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PSYCHOSOCIAL AND SUPPORTIVE CARE: RESEARCH ARTICLE

Pain at home during childhood cancer treatment: Severity, prevalence, analgesic use, and interference with daily life

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Abstract

Background: Pain is a common symptom in childhood cancer. Since children spend more time at home, families are increasingly responsible for pain management. This study aimed at assessing pain at home.

Procedure: In this longitudinal observational study (April 2016-January 2017), pain severity and prevalence, analgesic use, and pain interference with daily life (Brief Pain Inventory Short Form) were assessed for 4 consecutive days around the time of multiple chemotherapy appointments. Descriptive statistics (frequencies and percentages) were used to report pain severity (with clinically significant pain defined as: score ≥ 4 on "worst pain" or "average pain in the last 24 h"), pain prevalence, and analgesic use. Mixed models were estimated to assess whether patient characteristics were associated with pain severity, and whether pain severity was associated with interference with daily life.

Results: Seventy-three children (50.7% male) participated (1-18 years). A majority ($N = 57$, 78%) experienced clinically significant pain at least once, and 30% reported clinically significant pain at least half the time. In 33.6% of scores ≥ 4, no medication was used. We found an association between pain severity and interference with daily life: the higher the pain, the bigger the interference (estimated regression coefficient = 1.01 [95% CI 0.98-1.13]).

Conclusions: The majority of children experienced clinically significant pain at home, and families frequently indicated no medication use. A stronger focus on education and coaching of families seems essential, as well as routine screening for pain in the home setting.

KEYWORDS
pain, pediatric oncology, psychosocial, quality of life, support care

1 | INTRODUCTION

Due to major advances in treatment over the past years, the overall 5-year survival rate of children with cancer has now increased to approximately 80%.[1] With the improvement in survival, emphasis on

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Abbreviations: BPI-SF, Brief Pain Inventory Short Form; FPS-R, Faces Pain Scale Revised; NRS, Numerical Rating Scale; T, time point improving quality of life and managing cancer-related symptoms, such as pain,[2–4] has grown. This is an important development, as pain has been identified as the most frequent and severe cancer-related symptom by pediatric patients.[5] Pain in children with cancer can be divided into treatment-related pain (due to chemotherapy, radiation, surgery), procedure-related pain (due to blood draws, lumbar punctures, bone marrow aspirations), and illness-related pain (due to the infiltration of tumor in organs or tissues).[6,7] Studies have found treatment-related pain to be the most prevalent,[7–9] with neuropathic pain as a result of chemotherapy being one of the most common forms of treatment-related pain.[10,11]

A study on pain in children with cancer (in active treatment and post-treatment) revealed that 75% experienced pain over the past month (a score > 0/10 for worst, least, or average pain).[8] In another study, over 50% of parents said their child experienced chronic or recurrent pain in the past 3 months.[12] Similar pain prevalence percentages were reported by children and their parents/guardians in qualitative interviews during the first 3 months after diagnosis (49%),[7] and during the first year of cancer treatment (ie, 43%).[13] The percentage of pain in children with cancer varies between studies. This may be due to rapid changes in treatment options over the years, and the large variety of study populations (focus on specific cancer diagnoses, treatment phases, or age groups) and pain assessment tools. Taking into account this wide range of studies, pain prevalence varies between 43 and 75%.

Until now, research on pain in children with cancer has focused mainly on hospitalized children.[14] However, as a result of changing patterns in health care systems and therapeutic regimens, children with cancer spend less time in the hospital and more time at home.[15–19] Therefore, families are becoming increasingly responsible for the child's pain management.[15,18]

Little is known, even now, about pain experiences of children with cancer in the home setting. There have been some studies focusing on this group.[8,12,13,20] However, the youngest population is often disregarded (0-4/8 year olds). One study did include children aged 1-18 years old.[8] However, only parent proxy reporting was used. The aim of our study was to include the entire patient population (children aged 0-18 years) and use parent- as well as self-report measures of acute pain, as recommended by previous studies.[21]

