Improving aspects of palliative care for children

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Citation for published version (APA):

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Chapter 7

General Discussion
In this thesis, three aspects of pediatric palliative care are presented: the palliative course of incurable malignant disease, aspects of care by a pediatric palliative case management team, and the adherence to the national clinical guideline of pediatric palliative care. Insight in these aspects fills in the gaps in knowledge on which no or scarce literature is available and where there is no consensus on policy. This way the results of this thesis contribute to the improvement of the quality of pediatric palliative care. The presented studies are part of the overarching PANDA study (Palliative care, ANticipating Dedicated and Adapted) a collaboration between researchers from two universities. This final concluding chapter of the thesis gives a summary of the main findings as well as a reflection on those and considers limitations of the studies included in this thesis. Further, it provides directions for future research and clinical implications to improve palliative care.

**Summary of main findings**

**Insight in the palliative course of disease of children with incurable malignant disease**
To provide anticipated care it is essential to obtain insight in the palliative phase of children with an incurable malignant disease. The thesis provided an overview of what can be expected in the course of disease during the palliative phase of children with a malignant disease in chapter 2 and 3. The main results are presented in table 1.

The first study (chapter 2) describes the course of the palliative phase of children with a malignant brain tumor, while the second study (chapter 3) addresses patients with an incurable non-CNS tumor. The studies cover the wide scope of symptom occurrence, and timing of occurrence, and the associated management of the symptoms. Moreover the studies include information on duration of palliative phase, number, duration and indications for hospital admissions, administration of cancer directed therapy, DNR-discussions and place and circumstances of death. We illustrate, that except for patients with bone tumors whose palliative phase was significantly longer than in other tumors, the duration of the palliative phase is estimated a median of 72 days (range 1-603 days). In both cohorts the most frequent documented symptom was pain (both > 90%). For children with a brain tumor, poor mobility and somnolence were frequently reported. Early occurring symptoms in the palliative phase were altered mobility, speech disorders and loss of sight or hearing, while somnolence, dysphagia and dyspnea had the shortest duration. Children with a non- CNS tumor had changed appearance, vomiting and dyspnea, documented in most patients. Symptoms occurring early in the palliative phase were pain, seizures and skin problems, while changed cognition and dyspnea had the shortest duration. Do-not-resuscitate agreements were discussed with all parents and all patients above 12 years old. Almost 80% of both cohorts died at home.
### Table 1. Insight in the palliative phase of children with cancer

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Aim</th>
<th>Sample of children</th>
<th>Measures</th>
<th>Conclusions</th>
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<tbody>
<tr>
<td>2</td>
<td>To describe the specific trajectory of an incurable brain tumor in children and focus on timing of occurrence and duration of symptoms until death</td>
<td>N= 8 (24%) medulloblastoma N=7 (21%) GBM N=5 (15%) DIPG N=5 (15%) ATRT N=5 (15%) Other CNS tumor N=4 (12%) anaplastic ependymoma Total N=34</td>
<td>Outcomes: -Duration of curative phase -Duration of palliative phase -Administration of cancer-directed therapy -Occurrence and timing of symptoms -Management of symptoms -Location of death -Discussion of DNR agreements</td>
<td>1. Duration palliative phase= 1-603 (median 80) days 2. Palliative cancer-directed therapy = 23 (68%) patients 3. Most frequent symptoms pain (91%), poor mobility (74%), and somnolence (71%) 4. Intravenous treatment with morphine= 38%, median 4 days 5. Intravenous sedation before death in 15%, median 2.5 days 6. Location of death 27 patients (79%) at home1 in a hospice, six (18%) in the hospital 7. DNR agreements addressed in 100% of patients</td>
</tr>
<tr>
<td>3</td>
<td>To describe the specific trajectory of an incurable tumor in children and differentiate between hematologic malignancies, neuroblastoma, bone tumors and other non-cns tumors</td>
<td>N=11 (29%) bone tumor N=10 (26%) neuroblastoma N=3 (8%) hematologic malignancy N=14 (37%) other solid non-CNS tumor Total N=38</td>
<td>Outcomes: -Duration of curative phase -Duration of palliative phase -Administration of cancer-directed therapy -Occurrence and timing of symptoms -Management of symptoms -Location of death -Discussion of DNR agreements</td>
<td>1. Duration palliative phase= 6-855 (median 67) days. 2. Palliative cancer-directed therapy= 27 (69%) patients 3. Most frequent symptoms pain (95%), changed appearance (63%), vomiting (63%) and dyspnea (63%) 4. Intravenous treatment with morphine= 44%, median 12 days 5. Intravenous sedation in 24%, median 7 days 6. Location of death 28 (74%) patients at home, ten (26%) in the hospital 7. DNR agreements addressed in 100% of patients</td>
</tr>
</tbody>
</table>

Abbreviations: ATRT atypical teratoid rhabdoid tumor, DIPG diffuse intrinsic pontine glioma, sPNET supratentorial primitive neuro-ectodermal tumor, GBM glioblastoma multiforme, DNR do not resuscitate.

