete suggesting that the included parents may have more mental energy than the non-participants. However, the response rate on the whole was the same in the HBHC and SHC groups, suggesting that the groups are comparable in this aspect.

The study included a broad sample of children with cancer, which allowed us to examine the effect across diagnosis, age, and time since diagnosis. However, this diversity, the assignment distance and the inclusion of a historical control group induce further bias besides the non-randomised design. The choice of a non-randomised design based on geography reflects logistic and ethical considerations. A randomised design might reduce the willingness to participate. In addition, randomisation would prevent half of the potential recipients to receive HBHC. As an alternative and since we regarded HBHC to be safe we chose the geographical stratification to increase the participation rate. Due to the high participation rate, the included families in the HBHC programme are truly representative of the childhood cancer families.

The treatment groups were comparable except for the educational level of the parents, which suggests that families residing inside the assignment area are better educated. This may be reflected in the higher PedsQL scores in the HBHC group. However, studies from Canada found that greater household income was a predictor for better HRQOL assessed by PedsQL Generic Core and Acute Cancer Module[29,30]. There was no difference between the HBHC and SHC groups in household income, indicating that the educational level did not have a considerable effect on the PedsQL scores. When education and distance from the hospital were included separately in the statistical model, they showed no considerable confounding effect. Finally, the inconsistent timing of

inclusion to the HBHC programme and the questionnaire study meant that some families received home visits prior to completing a baseline assessment. A completion of baseline before an HBHC visit for these families was hard to justify due to logistical and ethical considerations. However, it is a critical methodological weakness as we cannot confirm that the groups were comparable with regard to PedsQL scores when included. Our findings should therefore be interpreted with caution. Despite the limitations, we strongly believe that our findings provide valuable information to facilitate clinical decision-making when introducing an HBHC programme.

In conclusion, the results of this study support the acceptability and feasibility of an HBHC programme with high parent satisfaction and a preference for HBHC. Children's HRQOL may be enhanced in the specific aspects when receiving HBHC though some children may also perceive more treatment-related anxiety. The study highlights the importance of further studies on the effect of routinely measuring HRQOL combined with health outcomes with a brief questionnaire and a follow-up to be able to assess the psychosocial impact of HBHC over time.

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Table 1. Characteristics of the participants in the HBHC group and the SHC group

	No. (%)				
	HBHC group	**SHC group**	**P-value**	**Historical SHC group**	**Concurrent SHC group**
Parents	***44 (100)***	***66 (100)***		***51 (100)***	***15 (100)***
Parents/Guardian			.47		
Female	25 (57)	42 (63)		33 (65)	9 (60)
Male	19 (43)	24 (37)		18 (35)	6 (40)
Age (years)			.32		
21-30	2 (5)	8 (12)		5 (10)	3 (20)
31-40	21 ()	26 (39)		24 (47)	2 (13)
41-50	19 (43)	25 (38)		16 (31)	9 (60)
≥ 50	2()	7 (10)		6 (12)	1 (7)
No data	0	3 (3)		0	0
Marital status			.62		
Married or cohabiting	40 (90)	58 (88)		46 (90)	12 (80)
Living alone	4 (10)	8 (12)		5 (10)	3 (20)
Education			.009		
Basic (ISCED 1-2)	0 (0)	0 (0)		0 (0)	0
Secondary (ISCED 3)	9 (20)	30 (45)		21 (41)	9 (60)
Higher (ISCED 4-6)	33 (75)	30 (45)		25 (49)	5 (34)
Unknown	2 (5)	6 (10)		5 (10)	1 (6)
Employment			.96		
Employed	35(80)	53 (80)		41(80)	12 (80)
Sick leave or unemployed	2 (5)	4 (6)		3 (6)	1 (6)
Retired or other	5 (10)	6 (10)		5 (10)	1 (6)
Unknown	2 (5)	3 (4)		2 (4)	1 (6)
Number of children			.96		
1	6 (14)	9 (14)		8 (16)	1 (6)
2	25 (56)	36 (54)		29 (57)	7 (47)
3 or more	13 (30)	21 (32)		14 (27)	7 (47)
Annual household income			.40		
Low (0-249 000)	1 (2)	1 (2)		0	1 (7)
Medium (250 000–549 000)	6 (14)	9 (14)		6 (12)	3 (20)
High (≥ 550 000)	33 (75)	42 (64)		34 (66)	8 (53)
Do not wish to answer	4 (9)	14 (21)		11 (22)	3 (20)
Children	***28 (100)***	***47 (100)***		***35 (100)***	***12 (100)***
Gender			.70		
Male	15 (54)	23 (49)		15 (43)	8 (67)
Female	13 (46)	24 (51)		20 (57)	4 (33)
Age (years)			.33		
0-1	5 (18)	3 (6)		1 (3)	2 (17)
2-4	7 (25)	16 (3)		13 (37)	3 (25)
5-7	6 (21)	8 (17)		7 (20)	1 (8)
8-12	7 (25)	9 (19)		7 (20)	2 (16)
13-18	3 (10)	11 (23)		7 (20)	4 (33)
Diagnosis			.94		
ALL/AML/ Lymphoma	20 (71)	32 (68)		25 (71)	7 (59)
CNS tumour	3 (11)	5 (10)		4 (11)	1 (8)
Solid tumour	5 (18)	10 (22)		6 (17)	4 (33)
Time since diagnosis (months)			.0003		
1-3	18 (64)	10 (22)		5 (14)	5 (42)
4-6	7 (25)	12 (26)		5 (14)	7 (59)
7-11	3 (11)	7 (14)		7 (20)	2 (17)
≥ 12	0	18 (38)		18(52)	0 (0)
Distance to hospital			<0.0001		
≤ 50 km	27 (96)	23 (49)		23 (66)	0 (0)
> 50 km	1 (4)	24 (51)		12 (34)	12 (100)