Since pain in children with cancer receiving outpatient care (ie, at home or at the outpatient clinic) has been reported in a limited amount of studies, the effect of families' increased responsibility for the child's pain remain unclear. One study reported that parents tend to undertreat pain in the home setting.[12] Parental concerns about analgesic use and misconceptions about the expression and treatment of pain in children could be related. For instance, a study focusing on parental attitudes regarding analgesic use in children with cancer showed that 63% of parents think that pain medication is addictive and 42% of parents think that pain medication should be given as little as possible in order to minimize side effects.[22] Another study carried out interviews with patients and parents and revealed that about half of the interviewees thought of pain as an unavoidable symptom during cancer treatment.[7] This is worrisome, as pharmacological as well as nonpharmacological treatments such as psychosocial interventions aimed at social, behavioral, cognitive, or psychoeducational aspects[23] seem to have an effect on pain control in children when handled correctly.[24,25] Moreover, the way pain is being dealt with during childhood can permanently impact the child's pain processing (ie, sensitization to pain), sometimes persisting into survivorship (posttreatment).[26]

Pain is an often present and disconcerting symptom during all stages of childhood cancer and many patients will experience pain as a consequence of their illness and/or treatment.[6,14,27–29] The existing literature suggests that pain management at home is not optimal and thus many children may be experiencing pain unnecessarily.[12] In some cases, undertreatment of pain during childhood cancer treatment can cause sensitization to pain stimuli, causing pain to persist postcancer treatment.[26] Pain has been reported as very stressful by children with cancer,[30] and it interferes with their quality of life.[31] Furthermore, it has been associated with high levels of patient distress,[27,32] greater burden from physical and psychological symptoms,[33] negative affect,[34] and sleeping problems.[7,33] In childhood cancer survivors, it has been associated with greater emotional distress and suicidal ideation.[26]

Since research on pain in the home setting is still scarce, the first aim of this study was to gain more insight into pain experiences of children at home during childhood cancer treatment in order to determine whether interventions focusing on pain management at home are needed. Therefore, we assessed the severity and prevalence of pain, as well as analgesic use. Furthermore, we investigated whether patient characteristics (ie, age, gender, and diagnosis) were associated with pain severity, and whether pain severity was associated with interference in daily life.

2 | METHODS

2.1 | Procedure and participants

This explorative longitudinal observational study included families of children with cancer receiving chemotherapy at the outpatient clinic of Sophia Children's Hospital/Erasmus University Medical Center in Rotterdam, the Netherlands between April 2016 and January 2017. Inclusion criteria were as follows: children with cancer between 0 and 18 years old receiving chemotherapy at the outpatient clinic at the time of study, with either patient or parent having a sufficient understanding of the Dutch language to complete the questionnaires. Approval for the study was obtained from the Internal Review Board of the Sophia Children's Hospital.

All patients meeting the inclusion criteria were invited to participate. Eligible families were identified through the electronic patient database and were approached by a research assistant. Families received both oral and written information about the study. If they agreed to participate, an informed consent form was signed.

Participating families received one set of questionnaires at the outpatient clinic. Each set of questionnaires consisted of four printed copies of the Brief Pain Inventory Short Form (BPI-SF). These four copies of the BPI-SF were completed at different instances (ie, time points [T]) around chemotherapy appointments at the outpatient clinic,

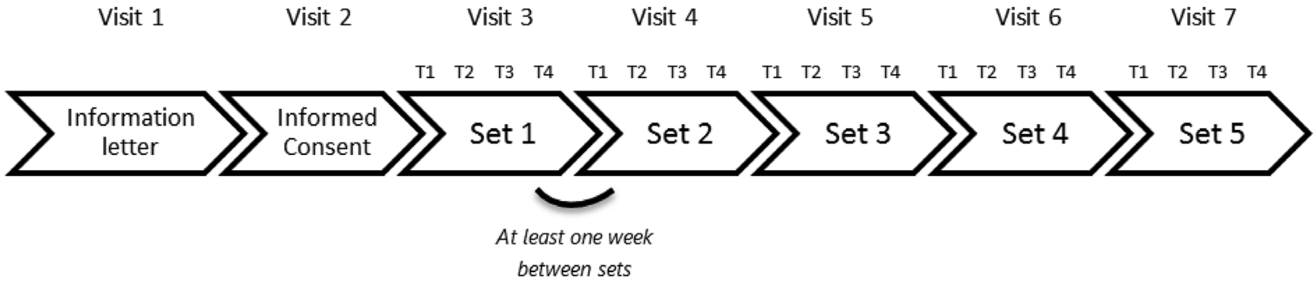

FIGURE 1 Data collection over the course of multiple visits to the outpatient clinic. Each set consists of four questionnaires (BPI-SF) completed at different time points (T): T1: in the waiting room before initiation of chemotherapy; T2: on the same day after chemotherapy had been initiated; T3: 1 day after chemotherapy; T4: 2 days after chemotherapy

