Palliative Care Rounds

Symptom Experience of Children With Cancer Younger Than Eight Years of Age: An Integrative Review

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Abstract

Context. Children with cancer endure multiple symptoms during treatment. However, there remains a lack of systematic approaches to capture the whole picture of the symptom experience of children with cancer younger than eight years of age.

Objective. The purpose of this study was to conduct an integrative review to explore symptom experience of children with cancer younger than eight years of age.

Methods. A literature search of PubMed, CINAHL, Web of Science, PsycINFO, Cochrane databases, and four Chinese databases was performed to identify empirical studies, followed by an evaluation of empirical quality and data extraction and synthesis.

Results. Twelve articles covering 11 symptoms met the inclusion criteria. Children with cancer under the age of eight years experienced multiple intense symptoms, especially pain, worry, and anxiety. PedsQL™ Cancer Module (for age five to seven years) was the most commonly used instruments. There were limited data on these children's symptom quality, timing, and distress. Discordance between a child's age and symptom intensity was noted. Inconsistent concordance existed between children and their proxy symptom reports.

Conclusion. Children with cancer younger than eight years of age experience multiple symptoms. There is a need to investigate the full symptom profiles of these young children in consideration of their developmental nuances; to examine the concordance among different symptom reporters; and to conduct more qualitative studies to explore their symptom experience. J Pain Symptom Manage 2019;58:157−166.

Key Words

Children, cancer, symptoms, integrative review

Introduction

Children with cancer endure multiple co-occurring, interrelated symptoms during treatment that can profoundly impact their lives leading to delays or reductions of treatment affecting prognosis and causing declines in physical and mental functioning affecting quality of life. Accurate symptom assessment is vital to provide high-quality supportive care and evaluate the effectiveness of treatment. Research that addresses symptoms among children with cancer has increased over the past 20 years; however, symptom studies specifically on younger children (less than eight years of age) are limited.[1,2]

It is widely acknowledged that the child's developmental stage influences their description of symptoms and the experience of symptom-related distress. Measuring and interpreting the symptom experience

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in younger children presents unique challenges as these children think more concretely and are more present-oriented compared with older children.[3] Currently, most self-report instruments' (e.g., pediatric PROMIS) age ranges are from eight to 17 years.[4] To measure the symptoms of children under the age of eight years, some researchers relied on proxy report by parent or health care provider to interpret the symptom experience on behalf of the child.[5] At the meantime, a few researchers used self-reported instrument (e.g., faces scales) or qualitative approach (e.g., focus groups) to explore young children's own symptom reports.[6,7] However, there remains a lack of comprehensive and systematic approaches to capture the whole picture of the symptom experience of children with cancer younger than eight years of age, specifically, the symptom quality (characteristics of symptoms), symptom intensity (the degree, strength, or severity of symptoms), timing (the symptom occurring time, duration, and frequency), and the distress dimension (the affective aspect or meaning of symptoms), according to the Theory of Unpleasant Symptoms.[8] This knowledge gap not only contributes to poor symptom management but also ignores how symptoms interfere with children's and families' quality of life in this particular age group.

Therefore, the purpose of this integrative review was to synthesize current evidence regarding symptom experience of children with cancer younger than eight years of age. Before we nearly accomplished this article, we also noted a recently published systematic review on this age group.[1] However, unlike the previous one that focused on the psychological property of the self-report symptom instruments, this integrative review was conducted to explore the symptom experience of these young children, that is, the content of the symptom profile reported by children or proxy reporters. Findings from this review will inform future research directions and help health care providers develop age-appropriate intervention strategies that support these young children and their families as they manage and cope with symptoms.

Methods

The objective of the present study was to conduct an integrative review to fully examine the symptoms experienced by children with cancer younger than eight years of age. Integrative review was selected because it allows the inclusion of heterogeneous research methods to identify, synthesize, and assess the empirical quality of selected publications. The methodological strategies proposed by Whittemore and Knafl was followed, that is, 1) problem identification, 2) literature search, 3) data evaluation, 4) data analysis, and 5) presentation of findings.[9] PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations were utilized for this review.[10] The protocol for this review got Institutional Review Board approval from Children's Hospital of Fudan University (No. (2018) 231).