### Insight in the intensity and content of care provided by the pediatric palliative care team

Yearly about 35 children, who are treated for a life-shortening disease in our university hospital, die an expected death. To optimally support this patient group as well as all patients in the chronic palliative phase of a life-shortening disease, a Pediatric Palliative Care Team (PPCT) has been initiated in June 2012. To align pediatric palliative care to the specific needs of patients and their families, it is necessary to obtain detailed insight in the demands of patients and their families as reflected in consultations between patients, families and HCPs. It is needed to know on which locations, on which subjects patients need support, by whom the contacts between the PPCT and parents are initiated and to what intensity support is provided. We conducted two studies to obtain more insight in
the intensity and content of care provided by the pediatric palliative care team (in chapter 4 and 5). The main results are presented in table 2.

### Table 2. Insight in the intensity and content of care provided by the pediatric palliative care team

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Aim</th>
<th>Sample</th>
<th>Measures</th>
<th>Conclusions</th>
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<tbody>
<tr>
<td>4</td>
<td>To gain insight in what aspects of case management are provided by the PPCT and in what intensity? And what are the amounts, durations, and indications of hospital admissions. Are there differences for patients with MD vs NMD?</td>
<td>43 children, Study period 9 months, -22 with MD, -21 with NMD</td>
<td>Outcomes: -Duration of support -Intensity of support in minutes per day -Location of support -Admissions and its indication</td>
<td>1. Patients with MD have a shorter duration of support than patients with NMD 2. The intensity of received support is higher for MD patients compared with NMD 3. Patients with MD receive more support from the PPCT at home whereas patients with NMD receive more support from the PPCT in the hospital. 4. Patients with NMD are admitted to the hospital more often and longer</td>
</tr>
<tr>
<td>5</td>
<td>To gain detailed insight in pediatric palliative case management as provided by the PPCT, and the contents of contacts between the PPCT and parents, and define differences between MD and NMD</td>
<td>455 contacts with 70 patients, In 89 days, -27 MD, -43 NMD</td>
<td>Outcomes: -Number of contacts per person -Discipline the contact is with -Timing of contacts -Subject of contact -How a contact was initiated</td>
<td>1. Median of 5 contacts per patient in the study period with the PPCT 2. 280(62%) of the contacts were with the specialized nurse, no contacts with the chaplain 3. 95% of all contacts took place during office hours 4. 38% of all discussed topics was psychosocial MD patients discussed school and daycare significantly more often, NMD patients discussed socio-economic issues more often 5. 50% of contacts was planned, 25% unplanned initiated by parents, 25% unplanned proactively initiated by the PPCT</td>
</tr>
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Abbreviations: PPCT pediatric palliative care team, MD malignant disease, NMD non-malignant disease.

**Chapter 4** showed that patients with MD and NMD receive a significantly different approach in palliative support. Whereas patients with MD have a relatively shorter duration in which they receive intensive support, patients with NMD have a significant longer phase in which less intensive support is needed. Also the location of support differs between the two cohorts. Our study shows that patients with NMD are admitted more often and longer during the palliative phase and receive support of the PPCT significantly more often within the hospital compared to MD patients.
In chapter 5, we provided more details on the content of support provided by the PPCT. 62% of all contacts were between patients or families and the specialized nurse. The child life specialists, psychologist and social worker also had regular contacts whereas the chaplain had no contacts with patients or their families. 95% of all contacts took place between 8 am and 6 pm during weekdays, a limited number between 6pm and 9pm. 25% of all contacts were proactively initiated by the PPCT, 25% were unplanned initiated by parents, while 50% of the contacts were planned in advance. In these contact characteristics, no differences were seen for MD and NMD patients. Psychosocial topics were addressed most frequently. Parents of MD patients consulted the PPCT more often about school and parents of NMD patients about socio-economic issues.

Compliance of the PPCT to the Dutch guideline for pediatric palliative care
To improve quality of palliative care through a national clinical guideline on pediatric palliative care, it is important to know to what extend the pediatric palliative care team complies to the guideline, and to research whether the compliance can be improved. We conducted a study to evaluate the compliance to the Dutch National clinical guideline pediatric palliative care, and we assessed whether an e-learning program with an interactive educational meeting, is an effective method to improve compliance (chapter 6). The main results are presented in table 3.