Table 2. Participants and HBHC programme activities

	HBHC programme		HBHC group	
	N	**Range (median)**	**N**	**Range (median)**
Children	57		28	
Male	28		15	
Female	29		13	
Age		0-17 (8)		0-13 (5)
0-4	17		10	
5-7	10		6	
8-12	15		8	
13-17	15		12	
Diagnosis				
ALL/AML/ Lymphoma	33		20	
CNS tumor	10		3	
Solid tumor	8		5	
Thalassaemia	5			
Histiocytosis	1			
Home care visits	942	1 – 75 (10)	478	1 – 75 (9)
Duration home care visit (minutes) [1]	784	10-200 (20)	474	10-200 (20)
Nurse transport time (minutes) [1]	786	3-150 (30)	476	5-150 (30)
Length in the HBHC intervention (months)[2]		0 – 17 (5)		0-17 (4)
Treatments				
Infusion of antibiotics Carbapenem and Ciproflaxine	117		69	
Infusion of chemotherapy Vincristine and Dactinomycin	317		211	
Other intraveneous medications	82		57	
Blood sample central venous catheter (CVC)	619		379	
Blood sample peripheral vein	128		37	
CVC occlusion	14		5	
Other care procedures e.g. cleansing CVC	63		20	

Table 3. Psychosocial Health, HBHC group and SHC group

	Time point 2				
	Mean (SD)				
PedsQL™ Scales	**N**	**HBHC group**	**N**	**SHC group**	**p-value**
Generic Core					
Child self-report					
Total score	13	75.3 (19.11)	25	61.1 (16.68)	.02
Physical functioning/ physical health	13	76.3 (25.14)	25	59.0 (25.96)	.06
Psychosocial health*	13	74.6 (17.30)	25	62.4 (14.50)	.03
Emotional functioning	13	78.1 (16.65)	25	62.2 (25.59)	.04
Social functioning	13	82.3 (20.27)	25	71.7 (18.83)	.12
School functioning	12	51.1 (19.78)	23	49.8 (46.83)	.91
Parent proxy					
Total score	41	69.2 (16.15)	66	60.9 (19.75)	.04
Physical health/ physical functioning	41	67.8 (20.09)	66	56.3 (26.89)	.03
Psychosocial health	42	70.6 (15.11)	63	64.6 (19.04)	.11
Emotional functioning	43	69.0 (17.29)	66	62.0 (20.27)	.08
Social functioning	42	77.9 (16.57)	63	72.4 (20.79)	.18
School functioning	27	57.9 (22.12)	30	44.8 (21.23)	.03
Cancer Module					
Child self-report					
Pain and hurt	13	73.1 (25.94)	25	62.5 (27.24)	.26
Nausea	13	71.2 (11.93)	25	66.4 (23.78)	.42
Procedural anxiety	12	52.8 (33.58)	25	65.0 (32.63)	.30
Treatment anxiety	13	87.8 (21.95)	25	77.7 (28.23)	.16
Worry	12	76.4 (28.17)	25	67.2 (22.38)	.29
Cognitive problems	13	74.9 (19.47)	25	62.2 (18.92)	.06
Perceived physical appearance	13	72.4 (22.41)	25	67.3 (27.10)	.56
Communication	13	79.5 (29.58)	25	63.7 (26.45)	.10
Parent proxy					
Pain and hurt	39	73.4 (19.91)	65	64.4 (28.49)	.05
Nausea	40	71.8 (19.14)	63	70.1 (26.39)	.68
Procedural anxiety	40	60.8 (33.93)	63	71.0 (32.75)	.11
Treatment anxiety	40	79.6 (20.32)	64	85.4 (22.03)	.15
Worry	39	86.3 (20.19)	63	77.8 (26.73)	.08
Cognitive problems	39	77.8 (16.53)	62	70.5 (24.11)	.06
Perceived physical appearance	40	73.4 (25.97)	61	74.2 (25.94)	.99
Communication	38	67.3 (27.43)	60	63.7 (33.61)	.77