namely T1: while waiting for the appointment at the outpatient clinic (focused on the 24 h before initiation of chemotherapy); T2: on the same day, after chemotherapy had been initiated; T3: one day after chemotherapy; and T4: 2 days after chemotherapy. Families were asked to complete multiple sets of questionnaires. On each visit to the outpatient clinic for chemotherapy, families were handed a new set. There was one requirement: a minimum time of 1 week between the start of two subsequent sets (Figure 1).

2.2 | Measures

2.2.1 | Brief Pain Inventory Short Form

The BPI-SF is a validated questionnaire focusing on three domains: (a) pain severity, (b) pain management (ie, analgesic use and other forms of pain treatment), and (c) interference of pain with daily life.[35–37] The BPI-SF has been used to assess pain in multiple cancer populations in different countries, and internal consistency of the questionnaire has been proven with coefficient alphas ranging between .75 and .91.[38–46] The current study showed similar coefficient alphas ranging between .83 and .94, dependent on the subscale and moment of measurement (time point). The questionnaire was originally developed in English to assess pain in adults. Since then, it has also been used in children.[47,48] Stinson et al (2015)[49] included items on pain severity, analgesic use, and interference of pain in daily life comparable to the BPI-SF items in their smartphone-based pain assessment app, and these were validated for self-report in children with cancer between the ages of 8-18 years old. For children aged 0-8, the literature suggests the usefulness of parent proxy reporting of pain. Birnie et al (2019) published a systematic review[21] on the measurement properties of self-report pain intensity measures in children and adolescents. For children aged 6 and up, strong recommendations were made for the Numerical Rating Scale (NRS)-11, which is used in the BPI-SF. For children younger than 6 however, no self-report recommendations were made. Hagglund et al (2020)[50] assessed whether the prevalence of pain in children (1-18 years) with cerebral palsy differed based on self-reporting or proxy reporting, and found no statistically significant difference. Building of these findings, the questionnaires in this study were completed by one of the parents (children aged 0-4), jointly (children aged 5-8), or by the children themselves (aged 9-18).

For the purposes of this study, the Dutch version of the BPI-SF has been slightly changed and adapted to the participants (ie, children). Instead of asking to what degree the pain has interfered with normal work (original BPI-SF), we asked how the pain interfered with school/playtime/hobbies.

The pain severity section of the BPI-SF consists of four items in which participants are asked to rate pain on NRS-11 ranging from 0 (no pain) to 10 (worst pain imaginable) for different situations: "*please rate your pain/your child's pain by circling the number that best describes the* <u>*pain at its worst*</u> *in the last 24 h*" (ie, worst pain), "*please rate your pain/your child's pain by circling the number that best describes the* <u>*pain at its least*</u> *in the last 24 h*" (ie, least pain), "*please rate your pain/your child's pain by circling the number that best describes the* <u>*pain on the average*</u> *in the last 24 h*" (ie, average pain in the last 24 h), and "*please rate your pain/your child's pain by circling the number that best describes the* <u>*pain right now*</u>" (ie, pain right now). As Hicks et al (2001)[51] have demonstrated that the Faces Pain Scale Revised (FPS-R) is an appropriate tool for children's pain intensity in children aged 4 and up, we decided to use this scale rather than the NRS-11 in the age group 4-8. Clinically significant pain was defined as a score $\geq$ 4 on the NRS or the FPS-R (face number 3 equals a score of 4) on either "worst pain" or "average pain in the last 24 h."[52,53]

The pain management section of the BPI-SF consists of one open-ended item in which treatments/medications received for the pain are assessed (ie, "*What treatments or medications did you receive for your pain/did your child receive for their pain?*"). Afterwards, responses were dichotomized to assess whether any pain treatments/medications were used (yes/no categories).