Chapter 6 described the process of selecting quality indicators to measure the compliance to the Dutch clinical practice guideline “pediatric palliative care”. Additionally we designed an educational program, including 4 e-learning modules and an interactive educational meeting, and assessed whether the PPCT showed a higher compliance to the guideline after the educational program. Eleven quality indicators were selected. The educational program did not result in significant improvement in compliance for any of these indicators. The indicators “treatment of nausea”, “pain medications two steps ahead” and “pain medication for 48 hours present”, as measured through parent reports, scored a compliance beyond 80% before and after e-learning. The remaining indicators measuring compliance, as well as six indicators measuring documentation by chart review, showed a compliance below 80% before and after e-learning.
**Table 3.** compliance to the guideline “palliative care for children”

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Aim</th>
<th>Sample</th>
<th>Measures</th>
<th>Conclusions</th>
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<tbody>
<tr>
<td>6</td>
<td>To test the effect of the education program on actual compliance as well as documentation of compliance to the guideline</td>
<td>-11 quality indicators</td>
<td>Effect of education program on guideline compliance</td>
<td>1 No significant effect of education program on compliance to the guideline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-4 e-learning modules</td>
<td>Parental report on compliance</td>
<td>2 “Treatment of nausea”, “pain medications two steps ahead” and “pain medication for 48 hours present”, measured through parent reports, scored a compliance beyond 80% before and after intervention</td>
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<td></td>
<td></td>
<td>-7-month pre-intervention evaluation</td>
<td>Case-managers’ report on compliance</td>
<td>3 Compliance of all other indicators retrieved from case-managers’ chart reports was measured below 80% pre- and post-e-learning</td>
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<tr>
<td></td>
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<td>-6-month post-intervention evaluation</td>
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<td></td>
<td></td>
<td>-5 case managers</td>
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<tr>
<td></td>
<td></td>
<td>-73 patients</td>
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**Reflection on main findings**

As stated in the introduction, there is an increasing interest in pediatric palliative care, as is also reflected by the updated WHO definition on pediatric palliative care as well as emergence of many pediatric palliative care management teams that have been initiated internationally[1-11]. Even though this increasing interest is also visible in more research on the subject, there is limited consensus on what optimal pediatric palliative care should look like, and what it should comprise. One of the important aspects of pediatric palliative care, as is stated in the WHO definition[1] and is substantiated in several studies, is that pediatric palliative care should be anticipating[12-14]. As Kassam et al stated, parents highly value being prepared for medical aspects surrounding death[15] and Rosenberg et al found that parents experience lower levels of distress when prognostic understanding is aligned with treatment goals despite the understanding that the child’s illness is incurable[16]. A study by Mack et al. showed that parents of children with advanced cancer rated the quality of care provided by oncologists more highly when they felt they had received clear information about what to expect during the end-of-life period [17].

Also Groh et al found that information on the expected course of disease was identified as one of the most helpful aspects during pediatric palliative care particularly[18], and research has shown that this preparation is of high value for parents and will potentially reduce post-traumatic stress symptoms for parents[19, 20]. To provide this type of information, clinicians themselves ought to know what to expect during the progressing malignant disease. Additionally, van der Geest et al and Kreicbergs et al state that the severity of uncontrolled pain was, among other symptoms, related to higher levels of long-term parental grief[21, 22], which emphasizes the importance of optimal symptom management not only for the child’s benefit, but also for the family’s wellbeing. Even
though the importance of this anticipatory approach is clear, information on the course of the palliative phase of incurable malignant disease is limited, the presented numbers are very diverse and no research is available on timing of symptom occurrence[23-27]. Also, tumor specific research regarding palliative care is scarce[24, 27-29]. Chapters 2 and 3 extend our knowledge of occurrence of symptoms and it’s timing of occurrence in relation to the start of the palliative trajectory of a pediatric malignancy, and on how long these symptoms will exist before death occurs. This new knowledge will support pediatric oncologists to prepare parents and primary healthcare professionals and enables anticipating palliative care with upfront symptom management, and early end-of-life decision making in the palliative phase of children with an incurable malignancy.