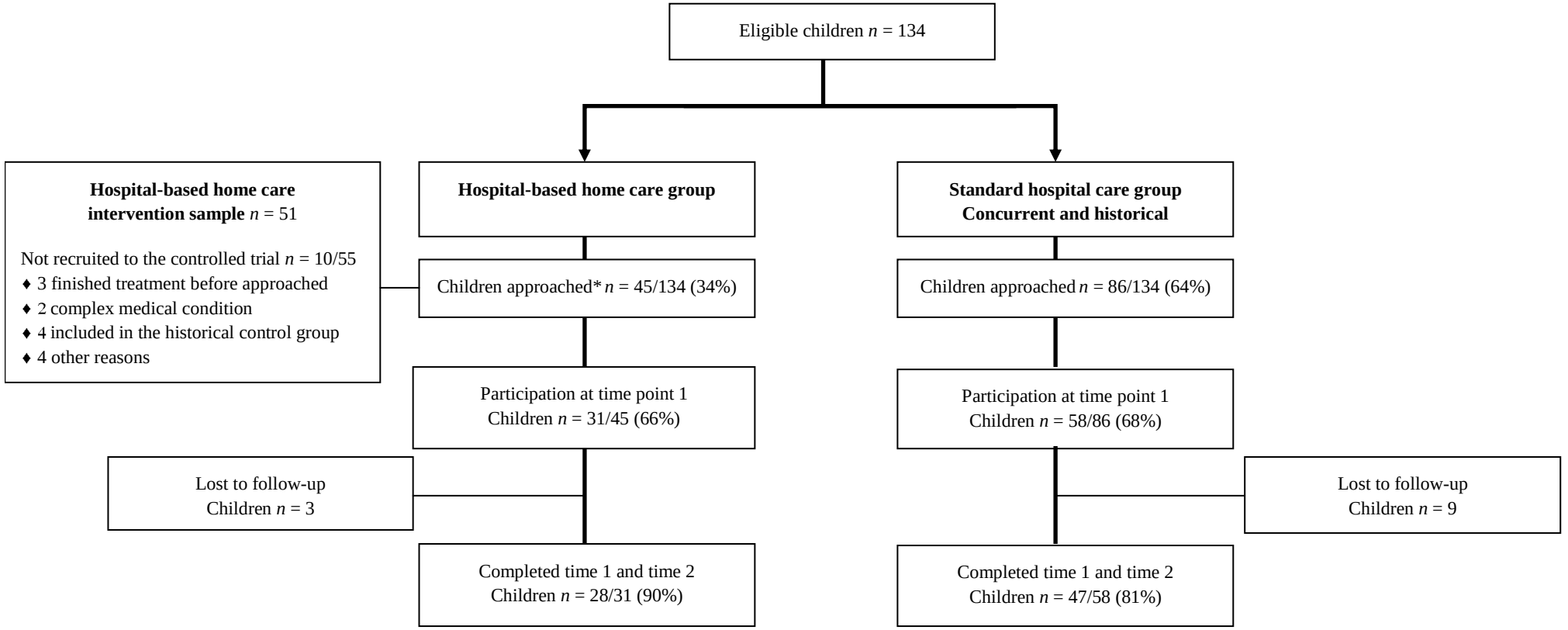
*Psychosocial health is a summary score of emotional, social and school dimensions
Scale ranging from 0 to 100 with higher scores indicating better HRQOL
1-2 parent proxy-reports per child in the treatment groups because both parents were invited

Table 4. Estimated difference between HBHC and SHC group

PedsQL™ Scales	Time point 2			
	Crude β 95% CI	p-value	Adjusted β 95% CI	p - value
Generic Core				
Child self-report				
Total score	14.2 (2.0–26.3)	.02	14.8 (-0.4–30.1)	.06
Physical Health Summary	17.3 (-0.5– 35.2)	.06	20.3 (-2.2–42.7)	.07
Psychosocial Health Summary	12.3 (1.5–23.0)	.03	11.7 (-1.8–25.3)	.09
Emotional functioning	15.9 (0.9–31.0)	.04	13.6 (-7.6–33.9)	.20
Social functioning	10.7 (-2.7–24.0)	.12	15.5 (0.0–31.1)	.05
School functioning	1.3 (-27.6–30.1)	.93	-6.1 (-45.4–33.1)	.75
Parent proxy				
Total score	7.7 (0.4–14.9)	.04	7.7 (0.6–16.1)	.07
Physical Health Summary	10.5 (0.8–20.2)	.03	14.2 (3.3–25.2)	.01
Psychosocial Health Summary	5.7 (-1.2–12.5)	.11	3.6 (-4.1–11.2)	.35
Emotional functioning	6.7 (-0.7–14.0)	.08	5.2 (-3.3–13.7)	.23
Social functioning	5.2 (-2.3–12.7)	.17	3.8 (-5.2–12.8)	.40
School functioning	13.1 (1.6–24.6)	.03	9.4 (-7.5–26.4)	.27
Cancer Module				
Child self-report				
Pain and hurt	10.6 (-8.0–29.2)	.26	2.7 (-21.0–26.4)	.82
Nausea	4.8 (-9.5–19.0)	.50	7.3 (-11.5–26.1)	.43
Procedural anxiety	-12.2 (-35.7–11.3)	.30	-2.6 (-32.5–27.5)	.86
Treatment anxiety	10.2 (-8.1–28.4)	.27	12.0 (-11.9–35.0)	.29
Worry	9.2 (-8.1–26.6)	.29	6.9 (-15.3–29.1)	.53
Cognitive problems	12.7 (-0.5–26.0)	.06	7.0 (-10.2–24.1)	.41
Perceived physical appearance	5.1 (-12.7–22.9)	.56	7.3 (-15.2–30.0)	.51
Communication	15.8 (-3-3–34.9)	.10	21.3 (3.9–46.6)	.09
Parent proxy				
Pain and hurt	9.6 (-0.6–19.9)	.06	9.9 (-2.0–21.8)	.10
Nausea	1.8 (-7.6–11.3)	.70	9.9 (-0.2–19.5)	.04
Procedural anxiety	-10.9 (-24.1–2.3)	.11	-5.0 (-20.3–10.3)	.52
Treatment anxiety	-6.1 (-14.6–2.3)	.15	-6.3 (-16.5–4.0)	.23
Worry	8.8 (-0.9–18.6)	.08	10.5 (-0.4–20.6)	.04
Cognitive problems	7.8 (-0.8–16.5)	.08	1.7 (-7.8–11.2)	.72
Perceived physical appearance	0.1 (-10.5–10.3)	1.0	-1.7 (-12.6–9.2)	.76
Communication	1.9 (-11.1–15.0)	.80	0.6 (-14.0–15.3)	.93

β is the estimated mean difference and positive differences imply a higher score in the HBHC group
CI: Confidence Interval
Scores are adjusted for diagnosis, time since diagnosis, age at inclusion, and gender

Figure 1. Flowchart of the controlled trial



* From HBHC programme *n* = 4 and four children approached December 2009 and HBHC in 2010