Finally, the interference of pain with daily life section consists of seven items in which the influence of pain on daily activities is assessed on a scale ranging from 0 (no interference) to 10 (complete interference). Daily activities include school, hobbies, and sleep. An average interference score was computed based on these items, as recommended in the BPI-SF user guide.[37] The higher the scores, the higher the interference with daily life.

2.2.2 | Demographics

Age, gender, and diagnosis were retrieved from the electronic patient database.

2.3 | Analytic strategy

2.3.1 | Pain severity

Descriptive statistics (frequencies and percentages) were used to report the severity of pain at each time point. A mean pain score was calculated per patient on all completed questionnaires for each specific time point (ie, T1, T2, T3, or T4). This was done separately for three pain items of the BPI-SF (ie, "worst pain," "least pain," and "average pain in the last 24 h"). We then divided the means into categories of pain severity: none (0), mild (1-3), moderate (4-6), and severe (7-10).[53]

2.3.2 | Prevalence of clinically significant pain

Descriptive statistics (frequencies and percentages) were used to report how many patients experienced clinically significant pain at least once across all completed time points (ie, reported a score ≥ 4 on either "worst pain" or "average pain in the last 24 h"). We also assessed how many patients experienced clinically significant pain at least 50% of the time (ie, percentage of clinically significant pain scores in the total amount of completed questionnaires per patient).

2.3.3 | Analgesic use

Chi-squared tests were used to assess how often patients/parents indicated medication use (yes/no categories) when logging a clinically significant pain score (yes/no categories). We reported in which percentage of these scores medication was used.

2.3.4 | Mixed models

To study the association between pain severity and patient characteristics (gender [male, female], age group [0-3, 4-8, 9-18], diagnosis [ALL, lymphoma, brain tumor, others/solid tumor]), mixed models were estimated to account for the repeated measure design. "Worst pain" and "average pain in the past 24 h" were used to assess pain severity (ie, outcome measures). For both items, a mixed model was estimated.

We used the same methodology to study the association between pain severity and interference with daily life. Here, "average pain in the past 24 h" was used to assess pain severity, and the average interference score was used to assess interference with daily life (ie, outcome measure).

SPSS version 25.0 was used for all analyses.

TABLE 1 Patient characteristics

Parameters	
Age in years mean (SD), range	8.33 (4.87), 0-18
Gender	
Male, n (%)	37 (50.7)
Female, n (%)	36 (49.3)
Diagnosed group	
ALL, n (%)	37 (50.7)
Lymphoma, n (%)	12 (16.4)
Brain tumor, n (%)	15 (20.5)
Others/solid tumor, n (%)	9 (12.4)

Note. N = 73.
Abbreviations: SD, standard deviation; n, number of patients per subgroup.

3 | RESULTS

One hundred ten eligible families were invited to participate in the study, of which 89 families agreed to participate and 21 families declined (response rate: 81%). Among the 89 families who signed informed consent, 16 families dropped out. The characteristics of the remaining 73 patients are summarized in Table 1.

Cancer-related treatment of patients during the study period was limited to chemotherapy (ie, no radiotherapy or major surgeries). Moreover, no major surgeries (amputation, limb sparing, thoracotomy) had occurred in any patient within 4 months preceding the study.

On average, the assessment period (number of days participants were in the study) was 42.9 days (min = 4 days; max = 178 days). There was a variability in the number of completed sets (*one set consisted of four printed copies of the BPI-SF*) per patient. The majority of families completed three sets (N = 35), and some completed four (N = 15) or five sets (N = 15). A small group completed one (N = 3) or two sets (N = 5). We evaluated whether the number of completed sets was associated with the level of pain severity. We divided the families into two groups: group 1 (one or two completed sets) and group 2 (three, four, or five completed sets). On the "worst pain" item, group 1 and group 2 had a mean pain severity equal to 3.41 and 1.81, respectively. On the "least pain" item, group 1 had a mean of 1.16, and group 2 a mean of 0.67. On the "average pain in the last 24 h" item, group 1 and group 2 had a mean equal to 2.40, and 1.21, respectively. On the "pain right now" item, group 1 had a mean equal to 1.78, whereas group 2 had a mean equal to 1.07. Group 1 consistently had a higher mean pain severity score than group 2. However, one-way analysis of variance showed no significant difference between groups. Thus, all sets were included in the analyses.