Another suggestion on what pediatric palliative care should offer, as is stated in the definition of palliative care, is that pediatric palliative care should be continuous, and demands a coordinated, broad approach by a multidisciplinary team. To be able to deliver this kind of support, several PPCTs have been initiated internationally[2-11]. However, even though there are some reports making suggestions on what disciplines should be represented in the team and what the team should offer, there is no consensus on its most optimal composition. This could be due to the fact that there is no research on to what extent and on which subjects the patients request the support provided by the team. Chapter 4 and 5 show a unique overview of the duration of received support, as well as the actual time spent on support, the activities on which time is spent, and the location of support. As is in line with the suggestions of Monterosso et al[30, 31], we found that patients with MD receive support for a shorter duration and with more intensity compared to patients with NMD. Also the subject of contents of care differs significantly. Even though research is scarce, this could imply that support for patients with MD should be set up differently than the support for patients with NMD. Future research should further define these differences and pediatric palliative care teams should be designed appropriately to offer these different approaches.

Chapter 5 suggests that 24/7 coverage is not necessary in our Dutch national care setting, since a very limited number of acute contacts took place outside office hours. However, different studies point out that 24/7 coverage is highly valued by caregivers and parents[15, 32]. Further research should investigate what prevented parents from calling outside office hours. It could be possible that the anticipating character of the support provided by the PPCT limits the need of support at night.

No contacts were reported in chapter 5 between the chaplain and the patients or parents, which suggests that the availability of a chaplain in a pediatric palliative care team could be overdone. However, Hexem et al found that spirituality plays an important role in most parents dealing with a child with a life threatening disease[33]. According to Knapp and colleagues, spiritual assessments should be conducted for all parents involved in such a burdensome trajectory of life shortening disease of a child, in order to provide appropriate supportive strategies [34]. Kassam et al found that involvement of a religious
or spiritual mentor was highly valued by parents, but not by the clinicians[15]. Robinson et al evaluated parental spirituality at the end of life and found that several parents noted that it was most helpful that the health care team provided access to and make welcome both community clergy and hospital chaplains on their behalf[35]. However, despite the availability of a chaplain in our center, there were no reported contacts between our chaplain and patients or parents during this study period. Groh et al found similar results and found that most of the parents explicitly refused any form of spiritual support[32]. There are several possible explanations for this contradiction and further research is needed to achieve full comprehension. First of all, it could be that in Western Europe, spirituality is experienced as less important than in other regions. Also, parents may turn to their own familiar spiritual mentor/ chaplain in these burdensome situations. Also, difficulty in distinguishing the definitions of religion and spirituality may be part of the explanation. Possibly other professionals of the PPCT offer enough supportive spiritual support to parents, minimizing the role of a chaplain. Also, the additional value of a chaplain during the multidisciplinary meetings is seen for professionals to educate aspects of care regarding spiritual wellbeing and to improve the skill to deal with these issues from the perspective of the professional, parents and/or the child[36].

Completeness in pediatric palliative guidelines is not reached yet, since the existing guidelines provide general directions, are mostly from single institutions, and often focus on coordination of care, continuity of care, and early integration of palliative care[37]. Practical guidelines to be implemented in daily clinical practice, are still lacking. To fulfill this gap, recently the Dutch Association of Pediatrics (NVK) has developed an interdisciplinary clinical practice guideline (CPG) palliative care for children in summer 2013 based on the best available evidence as well as expert opinions[38]. The main focus of this Dutch CPG is symptom management, decision-making and organization of care. The recommendations in the guideline aim at reducing variability of care, minimize under- and over-utilization of resources, and ultimately have the potential to improve the quality of palliative care[39]. We qualified indicators for the evaluation of the care according to this guideline. So far, no formal implementation program was launched to promote its use. It is known that CPGs don't implement themselves, and a well-organized implementation strategy is necessary to increase the guideline's general performance and its effectiveness to change clinician's behavior[40, 41]. Since research suggested that multifaceted educational programs are most effective in changing behavior[42-44] and that e-learning programs have shown improvement of knowledge when compared to non-intervention and other teaching interventions, we chose to design a multifaceted educational program including e-learning modules[45, 46]. However, based on chart review, chapter 6 shows no effect of the educational program on the compliance of the PPCT to the guideline. These results are in line with other research, showing low clinical guideline scores[47, 48] and limited effect of implementation strategies[49-53]. It is well supported by literature that no magic bullet has been found to optimize compliance to a guideline[41, 54-56].