Literature Search

The first author performed a librarian-assisted database search in PubMed, CINAHL, Web of Science, PsycINFO, Cochrane databases, and four Chinese databases, including China National Knowledge Infrastructure, China Science and Technology Journal Database, Wanfang Database, and Chinese Biomedicine Literature Database. In this study, symptom was defined as perceptions that indicate a change from normal conditions in the body. Assessment of these symptoms is paramount in diagnosing and treating illness.[11] A combination of both keywords and indexed terms (e.g., MeSH) was applied in each database using BOOLEAN terms. Table 1 shows the search strategies for PubMed. Search terms were modified as necessary for each electronic database. Searches were conducted from October 2017 to July 2018 with no publication date limits applied to any database.

Inclusion and Exclusion Criteria

Two reviewers independently identified the titles and abstracts of studies by the search strategies. Potentially eligible studies were evaluated at full text according to the inclusion and exclusion criteria, and the final inclusion of studies into the systematic review was by agreement of all the authors. Inclusion criteria were empirical studies including quantitative, qualitative, and mixed-methods designs focusing on physical or psychological symptoms experienced of children with cancer younger than eight years, and symptoms were reported by children, and/or family caregivers,

Table 1
Search Strategies for PubMed

No.	Search Strings
1.	"neoplasms"[MeSH] OR neoplasm* [tiab] OR cancer* [tiab] OR oncolog*[tiab] OR malignan*[tiab] OR tumor* [tiab] OR leukem* [tiab] OR sarcoma* [tiab] OR tumour* [tiab]
2.	"child, preschool"[MeSH] OR child [Mesh] OR preschool [tiab] OR child [tiab] OR children[tiab] OR pediatric* [tiab] OR boy* [tiab] OR girl* [tiab]
3.	"signs and symptoms"[MeSH] OR symptom [tiab] OR symptoms [tiab]
4.	#1 AND #2 AND #3

and/or health care professionals. Exclusion criteria are studies that 1) did not report on empirical studies, including reviews, opinions, case reports, or editorials; 2) did not examine patients' symptoms, including reporting the overall quality of life; 3) did not include children with cancer under the age of eight years; 4) did not report the symptom experience of this age group separately.

Data Extraction

The quality of the included studies was assessed by the five criteria of GRADE (Grading of Recommendations Assessment, Development, and Evaluation) tool.[12] Discrepancies in bias assessments (methodological flaws, inconsistency, indirectness, imprecision, and publication bias) were resolved by consensus.