Paper III

Pediatr Blood Cancer 2011;57:369–377

REVIEW
Hospital-Based Home Care for Children With Cancer

Helena Hansson, RN, MSc,[1] Inger Hallström, RN, DMSc,[2] Hanne Kjærgaard, RM, PhD,[1] Christoffer Johansen, MD, DMSc,[3] and Kjeld Schmiegelow, MD, DMSc[4]*

Hospital-based home care (HBHC) is widely applied in Pediatric Oncology. We reviewed the potential effect of HBHC on children's physical health and risk of adverse events, parental and child satisfaction, quality of life of children and their parents, and costs. A search of PubMed, CINAHL, and EMBASE led to identification of five studies that met the inclusion criteria. All sample sizes were small, and both the interventions and the outcome measures were diverse. Although burdened by these limitations, the studies indicate that HBHC is feasible and carries no crucial negative effects for children with cancer. Pediatr Blood Cancer 2011;57:369–377. © 2011 Wiley-Liss, Inc.

Key words: chemotherapy; pediatric oncology; quality of life; support care, review

INTRODUCTION

Since the early 1970s, there has been a dramatic improvement in the survival rate of children with cancer, primarily because of intensification of therapy. However, the diagnosis, aggressive treatment, and high frequency and long duration of hospital stays have considerable emotional and social effects on the whole family, which calls for alternative ways to provide care [1–4]. Pediatric home care (PHC) facilitates continuation of a normal life for children and their families by reducing disruptions resulting from hospital admissions. Accordingly, provision of PHC for children with cancer, as well as for children with other acute and chronic illnesses, is increasing because of technological developments, improvements in the understanding of factors for complications, the costs of hospital-based health care, changing policies, and the potential psychosocial advantages [5–8]. There is no consensus on the definition of PHC, but PHC is in general either a community-based service that primarily supports children with long-term conditions, or a hospital-based service that provides specialist care such as cancer treatment [9]. The different models of PHC provide, for example, drug administration, education of the family, and coordination of services. It is important to distinguish between outpatient treatment and PHC because outpatient treatment is provided by healthcare professionals in the outpatient clinic at the hospital, while PHC provides treatment by healthcare professionals in the patients' own home. Thus, outpatient treatment may avoid potential problems but also misses benefits of home treatment [10].

Despite the increasing provision of PHC in general, three systematic reviews of PHC have found that controlled studies are rare and that the evidence base is limited [5,7,9]. Knowledge is sparse about the effect of PHC on the frequency of hospital admissions, length of hospital stays, children's health outcomes and quality of life (QOL), and cost effectiveness. But current research, indicates that PHC is feasible and may lead to greater parent and child satisfaction with the medical care [5,7,9,11,12].

However, the three systematic reviews of PHC [5,7,9] did not include Pediatric Oncology treatment. Such children and their families have specific needs that differ from those of children with chronic disabilities or acute illnesses because of their complex intensive treatment and their potentially fragile somatic and psychosocial condition. Hospital-based home care (HBHC) for this patient group often involves highly potent medical treatments that may increase the risk of adverse events and strain on the families. Evidence of the strengths and weaknesses of HBHC for children with cancer and its effects is needed, but a systematic review is lacking. The present study evaluates the impact of HBHC on children with cancer.

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METHODS

Literature Search

We searched three databases (PubMed 1966–March 2010, CINAHL 1980–March 2010, and EMBASE 1980–March 2010) using medical subject headings and text words relating to HBHC services (home care agencies, home nursing, home infusion

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therapy, home chemotherapy) in combination with terms for children (infant, babies, adolescents, pediatric nursing, pediatrics) and cancer (neoplasms, oncology service, oncology nursing). We selected the databases PubMed and EMBASE to identify studies of healthcare interventions [13] and CINAHL, which focuses on home care nursing services. To capture the widest range of studies, we did not use specific terms for study design or outcomes of studies. Additional studies were identified through the reference lists of relevant studies. No language restrictions were used in the initial search, and all non-English language reports were identified to achieve an overview of the international research status. We did not search for unpublished data, ongoing studies, or data from conferences.

Inclusion and Exclusion Criteria

We applied the following criteria for inclusion in the review [13]: (a) type of studies: an intervention evaluating the impact of HBHC for children with cancer with at least one outcome measure (not necessarily pre-defined); (b) type of outcome measures: children's physical health, adverse events, parental and child satisfaction, QOL of children and their parents, and costs of using hospital data, questionnaires, or satisfaction surveys; (c) type of participants: children and adolescents aged 0–18 years with a cancer diagnosis; and (d) type of intervention: a service that provides medical treatments relevant for childhood cancer by hospital- or community-based healthcare professionals who take an active part in the care in the patient's own home as an alternative to a hospital admission. Interventions were intravenous chemotherapy, antibiotics, analgesics, or antiemetics compared with treatments delivered at the hospital. Therefore, the following services were excluded: (a) services providing end-of-life care because the aim of the cancer treatment was cure; (b) studies that included children and adults or adolescents if they did not specifically report separate results for the children; (c) services provided in ambulatory or outpatient settings; (d) oral therapy; and (e) care in which the parents administered the medical treatment.

We expected that only a limited number of randomized, controlled studies would be available and therefore also considered cohort and case–control studies and case series. Such studies were included if the design was comparable with inpatient care as well as studies in which patients were their own controls. Excluded qualitative studies or descriptive studies were taken into account in the narrative synthesis if they provided additional information that might be of value in a decision-making process or in planning future research. Finally, non-English studies were excluded because of a lack of resources for translation. Reasons for exclusion were recorded.