3.1 | Pain severity

Figures 2–4 show the severity of reported pain at home. These figures illustrate the mean pain score per patient for each specific time point

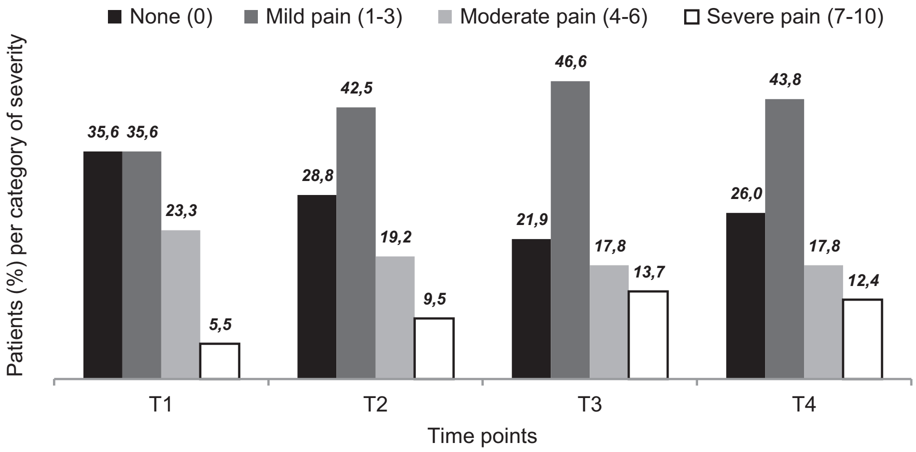

FIGURE 2 *Pain at its worst in the last 24 h*, mean pain score per patient for each specific time point (T1, T2, T3, and T4) divided into categories of pain severity (N = 73)

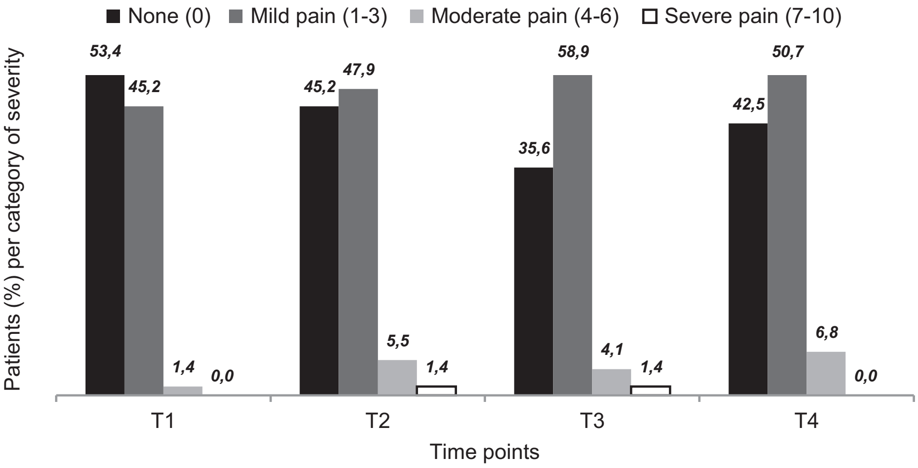

FIGURE 3 *Painat its least in the last 24 h*, mean pain score per patient for each specific time point (T1, T2, T3, and T4) divided into categories of pain severity (N = 73)

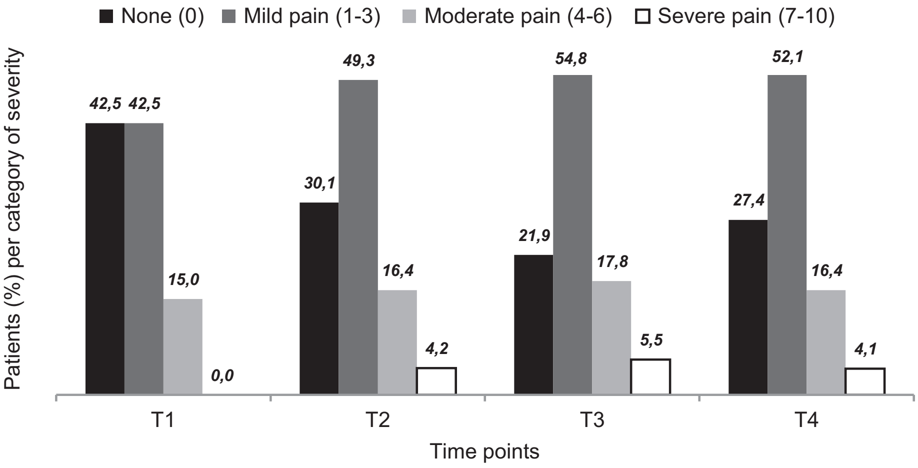

FIGURE 4 *Average pain in the last 24 h*, mean pain score per patient for each specific time point (T1, T2, T3, and T4) divided into categories of pain severity (N = 73)