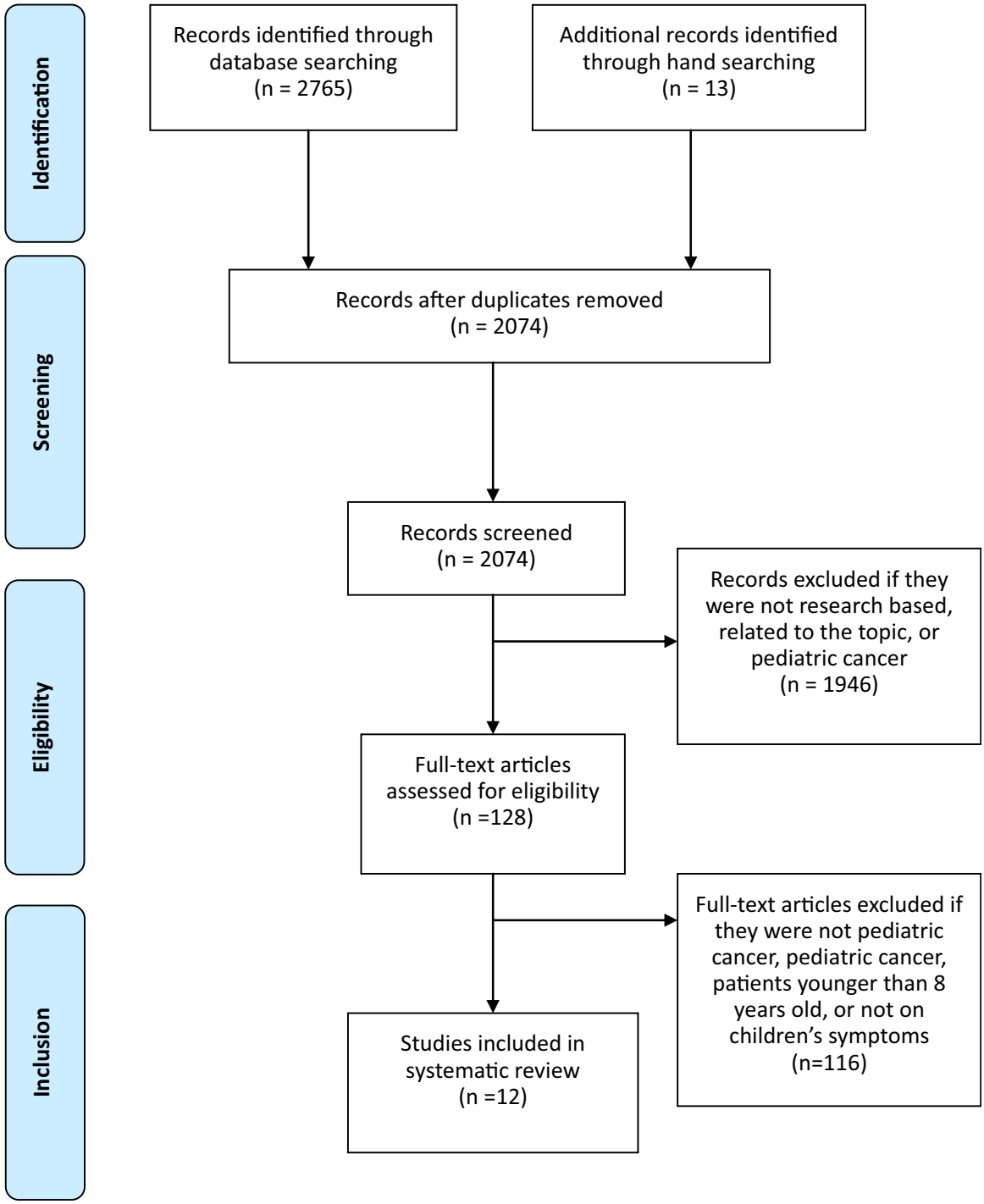

Fig. 1. PRISMA flow diagram.

Table 2
Summary of Studies

First Author (Year) Country	Study Design	Population	Symptom(s)	Measurement	Symptom(s)-Related Outcomes
Badr (2006)[21] Lebanon	Descriptive, observational study	45 children (four to 10 yrs) with cancer undergoing port-a-cath access Not stated the exact number of children aged under eight years	Procedure pain	Wong-Baker FACES Pain Rating Scale DOLLS (six fabric dolls with different facial expressions) Children reported pain level at the three different time points (10 minutes before the port-a-cath access, during the procedure, and 10 minutes after the procedure).	1) Four- to five-year-old children reported higher procedure pain than six- to 10-year-old children ($F = 5.26$, $P < 0.05$).
Dupuis (2001)[13] Canada	Descriptive, observational study	124 children (one to 17.7 yrs) receiving antineoplastic Not stated the exact number of five- to seven-year-old children	Delayed nausea	6-faced "happy face" analog scale Children report daily	1) Nausea intensity scores 2) Nausea frequency 3) Three- to 4.9-year-old children did report more frequently than did older children in moderate to severe delayed nausea ($P = 0.415$).
Dupuis(2006)[6] Canada	Instrument validation	177 children (four to 18 yrs) with cancer Aged under eight years (66 children)	Nausea	PeNAT four-face scale Children's report four to 24 hours after chemotherapy	1) Nausea intensity scores 2) Correlation between the number of emetic episodes and the PeNAT score was observed to be higher in four- to eight-year-old children ($r = 0.513$) than in children aged over eight and 12 yrs ($r = 0.155$) or adolescents ($r = 0.356$).
Hedström (2003)[22] Brazil	Qualitative study	121 children (zero to 19 yrs) with cancer Zero to three yrs (26 children) Four to seven year (41 children)	Distressing events	Interviewing parents No timing was mentioned.	1) Distressing symptom frequency
Hermont (2015)[23] Brazil	Descriptive, observational study	83 children (five to 18 yrs) with cancer and parents dyads Five to seven yrs (23 children and parents dyads)	Procedure anxiety, treatment anxiety, and worry	PedsQL Cancer Module Scale Children and parents dyads reported symptoms in the past month.	1) Symptom intensity scores 2) Tendency for children to report increasing feelings of worry (comparing five to seven, eight to 12, and 13–18 yrs) as they got older 3) No statistically significant difference between the age group five to seven years and the proxy-reported scores
Lau (2010)[19] Hong Kong	Instrument validation study	359 children (five to 18 yrs) with cancer Two to four yrs (55 parents) Five to seven yrs (70 patients and 70 parents)	Pain/hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, physical appearance, and communication	PedsQL Cancer Module (Cantonese) Two- to four-year-old children's parents and five- to seven-year-old children and parents dyads reported symptoms in the past month.	1) The intraclass correlation coefficient values (consistency between the patient and parent versions) for the five- to seven-year-old age group