General Discussion
Future research should further focus on how implementation strategies should be designed to persuade clinicians to change daily practice. Although many different strategies are seen and described in literature, such as e-learning programs, and audit and feedback, a recent Cochrane review found 4 RCTs describing the effect of different interventions on guideline compliance, of which a specific guideline adhered tool described as face-to-face instruction, pocket card and/or prealigned forms showed about 13.5% improved adherence[57]. Even though it is scientifically supported that a combination of strategies will most probably lead to better adhesion to the guideline[42-44], there is no consensus on what combination of interventions will be most optimal. Moreover, there is probably a limited generalizability on this subject. Francke et al suggested in a systematic meta-review that complexity of the guideline is an important limiting factor in the success of implementing a guideline. Even though the PPCT case managers are highly qualified nurse-practitioners, the guideline as written for physicians may be too complex, influencing compliance negatively[41]. This would advocate for a different approach and/or document for nurses in guideline education. Also we may presume that intercultural differences may influence the success rate of different interventions, however international comparative research is scarce [58, 59]. Since the field of pediatric palliative care is very broad, future research should best focus on improved guideline implementation regarding the most burdensome aspects of symptoms during palliative care.

METHODOLOGICAL CONSIDERATIONS

The findings of the studies described in this thesis must be considered in light of some overall limitations.

Representativeness of participants
First, we have to be cautioned about the generalizability of the results as there is no (inter)national consensus on how children are selected to be referred to receive palliative care. Even though the WHO definition states all children with a life threatening disease should receive palliative care from diagnosis[1], it is not clinical practice within our hospital to do so. Especially for children with MD, extensive supportive care is provided along treatment with curable intent, and in clinical practice when an infaust prognosis is discussed with parents, supportive care is switched to palliative care, usually referred to as the palliative phase. For children with NMD the switch to palliative care is more gradually and less well defined. It is unclear when a treating physician refers such patients to palliative care as Thompson found a high variation in timing of referral[60]. Referral is likely to be dependent on the diagnosis and individual clinical course of disease as well as
family circumstances and knowledge and expertise of the individual health care professional. As Keel at al showed, older children and children with neurologic disease are more likely to be referred than infants and children with neonatal or cardiac disease[61]. We may presume a selection bias exists within our NMD group, with patients suffering a more complicated course of disease will be selected earlier than patients who are clinically stable. Also patients with more psychosocial difficulties, such as less resources, a limited support system, and educational influences could be more likely to be selected for support from the PPCT. These assumptions are in line with adult research showing that the main difference between referring and non-referring physicians was that the non-referring physicians estimated that the patients’ caretakers were coping well enough[62]. This selection and the timing of referrals will strongly influence the intensity and content of care, since the needs of each individual child are different at diagnosis and in the dying phase. Also international differences in organization of care and finances may contribute to differences in referral and thus limit the generalizability of our results. For example, in the United states before the enactment of the Patient Protection and Affordable Care Act in 2010, children with life-limiting health conditions under Medicaid were eligible for a hospice benefit only in the last six months of their life. Additionally, to receive the benefit, families had to end all curative treatment for the child’s life-limiting condition, a choice many found difficult to make[8].

Cultural differences and differences in organization of care between different countries may also limit the generalizability of the results. As Robinson and Carr stated, discrepancies between symptom experiences could be related to culture, treatment differences, population size, and difficulty of symptom measurement[63]. Treatment differences such as type of cytostatic drugs used for chemotherapy, antiemetic medications, and pain management may be important factors regarding variations in reporting of symptoms[63]. Also, in the Netherlands it is common that the general practitioner is intensively involved in all patients, even when a complex chronic condition is diagnosed, especially when the child is at home. Moreover, the Netherlands is a small country with health care facilities usually within a short geographical distance, mostly insured care and with availability of pediatric home care nurses facilitating outpatient care. As Knapp et al stated, the availability of pediatric palliative care is highly variable around the world, with Western Europe having one of the highest availabilities[64].

**Assessment of data**
The results presented in chapter 2,3, 4, and 6 are retrieved retrospectively and mainly from chart review. This might have led to lower registration of symptoms (chapter 2,3) and lower compliance scores (chapter 6) than what would have been registered prospectively by patients and/or their parents directly. Significant literature is available on the disappointing quality of most documentation in medical charts [65-67] and a comparative study has also shown that e-learning programs do not improve the quality of
nurses documentation[68]. This may imply that the results of chapter 2 and 3, distracted from patient files, might not provide a complete overview of the course of the palliative phase of incurable disease. Moreover, we may assume from retrospective chart research, that appearance of new symptoms will be registered better than the disappearance of symptoms. To expand, in the first study on CNS malignancies we did not look at the disappearance of symptoms, we only registered the first start of the symptom. In the second study regarding non-CNS malignancies we additionally registered the disappearance of symptoms, when available. Also, a limitation of the study is the use of physician reported outcomes. Wolfe et al. found a significant disparity between parents and healthcare providers when prospectively reporting on the occurrence and severity of symptoms of a child with cancer. They postulate that unsuccessful symptom treatment might be the result of a lack of recognition and perception of symptoms by parents and / or health care professionals[69]. Heden et al even state that the two parents of the child perceive the burden of a child’s symptom during and after cancer treatment differently[70]. It has been well documented that the information provided by physicians or parent-proxy in children with chronic health conditions is not equivalent to that reported by the patient him or herself[71, 72]. Future research should be prospective and patient- or parent reported to avoid these limitations.