Data Extraction and Quality Assessment

The first author (H.H.) performed the initial screening of titles and abstracts of all studies to identify interventions of HBHC for children with cancer, and another author (K.S.) conducted a random rescreening of 20% of the initially identified studies. In the second step, potentially relevant studies identified in the preselection process were obtained as full text and screened by two reviewers (H.H. and K.S.) for inclusion criteria according to a standardized checklist (Fig. 1). One reviewer extracted the data (H.H.) into a standardized data collection form that included information about study design, sample size, participant details, home care intervention, and outcome variables. The second reviewer (K.S.) checked the data extraction forms for correctness. The methodological quality of the included studies was independently assessed according to the following criterion: potential bias caused by inadequacies in study design, outcome data/results, statistical methods, effect size calculation, quality of reporting, and quality of intervention [13,14]. The quality of the studies was not scored, but individual aspects of methodological quality were considered. The two reviewers (H.H. and K.S.) resolved any disagreement in the screening, extraction, and assessment process by consensus.

Because of the small number of studies, diversity of interventions, and lack of common outcome measures, a meta-analysis was inappropriate as was a sensitivity analysis to evaluate the impact of study quality on outcome, statistical assessment for heterogeneity, and statistical subgroup analysis. Thus, a narrative summary is provided [13].

RESULTS

The initial search yielded 496 titles and abstracts, of which 466 were not relevant to the review. There were 8 potentially relevant reports in a non-English language, and 5 of these seemed to comprise home care, as this was mentioned specifically in the title. Two articles respectively published in 1979 by LM. Martinson and in 1984 by C. Nunneley could not be retrieved. The remaining 30 studies from the search and the 3 studies identified in the reference lists were reviewed in full and assessed for inclusion. Twenty-eight [6,8,20–27,30–47] of the 33 studies did not meet the inclusion criteria (Table I), leaving 5 studies relevant to the final review (Table II). The number of participants in the included studies ranged from 14 to 45. Three of the studies were from the United States, 1 from Canada, and 1 from Italy. Only one randomized crossover trial [15] was included. Other studies were designed with children as their own control group (1 study) [16] and 3 studies [16–19] had no true control group, but compared the home care with corresponding inpatient care. All 5 studies involved provision of HBHC to children with cancer, but the cancer diagnoses, types, and numbers of treatments, healthcare providers, and outcomes varied. Additionally, the description of interventions also differed with respect to details and content. A single study [15] reported effect size calculation. Thus, there are potentially significant problems with bias that may have affected the results.

Quality of Life of Children and Their Parents

Two studies examined the children's and parents' QOL when receiving intravenous chemotherapy at home, and both studies [15,16] reported that QOL was overall improved with HBHC. Close et al. [16] assessed QOL using a questionnaire developed specifically for their study and found that the patients had significantly greater well-being and better appetite, felt more independent, were more satisfied, and had greater ability to keep up with their school work when they received chemotherapy at home. Additionally, the parents were significantly better at keeping up with household tasks, maintaining their jobs, and spending time with one another and with their other children during HBHC. In a crossover study by Stevens et al. [15], children were randomly