Meeske (2004)[15] U.S.	Descriptive, observational study	Parents of children (two to 18 yrs) with brain tumors ($n = 86$) or acute lymphoblastic leukemia ($n = 170$) Two to four yrs (acute lymphoblastic leukemia, $n = 42$; brain tumors, $n = 11$); Five to seven yrs (acute lymphoblastic leukemia, $n = 51$; brain tumors, $n = 21$)	Physical, psychosocial, and emotional functioning, social functioning, school functioning, pain, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, physical appearance, communication, and fatigue	PedsQL Cancer Module PedsQL Multidimensional Fatigue Scale Parent proxy reported symptoms in the past month.	1) Symptom intensity scores 2) Children's age at interview was inversely related to the Multidimensional Fatigue Scale total score (trend $P = 0.0008$). 3) Child's age at diagnosis was inversely related to the Multidimensional Fatigue Scale total score (trend $P = 0.003$).
Pu (2015)[17] China	Instrument validation	141 children with leukemia (aged two to 18 yrs) and parents dyads Two to four yrs (61 parent proxy reports) Five to seven yrs (27 children and parents dyads)	Fatigue	PedsQL Multidimensional Fatigue Scale (Chinese) Two- to four-year-old children's parents and five- to seven-year-old children and parents dyads reported symptoms in the past month.	1) Symptom intensity scores 2) Parents reported more severe levels of general fatigue than the children aged five to seven years ($t = -2.85$, $P < 0.05$). 3) Parents' total fatigue score is related to the score reported by children aged five to seven years ($r = 0.524$, $P < 0.05$)
Razzouk (2006)[16] U.S.	Randomized, double-blind, placebo-controlled study	111 anemic children (five to 18 yrs) receiving myelosuppressive chemotherapy and parents dyads Five to seven years (47 child-parent dyads)	Pain/hurt, nausea, procedure anxiety, treatment anxiety, worry, cognitive problems, physical appearance, and communication	PedsQL Cancer Module Two- to four-year-old children's parents and five- to seven-year-old children and parents dyads reported symptoms in the past month.	1) Symptom intensity scores
Tsuji (2011)[20] Japan	Instrument validation	253 children with cancer (two to 18 yrs) and parents dyads Two to four years (41 parents of these children) Five to seven years (62 children and parents dyads)	Pain/hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, physical appearance, and communication	PedsQL Cancer Module (Japanese) Two- to four-year-old children's parents and five- to seven-year-old children and parents dyads reported symptoms in the past month.	1) Symptom intensity scores 2) Scale scores were consistently higher for child reports than for parent reports. 3) Intraclass correlation coefficient values among the children ranged from good to excellent except for the "treatment anxiety" subscale for five- to seven-year-olds.
Zhou (2014)[18] China	Descriptive, observational study	52 children (five to seven years) with cancer and parents dyads	Pain/hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, physical appearance, and communication	PedsQL Cancer Module (Chinese) Children and parents dyads reported symptoms in the past month.	1) Symptom intensity scores 2) Children had more distress and burden on procedural anxiety and worry than their parents ($P < 0.05$), and they had less distress and burden on cognitive problems than their parents ($P < 0.05$).
Zupanec (2010)[14] Canada	Descriptive, observational study	62 children (four to 18 yrs) receiving maintenance chemotherapy for ALL Four to seven years (36 children)	Sleep disturbance and fatigue	Children's Sleep Habits Questionnaire Childhood Cancer Fatigue Scale—Parent version Parent proxy reported symptoms in the past week.	1) Symptom intensity scores 2) Four- to seven-year-old children whose sleep was reported as different because diagnosis had higher median fatigue scores

All included studies were analyzed by qualitative descriptive analyses. First, data were abstracted with a report table, including variables of publication year, country of study population, study design, study participants, symptom(s), measurement procedure, and symptom(s)-related outcomes. Then, symptom profile, including symptom intensity, timing, quality, distress, and associated factors, was extracted from each studies based on the Theory of Unpleasant Symptoms. Content analysis was performed to analyze the qualitative data.