Considering chapter 6, the retrospective chart design may have led to compliance scores that illustrate documentation of compliance instead of actual compliance. This would suggest that the actual compliance in clinical practice could be higher than the documented compliance, which is in line with the finding that the parent reported outcomes showed a compliance of above 80%. Additionally we assessed compliance during a specific period, while earlier provided information was not accounted for which could have led to bias. Certain guideline recommendations such as advises that should be given, could have been followed before the start of the assessment period, resulting in false-negatives. Our data advocate for future longitudinal research on compliance of the guideline.

Clinical implications and future perspectives

Even though an increasing interest in pediatric palliative care is seen in clinical practice and research, there is still little consensus on how different aspects of pediatric palliative care should be designed. This thesis fills in some of these gaps providing data for the design of pediatric palliative care teams and thereby contributing to an improved quality of pediatric palliative care. Strategies to improve pediatric palliative care and suggestions for future research are described in the sections below and summarized in the bullets section at the end of this paragraph.
Insight in symptom occurrence and burden using Patient Reported Outcome (PROs) and effect of feedback of Pros

As is pointed out within the limitation section above, there is a high discrepancy between healthcare provider reported outcomes and patient reported outcomes. However, few studies have ascertained patient-reported outcomes (PROs) in children with advanced cancer[73-76]. Wolfe et al have developed Pediatric Quality of Life Evaluation of Symptoms Technology (PediQUEST), a computer-based system that generates feedback reports after collecting PROs[76]. They found that routine feedback of PROs affected the child’s symptoms or HRQoL positively, although not significantly[77], which is in line with earlier adult expert’s suggestions[78, 79]. However, routine feedback of HRQOL in discussion with parents and / or patient after end of treatment increased discussion of emotional well-being of the child [80] and Detmar et al showed an increasing attention for HRQoL discussions after structural patient-physician feedback of quality of life assessment[81].

In order to measure perception of symptoms over time prospectively, we have developed an online patient/parent questionnaire which is imbedded in the KLIK portal [82]. The questionnaire, the symptom PREVIEW (Patient/Parent Reported Evaluation of VAS, Interventions and Effects) allows to prospectively evaluate the occurrence and severity of symptoms (figure 1), medication use, interventions, information on nutrition, and need for medical aids. The web based questionnaire is comprehensive for patients and parents and is easy to fill in. In an earlier pilot phase in children with chronic illness, the pediatric oncologist was provided symptom VAS scores, scores on functional ability as well as an impression of overall HRQoL[83] during consultation (figure 2). Research has shown that involvement of a PPCT can lead to a decrease of symptoms or less burden of symptoms and can improve quality of care[2-8, 10, 18, 84]. Moreover, different studies have implied that support provided by a PPCT can decrease the parental burden and stress symptoms[19, 20]. In our study, we did not investigate the effect the support by the PPCT had on the HRQoL or whether the need for support was higher for children with more symptoms or a lower HRQoL. Information on how symptom burden or HRQoL affects the needs for palliative care and affect parental and siblings’ burden can help optimize the organization of palliative care in the future.

The answers on the online questionnaires are automatically converted into an ePROfile and keyed to colors, with red (“high” and “very high”) indicating that a child experiences symptoms with a high burden, orange (“somewhat”) representing mild symptoms, or green (“none” and “little”) indicating no reported symptoms. Future research should focus on implementing and validating this on line symptom questionnaire for children with advanced cancer and eventually other diseases. Incorporation of the sPREVIEW in a system of professional feedback by physicians and / or case manager might improve pediatric palliative care, however this needs further research. Ultimately in case of a successful pilot phase, a sPREVIEW might be applied in daily clinical practice. It provides
the possibility to register data on symptoms, symptom burden and treatment interventions for diverse patient groups with a (rare) life shortening disease. This will lead to a true estimate of the symptoms in a wide variety of life shortening disease. Also the effectiveness of symptom management can be extrapolated from the changes in symptom burden over time. Alongside, the sPREVIEW allows measuring compliance at a patient/parent based level to most of the eleven selected quality indicators of the clinical guideline. Moreover, by enquiring the HRQoL on a frequent base, in the future we may be able to estimate whether compliance to the guideline will actually increase HRQoL, which is of course one of the ultimate goals of implementing the CPG.