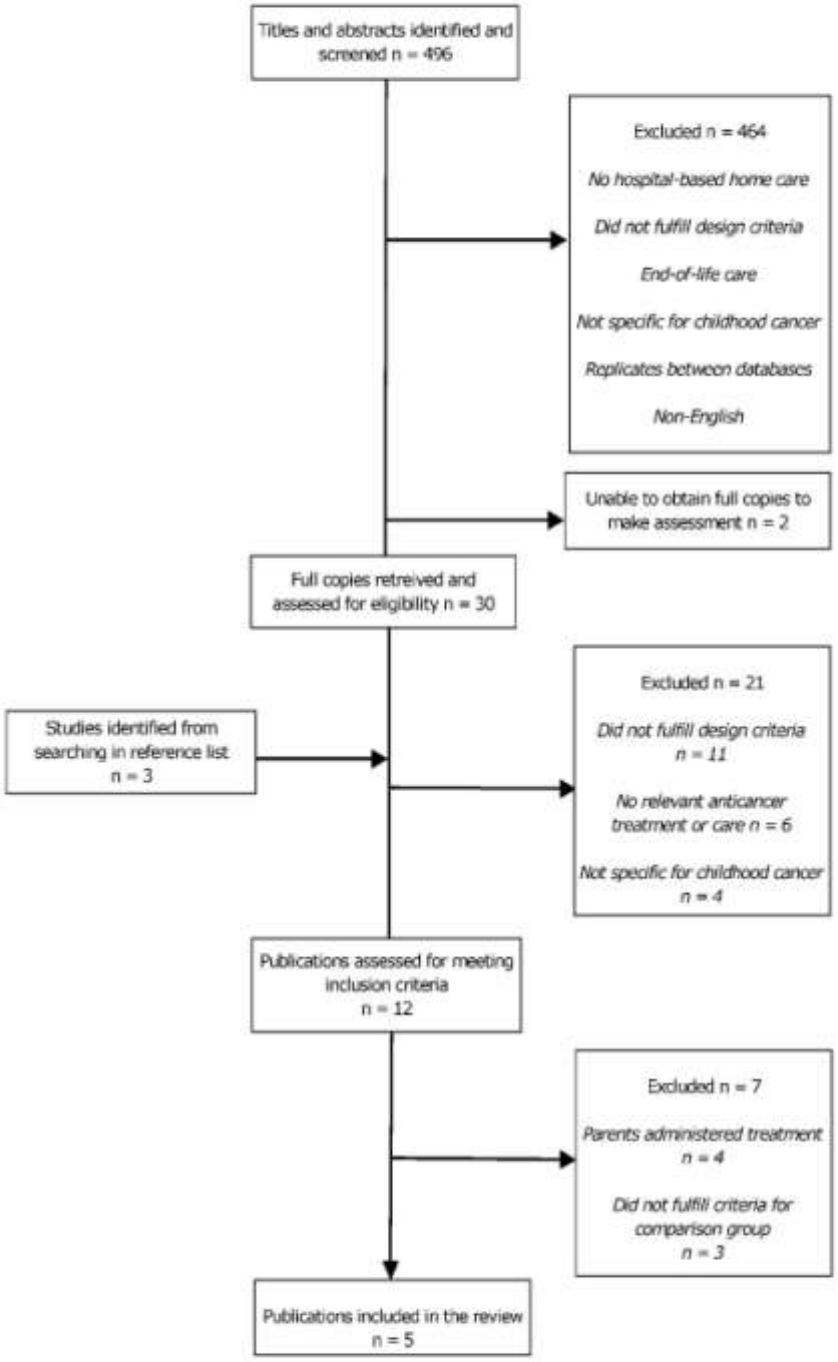

Fig. 1. Flow chart of study selection process.

assigned either to hospital standard care or home chemotherapy during phase 1, which lasted 6 months. Children randomized to the hospital care group in phase 1 were transferred to the home treatment group for phase 2 (6 months) and vice-versa. The children's QOL was assessed, as well as the parents' caregiver burden, through validated questionnaires on three occasions for each 6-month period, that is, before and at 3 and 6 months after the start of each phase. The definition of QOL included physical, social, and emotional functioning and the reaction to current medical treatment. The authors reported

TABLE I. Characteristics of Excluded Studies

Refs.	Exclusion criteria
Aguilera et al. [30]	Case report
Bendorf et al. [31]	Descriptive study, end-of-life care
Clarke [32]	Qualitative study (not hospital-based home care)
Fergusson et al. [33]	Descriptive case study
Frierdich et al. [8]	A report on community and home care services
National Association of Children's Hospitals and Related Institutions Patient Care Oncology FOCUS Group 2000 [22]	A report on home care recommendations for children with cancer
Gelesson et al. 2009 [34]	Qualitative study
Goldsmith et al. [35]	Qualitative study (not hospital-based home care)
Hooker et al. [24]	Parents administered the home care
Jayabose et al. [23]	Parents administered the home care
Kandsberger [6]	Review design
Køhlen et al. [36]	Qualitative study, no children with cancer
Lashlee et al. [25]	Descriptive study, no clear comparison group
Pasut [37]	Case report
Raisch et al. [26]	Parents administered the home care
Ratcliffe [38]	Case report, not specific for childhood cancer
Rizzari et al. [39]	Included children with other diagnoses than childhood cancer, no relevant anticancer treatment (not hospital-based home care)
Shah et al. [40]	No clear comparison group. Included end-of-life care.
Simon et al. [41]	No relevant treatment and care (not hospital-based home care)
Simon et al. [27]	Pilot study, no clear comparison group
Smith et al. [42]	Outpatient care, no relevant anticancer treatment (not hospital-based home care)
Stevens et al. [20]	Qualitative study
Stevens et al. [21]	Qualitative study
Sung et al. [43]	Oral outpatient treatment
Talcott et al. [44]	Pilot study, not specific for childhood cancer
Weaver et al. [45]	Case report, not specific for childhood cancer
Wiemikowski et al. [46]	Parents administered the home care
Wolfe [47]	Descriptive study, no clear comparison group

statistically significant improvements in the children's physical and social functioning when they switched from hospital treatment to receiving home chemotherapy during the first 3 months after crossover, but not after 6 months. Furthermore, at the end of each 6-month phase, the children had significantly more emotional distress in the HBHC group compared to the hospital care group. Thus, in this study, the children's physical and social functioning did not differ significantly between the two care programs in the long term, although children receiving home chemotherapy tended to experience more emotional distress regardless of the phase in which they received it.

Parental and Child Satisfaction

In two studies [16,18], the great majority of the parents and children preferred home care. In the study by Close et al. [16], 13 out of 14 families chose to receive the subsequent chemotherapy at home, and the author could thus conclude that most parents prefer home care. The Lange et al. study [18] reported that no family requested to return to inpatient care.

Children's Physical Health and Adverse Events

Four studies examined children's physical health and adverse events, and all reported HBHC to be a safe alternative to hospitalization for the children. Close et al. [16] found only a single adverse event (an occluded Broviac catheter). Lange et al. [18] reported six episodes of subcutaneous inflammation along the intravenous lines and two cases of miscommunication in teaching the parents, which led to parental anxiety. Holdsworth et al. [17] reported that no acute complications occurred during home chemotherapy and that successful control of the children's nausea and vomiting was achieved. Finally, Stevens et al. [15] found no significant differences between the home chemotherapy and standard hospital chemotherapy groups in the incidence of adverse events such as minor drug reactions, problems with venous access routes, adverse effects of chemotherapy, and unscheduled hospital visits. However, none of the studies reported their rules for stopping the home care program as a result of an increased frequency of adverse events.

Costs

Four of the studies [16–19] reported that HBHC reduced costs of care compared with inpatient care, but their applied methods and assessment differed. The only randomized study [15] could not demonstrate any reductions in costs in relation to HBHC.