TABLE 2 Medication use during scores ≥ 4

BPI-SF item	Number of scores per item	Number of scores ≥ 4 per item	Medication use (%) in scores ≥ 4	Missing
"Worst pain"	1013	352	218 (61.9%)	1
"Average pain in the last 24 h"	1013	247	164 (66.4%)	1

Note. N = 1013 (total number of completed BPI-SF). Missing = in the same questionnaire in which a score of ≥4 occurred, the question on analgesic use had been left unanswered.

(T1, T2, T3, or T4) divided into categories of pain severity. Figure 2 illustrates "worst pain," Figure 3 "least pain," and Figure 4 "average pain in the last 24 h."

3.2 | Prevalence of clinically significant pain

Fifty-seven patients (78.1%) experienced clinically significant pain (ie, reported a score ≥ 4 on "worst pain" or "average pain in the last 24 h") at least once. The remaining 16 patients (21.9%) did not report clinically significant pain. Twenty-one patients (30%) reported clinically significant pain at least 50% of the time.

3.3 | Analgesic use

"Worst pain" scores reveal that in 38.1% of scores ≥ 4, no pain medication was used. For "average pain in the last 24 h" scores, this is 33.6%. Thus, in roughly one-third of scores ≥ 4, no medication was used (Table 2).

3.4 | Mixed models

No association between pain severity and patient characteristics (gender [male, female], age group [0-3, 4-8, 9-18], diagnosis [ALL, lymphoma, brain tumor, others/solid tumor]) was found.

We found an association between pain severity and interference with daily life, adjusted for gender, age, and diagnosis. The more severe the pain, the bigger the interference (estimated regression coefficient = 1.01 [95% CI 0.98-1.13]).

4 | DISCUSSION

This study is among the few that assessed pain in children with cancer in the home setting.[8,12,13,18] We found that a majority of patients (78%) experienced clinically significant pain at least once during the study period, and that a large proportion (30%) experienced clinically significant pain at least 50% of the time. We also found that in roughly one-third of all clinically significant pain incidences, the pain was not being treated with medication. This is in line with previous studies. One study found that parents tended to use physical and psychological strategies rather than medication to reduce pain.[8] Another study found that despite the fact that most children experienced chronic pain, analgesic use at home was still low.[12] As our questionnaire did not assess the rationale behind medication use, no conclusions can be drawn as to why medication was used so scarcely. Yet, previous studies imply that misconceptions (ie, "pain is simply unavoidable") and fears regarding medication and side effects may lie at the root of this.[7,22]

Furthermore, no association was found between pain severity, gender, age, and diagnosis. This is in line with previous studies in children during cancer treatment that also did not find significant differences in pain severity when controlling for patient characteristics.[5,8,54] A study with survivors of pediatric brain tumors found pain to be more prevalent in females and in younger age groups.[55] However, participants were posttreatment with ages ranging between 13 and 32, as opposed to participants in the current study (aged 0-18 years), who were assessed during treatment.

We did find an association between severity of pain and interference with daily life. The more severe the pain, the bigger the interference with daily life. This is in line with previous studies, which show pain to be correlated with stress,[30] sleeping problems,[7,33] and greater burden from physical and psychological symptoms[33] affecting the quality of life of patients in both pediatric[7,30,33] and adult populations.[56]

Overall, our findings have several clinical implications. The calculation of mean scores per patient (Figures 2–4) reveals that a majority fits the none/mild category of pain severity. Thus, based on the days that data were collected, the majority seems to have no issues to adequately cope with pain at home. However, assessment of clinically significant pain scores per patient reveals that the majority did experience clinically significant pain (78%), some more than half of the time (30%). This implies that pain management could potentially be improved for this group. Previous studies have also revealed the negative impact of pain on quality of life, distress, burden of physical and psychological symptoms, affect, and sleep.[7,27,31–34] It is therefore imperative to closely monitor pain in these children in the home setting. We believe that the use of ecological momentary assessments (ie, real-time pain assessment in the subject's natural environment[57]) over a prolonged period of time is the most reliable source to collect data on pain in the home setting. In the current study, subjects reported pain in their natural environment (ie, at home) with a recall period of 24 h. In the future, real-time pain assessment will be taken into account to minimize recall bias and gain a more reliable dataset.