**Figure 1:** example of symptom PREVIEW questionnaire.

**Insight in the palliative phase of children with non-malignant life shortening disease**

Your child has suffered of pain.

<table>
<thead>
<tr>
<th></th>
<th>No degree of burden</th>
<th>Extreme degree of burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>0 1 2 3 4 5 6 7 8 9 10 7</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>0 1 2 3 4 5 6 7 8 9 10 7</td>
<td></td>
</tr>
<tr>
<td>Pain arms</td>
<td>0 1 2 3 4 5 6 7 8 9 10 7</td>
<td></td>
</tr>
<tr>
<td>Pain legs</td>
<td>0 1 2 3 4 5 6 7 8 9 10 7</td>
<td></td>
</tr>
<tr>
<td>Facial pain</td>
<td>0 1 2 3 4 5 6 7 8 9 10 7</td>
<td></td>
</tr>
<tr>
<td>Nerve pain</td>
<td>0 1 2 3 4 5 6 7 8 9 10 7</td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>0 1 2 3 4 5 6 7 8 9 10 7</td>
<td></td>
</tr>
<tr>
<td>Pain on other location</td>
<td>0 1 2 3 4 5 6 7 8 9 10 7</td>
<td></td>
</tr>
</tbody>
</table>

In this thesis, we focused on the course of disease of children with a malignant disease. However, the research in pediatric palliative care should also concentrate on those children with other types of life shortening disease, with no reasonable hope of cure[85]. From the children who receive palliative support from the PPCT of our academic pediatric hospital 50-60% has a non-malignant disease which is in line with other studies[86]. As Morgan et al stated, and is shown in our own studies, the palliative needs of children with cancer are different from those with other life-limiting conditions[87]. One of the factors, contributing to these differences in needs, is the different course of disease.
Figure 2: example of symptom PREVIEW, online feedback to pediatric oncologist.

As is shown in our own study, the palliative trajectory of children with a NMD is often longer than that of a MD[86]. The cohort of children with a non-malignant primary condition is also much more heterogeneous than the cohort of children with a malignant disease, with individual conditions being even more rarely described and they are roughly categorized in groups. According to a longitudinal study by Feudtner et al, the most common categories are genetic or congenital disorders and neuromuscular disorders. Other less frequent reported categories cover even more seldom diagnoses included respiratory, gastrointestinal, cardiovascular, metabolic, renal, and immunologic diseases[85]. Importantly this is also the group of children with (severe) psychomotor retardation, which hampers communication. Comparable with children with malignant disease, these children suffer from a wide range of many symptoms[88]. Future research should strive a detailed, preferable prospectively retrieved, oversight of the course of these conditions.

Adaption of the formation of the pediatric palliative care team

The different chapters provide important insight in the content of the support the PPCT offers to different groups of patients. From this information we may conclude that patients with MD receive shorter but more intensive support compared to patients with
NMD, which is in line with other research[30, 31]. This implies that a PPCT should be flexible to be able to offer both, long term low intensity support as well as short but highly intensive and quickly available support. This has implications for the number of case managers, in which there should always be one or two case managers who can step in acutely when necessary. Also, there should be time available for the case managers to answer to the unplanned “parent initiated” contacts that, in our study, comprised 25% of all contacts between the case manager and the parents.

An important finding in chapter 5, is that only a limited number of contacts between patients or parents with the PPCT are held outside office hours. Even though literature exploits that parents highly value the 24-hour availability of a PPCT[15, 32], our study suggest that this 24-hour coverage is not necessary in the Dutch health care setting. Possibly the anticipating approach of the PPCT ensures that all needs are accounted for during daytime, which could explain the limited requests during the after-office hours. Although future research should define the value of 24-hour availability for parents, our PPCT has followed the suggestion to limit availability from 8 am to 9pm.

Also, chapter 5 shows there were no contacts between the chaplain and patients or parents, suggesting there is no structural need by the parents for a chaplain within the PPCT. Since there is contradictive research suggesting a spiritual mentor within pediatric palliative care is highly valued by parents[15], future research should focus on the need for a spiritual mentor within a PPCT, researching the value for patients and parents, as well as the value for the team professionals themselves.

**Insight in the effect a PPCT has on health care costs**

In current timeframe with worldwide increasing healthcare costs, healthcare providers cannot ignore the economic aspects. Even though several merits of pediatric palliative care have been described, it is important to know what the support of a PPCT will cost, and how a PPCT will affect overall palliative care expenses. Within adult palliative care, a great deal of information is available on the influence of palliative care programs on health costs. Different studies describe several cost reductions of overall medical care when extend of palliative care beyond the hospital walls or home care is provided[89-93]. Moreover a reduction in hospital costs is seen when palliative care is provided ongoing also during times of hospital admission[94-97]. The decrease in costs is mainly caused by reduction of re-admissions in hospital, shorter length of stay, less ICU referrals, less emergency department visits, less laboratory and imaging diagnostics and less aggressive therapies[98-100].