Close et al. [16] reported that the mean billed medical cost per day, the mean out-of-pocket expense per day, and the loss of wages per course of chemotherapy were significantly lower with home care. Holdsworth et al. [17] summed up all charge categories for inpatient and home chemotherapy delivery and then

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TABLE II. Characteristics of Included Studies in Alphabetical Order

Refs.	Country	Study design	Participants, age	Diagnosis	Type of care and treatment provided at home	Comparison group	Outcomes	Results
Close et al. [16]	USA	Prospective controlled study	14 children, ages 2–16 years	Solid tumor, brain tumor, and non-Hodgkins lymphoma	Community nurses provided intravenous 24-hr owncontrol infusion of methotrexate, etoposide, ifosfamide, cytoxan, vincristine, cisplatin, and lomustine. Supportive care included 48 hr of hydration, one dose of calcium leucovocin, and MESNA administered by the parents	The 14 children are their own control group. Compared one corresponding treatment in the hospital with one identical treatment at home	Quality of life (QOL) measured with self-developed questionnaire, and costs by billed medical charges, out-of-pocket costs, and loss of wages	The patients received 76 courses in total at home. Home care improved QOL for both children and parents and reduced costs
Holdsworth et al. [17]	USA	Prospective study	44 children, age 9 ± 5 years	Most common diagnoses were Ewing's sarcoma, osteosarcoma, acute leukemia, and hepatoblastoma	Home care agency nurses provided intravenous chemotherapy. Most frequent were vincristine, cyclophosphamide, dactinomycin, ifosfamide, etoposide, and methotrexate	No actual control group but compared treatments in the hospital with identical treatments at home	Control of nausea and vomiting monitored by a survey, adverse effects from nursing records and costs by summing up all charges for inpatient and home care and then comparing the difference	Mean number of courses per patient was 5.8 ± 4.4. Control of nausea and vomiting comparable or superior in home care. No serious adverse events. Home care reduced costs for patients and/or third-party payers
Lange et al. [18]	USA	Prospective study	22 children, ages 2–20 years	Acute lymphoblastic leukemia	Home care agency nurses provided intravenous 24-hr infusion of methotrexate in a peripheral vein. Parents administered hydration	No actual control group but compared corresponding treatments in the hospital with identical treatments at home	Costs calculated by billed charges and inpatient days	120 infusions in total were provided. Home care reduced inpatient days and costs. No family requested inpatient therapy
Miano et al. [19]	Italy	Prospective study	45 children, ages 1 month–19 years	Solid tumor, brain tumor, and leukemia	Hospital-based nurses and physicians provided, e.g., antiviral, antifungal, or other intravenous therapy, blood withdrawals, and blood transfusions	No actual control group but compared corresponding treatments in the hospital with identical treatments at home	Costs calculated by the average cost per patient of 1 day of home care-based charges to the hospital	A total of 881 nurse and/or physician visits. Home care reduced the average cost per patient

(Continued)

TABLE II. (*Continued*)

Refs.	Country	Study design	Participants, age	Diagnosis	Type of care and treatment provided at home	Comparison group	Outcomes	Results
Stevens et al. [15]	Canada	Randomized crossover trial with two phase crossover design	23 children, ages 2–16 years	Acute lymphoblastic leukemia	Community nurses provided intravenous therapy, e.g., methotrexate, vincristine, and cytosine arabinoside, depending on the phase of treatment according to the child's protocol	Children were their own controls	Children's QOL measured with the questionnaire, "The Pediatric Oncology Quality of Life Scale and Child Behavior Checklist" and the parental caregiver burden by the Caregiver Burden Scale. Adverse effects abstracted from hospital and community charts and costs by the Health Service Utilization and Costs of Care Inventory	A total of 24/29 patients were on maintenance phase of their protocol when they began the study. No differences in caregiver burden or adverse events. QOL was overall improved for the parents and children, but the children seem to experience more emotional stress during home care. No difference in total cost from a societal perspective

compared the difference in total charges for each chemotherapy protocol. They reported substantial reductions for both the patient and/or third-party payer. Lange et al. [18] reported that the home program reduced the billed costs of chemotherapy infusion. Miano et al. [19] reported a significantly lower average cost per patient by calculating the average cost per patient of 1 day of HBHC based on the price charged to the hospital for drugs, blood tests, and transfusion support, plus the cost of the staff based on the amount of time spent with each patient. In contrast, Stevens et al. [15] reported no significant differences on total societal costs when comparing hospital care and home care. They evaluated costs from a societal perspective by the Health Service Utilization and Costs of Care Inventory, and the assessment included total cost of services, parent information on visits, and direct out-of-pocket expenses as well as indirect costs.

DISCUSSION

Main Findings

Although HBHC for children with cancer is widely used, there is limited valid data on its psychosocial, clinical, and economic effects. We identified only five studies, and the variations in the methodological rigor, interventions applied, and outcomes explored precluded drawing reliable conclusions. Evidence remains insufficient to show whether HBHC improves the children and family QOL and clinical outcomes or reduces costs for the families or the health service. These findings are consistent across the studies and with three systematic reviews [5,7,9] of HBHC for acute and chronically ill children. The only randomized study included in this review showed that the children appeared to experience more emotional distress when receiving home chemotherapy. The authors suggested that the stress may be caused by the medical interventions at home or the challenges related to the organizing process and partnerships with the community. Stevens et al. [20,21] also conducted two qualitative interview studies with the participants from their randomized home chemotherapy study. The children, parents, and the healthcare professionals reported that home care overall had a positive effect on daily lives of the children and their families and on their well-being, and they preferred home care, even though the children had reported more emotional stress in the questionnaire study.

The few studies that addressed safety during HBHC had insufficient power to truly evaluate the risk of serious adverse events. In spite of that children with cancer are frequently treated on an outpatient basis and at home, especially in the United States [8,22]. Yet, the included studies [15–19] and a number of the studies [23–27] excluded from the review indicate that it is feasible to provide complex medical treatments at home for children with cancer and that may be less disruptive for the children and their families. Moreover, families seem to prefer HBHC to hospital care.