Firstly, we propose interventions aimed at educating families on recognizing and addressing pain in their children, and on the available pain management strategies, both pharmacological and nonpharmacological. Currently, families are often insufficiently prepared to effectively manage pain symptoms in the home setting.[19] As parents' knowledge about pain recognition and management is less extensive than that of health care professionals, the focus should be on educating and coaching parents during the early stages of the illness in order to effectively recognize and manage their child's pain.[58] By providing them with timely education about pain recognition and management, treatment may be improved and pain decreased.[15]

Secondly, our study highlights the importance of better communication about pain in the home setting. Regular screening increases the opportunity to intervene with pain before escalation. Studies have already shown that routine use of patient-reported outcomes (PROs) in clinical practice increases the detection of psychosocial problems, the discussion of the reported problems during consultations, and enhances the satisfaction with care.[59–61] Several research groups have acted on this and developed e-health interventions to keep track of pain in children with cancer.[62,63] Following the results of the current study, our group has developed a mobile app (the KLIK Pain Monitor) to assess pain in the home setting, enabling health care professionals to respond to families of patients in need as quickly as possible. Furthermore, the app features information concerning pain recognition and treatment, taking into account the need for education and coaching. Results of the feasibility study of the KLIK Pain Monitor will soon be available, and we are currently planning an effectiveness study.

The current study has some limitations. Firstly, there is no data available on the time since diagnosis. This can be relevant information, as one previous study has shown children to experience pain most often in the first 3 months after diagnosis.[7] However, as all patients who received chemotherapy between the ages of 0-18 years were approached for participation at random, we expected our group to be representative for the patient population, with a wide variety of time since diagnosis. Still, in the future this data should be collected and analyzed.

Secondly, we did not ask why families chose not to participate, and thus there might be a participation bias. To minimize this bias, we approached all families visiting the outpatient clinic for chemotherapy consecutively.

Thirdly, the BPI-SF Dutch version has not been formally validated for children. However, taking into account the massive use in context with different languages and wide range of cultures,[38,39,41–43,45] and the validation of items (English language) comparable to the BPI-SF for children with cancer aged 8-18,[49] we believe that the BPI-SF can be used in our population.

Fourthly, the pain management section of the BPI-SF does not distinguish clearly between analgesic and nonanalgesic interventions used to decrease pain. In this study, only one participant reported using a nonanalgesic method (ie, cannabis oil). As another study found parents to use more physical and psychological strategies (eg, deep breathing, massage/rubbing) than pharmacological strategies to manage their child's pain,[8] we suspect that due to a lack of clear instructions, participants might have underreported on nonanalgesic interventions. Thus, based on our results we cannot conclude definitively in which percentage of cases pain was being undertreated (ie, no interventions, analgesic or nonanalgesic, used). In future studies, a clear distinction should be made between analgesic and nonanalgesic interventions.

Fifthly, as cancer treatment was limited to chemotherapy in our study population, the results cannot be generalized to patients receiving other treatments such as radiation therapy or major surgery. Therefore, future studies should also look at the specific effects these treatments may have on pain prevalence and severity in children with cancer.

Finally, there was a variety in the number of completed questionnaires (ie, time points) per patient. However, we found no difference concerning mean pain severity between patients who completed one or two sets versus patients who completed three, four, or five sets.

In conclusion, a large proportion of children receiving outpatient cancer treatment experience clinically significant pain. Moreover, medication is not always used in situations of clinically significant pain. Therefore, pain might not be optimally managed, with the result that children might be experiencing pain unnecessarily. Thus, interventions aimed at pain management at home are warranted. By educating and coaching families in pain management during the early stages of the illness, and using e-health tools to monitor pain and bridge the distance between the hospital and home, we hope to improve pain management at home and decrease pain in children with cancer.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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