Knapp et all 2009 compares the mean medical costs in the last year of life between adults, children en infants[101]. Whereas the mean medical costs for an adult during the last year of their live with palliative care is $28.000, for children and infants the costs are extremely higher namely $110.000 and $62.000 respectively. The costs measured in this cohort were inpatient, outpatient and hospice care. In this cohort 5% of the infants and
18% of the children made use of hospice care towards the end of life. Considering the data known from adult palliative care of which 12%-36% use of hospice care[102, 103], it could be hypothesized that increasing home care and/or hospice care also reaching out for children at home, would minimize inpatient care and reduce the palliative care costs in children as well. Pascuet et al[101] 2010 compare the expenses made for children receiving palliative care before and after opening a hospice ward[104]. They describe a decrease in monthly costs of $4252. Miano 2002 describes how a home care team could influence medical costs[105]. This cohort includes both curative and palliative care (82% and 18% respectively). The average cost per patient assisted in the health care program (2,936 €, range 150 - 20,700 €) proved to be significantly lower (p<0.001) than the average cost that would have been charged to the NHS in case of hospitalization to carry out the same procedures (9,785 €, range 350 – 96,750 €). However, this study should be interpreted with caution due to the inclusion of curative patients, since the health care costs will increase in the last months of life [106]. A prospective descriptive case control study shows a reduction of healthcare spending of money for 11% in patients after enrollment in Partners for Children (PFC) program in California[8, 107]. Although the available data seem to support the economic benefit of palliative care in children, conclusive data is needed, and might differ per country and local organization of health care. At this time we can only hypothesize that introducing the PPCT might potentially reduce health care costs within our population of children in palliative care. The aim of a future study should be to perform a comparative prospective study comparing health costs of patients in the Netherlands receiving PPCT and of patients receiving care as usual.

Conclusions

In this thesis the results of three aspects of pediatric palliative care are presented: insight in the course of the palliative phase of malignant disease, insight in the intensity and content of pediatric palliative care provided by the PPCT, and the adherence to the Dutch clinical practice guideline “Pediatric palliative care”. The chapters in this thesis fill in gaps in knowledge needed to optimize palliative care. This unique insight in the course of the palliative phase of incurable malignant disease assists in facilitating anticipating palliative care. The insight in the content of support delivered by the PPCT allows the current team to adapt the organization of a team and will possibly be helpful in the initiation of future teams. Our study on guideline compliance resulted in the availability of 11 quality indicators allowing future compliance research. Moreover, a multifaceted guideline education program with e-learning modules is available for future distribution. Altogether, this thesis provides a solid ground for adaptation of current clinical practice and gives direction for future research to further improve the quality of pediatric palliative care.
Chapter 7

Key messages

Recommendations for clinical practice

- A PPCT should be highly flexible, able to both acutely start intensive (short)support as well as to provide long term low intensity support
- A PPCT should be equipped to answer to unplanned parental initiated contacts
- A PPCT should be multidisciplinary and able to answer both, medical questions on physical topics, as well as questions on living with a life limiting disease such as questions on school and socio-economic issues.
- A full 24-hour coverage can be overdone, availability of an anticipating PPCT between 8 am and 9 pm, is sufficient for most patients and families in the Netherlands
- The structural availability of a chaplain within a PPCT might not be necessary for the parent contacts but may be supportive for the team
- Guideline adherence as scored by parents is seen in over 80% not improving via multifaceted learning program
- The PPCT and other health care professionals providing pediatric palliative support, should be educated on guideline policy, for which the designed multifaceted education program is available

Recommendations for future research

- Prospective research using PRO’s is needed on the course of the palliative phase of disease, including assessment of HRQoL, for children with MD as well as NMD
- Additional research is needed on how parents value the different aspects of received palliative care, to further optimize the PPCT’s approach
- Research is needed on the effect of a PPCT on healthcare costs
- Longitudinal research using PRO’ can help to measure compliance to the national clinical guideline pediatric palliative care for children and evaluate the degree of compliance and whether this is associated with HRQoL
Reference list


Chapter 7


(53) Brouwers, M.C., et al., E-learning interventions are comparable to user’s manual in a randomized trial of training strategies for the AGREE II. Implement Sci, 2011. 6: p. 81.