We argue that the gap between the increasing number of HBHC programs that are clinically implemented and the empirical evidence raises concern. First, the child's safety is an essential factor in HBHC, but published studies overall are lacking sufficient power to explore issues of serious adverse events such as bloodstream infections. Thus, the toxic death rate for children with cancer in remission may be in the order of 2–4%, mostly

because of infections [28], and monitoring of the many hundreds of children in HBHC programs is thus needed to explore if this incidence is moderately but significantly increased.

All studies so far have small sample sizes and thus were underpowered to detect significant differences in such severe toxicities. Moreover, 4 of the 5 included studies did not calculate effect size. These small study sizes are burdened by the risk of type 2 errors and may thus overestimate the safety and benefits of HBHC. A randomized, controlled trial would require multiple sites for sufficiently large samples to detect differences in clinical outcome and effects on the children and the family members. However, in studies of childhood cancer, the sample size is often small, and conducting randomized controlled trials with children carries both practical and ethical considerations. Ethical issues need to be considered in future studies, including rules for cessation in cases of fatal or unexpected serious complications. Accordingly, studies based on other designs are important when trying to summarize research evidence, but the scientific standards for such studies should be as high as those for more conventional therapeutic clinical trials.

Second, we identified important challenges in the quantification and qualification of the psychosocial, clinical, and economic outcomes in the conduct of studies on HBHC for children with cancer. Because of the diversities in the practical provision of HBHC with respect to the care providers and whether the care includes chemotherapy or only less toxic treatments, these features should be explored and clearly reported. The great variety of outcome measures and the lack of descriptions and consistent definitions in some of the included studies make it difficult to evaluate and compare these features and the measurement.

None of the studies report a strategy for comparing and prioritizing among various empirical outcome measures of HBHC versus hospitalization to evaluate which is the most important outcome to be considered when implementing HBHC. Thus, there is a need for standards that allow reliable comparisons between hospital and home care, including the use of validated QOL measurements. There may also be potential significant problems with bias in the study designs regarding incomplete outcome data, group/individual matching, follow-up methods, and crossover effects. The Close et al. study [16] compared one course of chemotherapy at the hospital with one identical home chemotherapy treatment for the same 14 children. The children are their own controls, it is a small sample size, and only one home treatment constitutes the basis for comparison and is thus susceptible to bias that may affect the outcomes. In the Stevens et al. [15] crossover study, there is also the possibility of a carryover of the effect of the intervention provided in the first period into the second intervention period. The other three studies [17–19] did not compare groups from the same population with and without HBHC but only compared a home treatment with a historical inpatient treatment. Moreover, the allocation for participation in the HBHC program and outcome assessment were unclear and are thus sensitive to bias.

Third, we believe that evaluation of the costs may differ depending on the healthcare structure of the society in question, be it based on private or public hospitals, and public or insurance-based financial coverage. Three of the included studies were from the United States, where the care provision in general is based on insurance, the provision of HBHC is extensive, and the cost savings may be substantial simply because of the methods for calculating the costs. Thus, both hospital and home care charges are based on average costs, and transferring the most complicated patients to HBHC may give a misleading impression of the actual savings when only billed costs are included in the calculations. Furthermore, the type of treatment included in the HBHC and the distance between the hospital and the patient's home will also influence actual overall costs but not necessarily the billed costs. Thus, the published studies differ as to whether or not they included only the direct costs for the healthcare sector or also the indirect cost for the families and the society. Only the Canadian study by Stevens et al. [15] discussed these financial aspects, and they reported no overall cost savings from a societal perspective. Therefore, the results need to be interpreted with caution with respect to cost savings.

Finally, because of our search strategy and inclusion criteria, this review also has potential limitations other than the methodological limitations of the included studies. We did not include meeting reports, ongoing studies, or publications in languages other than English. The review is therefore potentially subjected to publication bias as well as language bias. Furthermore, overlooked reports or studies could have affected the results. The issue of outpatient care and initiating therapy at the hospital that later is handled by parents is a different but equally important and interesting topic that would require a separate review. We believe that the current review provides important and reliable information about the current research status and is thus valuable when planning HBHC programs and future research. It can be challenging to systematically review complex interventions [29] such as HBHC, and future reviews on HBHC for children with cancer may consider including relevant qualitative studies and data from a broader range of study designs to improve the synthesis and interpretation of the interventions [29].

CONCLUSION

This review demonstrates that there is limited evidence on the effect of HBHC for children with cancer and that it is difficult to draw clear conclusions from the published studies given the disparity in the interventions, the methodological limitations, and the differences in healthcare systems. Despite these potential biases, the limited evidence suggests that HBHC for children with cancer is feasible and associated with no crucial negative effects. The medical as well as psychosocial costs related to Pediatric Oncology require evaluation of the value of HBHC that is as vigorous as the more traditional survival endpoints and that should be reported as part of the outcome of collaborative trials.

There is a need for further research with controlled, prospective evaluations of HBHC with a standardized and consistent method of measuring relevant clinical outcomes as well-defined health outcomes, QOL measures, satisfaction with care, and health economic evaluations of direct costs for health organizations and indirect costs for the families and the society. Another important issue is the children's own perceptions and the parents' experiences with the benefits and disadvantages of HBHC. These issues are as relevant as conventional endpoints and could be evaluated by using parent proxy-reported and child self-reported standardized cancer-specific questionnaires measuring how HBHC affects the children and their families and their satisfaction with care, and by qualitative interview studies. Collaborative

childhood cancer groups that routinely use HBHC should in their reports on clinical outcomes include data on all patients that address costs and QOL in relation to the structure of care.

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