Results

A total of 2778 articles were identified by the search strategy. After removing duplicates, the remaining 2074 articles were screened by titles, which resulted in a total of 128 articles remaining. Of the retrieved full-text publications, 116 were excluded, leaving a total of 12 publications, which were included in this integrative review. Fig. 1 illustrates the flow diagram of study identification and selection. Table 2 illustrates the characteristics of the included publications. Eleven of the 12 studies were quantitative, with seven descriptive observational studies, four instrument validation studies, one randomized controlled study. Only one studies used qualitative design. The quality appraisal rating began at a low quality level because most of the studies were descriptive designs. As the appraisal revealed no serious methodological flaws and no issues with inconsistency, indirectness, imprecision, or publication bias within the evidence, the overall body of evidence remains at a low-quality level.

Five of the included studies were conducted in North America (three in Canada[6,13,14] and two in U.S.[15,16]), five in Asia (two in China,[17,18] one in Hong Kong,[19] one in Japan,[20] and one in Lebanon[21]), and two in South America (Brazil).[22,23] Most of the studies recruited children with a wide age range (two to 18 years), among which seven studies including children aged under five years.[6,13–15,20–22] One study only collected the symptom reports from children aged five to seven years.[18] Most studies recruited children with all types of cancer, for example, leukemia, lymphoma, brain tumors, neuroblastoma, rhabdomyosarcoma, osteosarcoma, and Wilms' tumor. Two studies recruited children only with acute lymphoblastic leukemia.[14,17] One study specifically enrolled children with brain tumor or acute lymphoblastic leukemia.[15] Three studies only collected children's own symptom reports.[6,13,21] Six studies measured both children's and parents' reports,[16–20,23] of which four studies only using parent proxy reports for two- to four-year-old children.[16,17,19,20] Three studies only examined parent proxy reports for their children's symptoms.[14,15,22] Most of the 12 studies studied symptom experiences during cancer treatment, with one study focusing on children receiving maintenance chemotherapy[14] and one study focusing on children undergoing port-a-cath access.[21]

Table 3
Symptoms and Instruments for Measuring Children's Symptoms Under Eight Years

Symptom	Instruments
Communication	PedsQL Cancer Module[15,16,18–20]
Cognitive Problems	PedsQL Cancer Module[15,16,18–20]
Fatigue	PedsQL Multidimensional Fatigue Scale[15,17] Proxy report Childhood Cancer Fatigue Scale[14]
Nausea	6-faced "happy face" analog scale[13] PeNAT four-face scale[13] PedsQL Cancer Module[15,16,18–20]
Pain/hurt	PedsQL Cancer Module[15,16,18–20]
Physical appearance	PedsQL Cancer Module[15,16,18–20]
Procedure pain	DOLLS[21] Wong-Baker FACES[21]
Procedural anxiety	PedsQL Cancer Module[15,16,18–20,23]
Sleep	Children's Sleep Habits Questionnaire[14]
Treatment anxiety	PedsQL Cancer Module[15,16,18–20,23]
Worry	PedsQL Cancer Module[15,16,18–20,23]

Symptom Identified and Instruments

Table 3 displays the symptoms and instruments for measuring children's symptoms under eight years of age. Symptoms that were identified included nausea ($n = 6$), procedural anxiety ($n = 6$), treatment anxiety ($n = 6$), worry ($n = 6$), pain/hurt ($n = 5$), communication ($n = 5$), cognitive problems ($n = 5$), physical appearance ($n = 5$), fatigue ($n = 3$), sleep ($n = 2$), and procedure pain ($n = 2$).

Interviews were used by the only qualitative study to assess children symptom experience.[22] The other 11 studies used two categories of instruments to measure symptoms. Six studies measured children's multiple symptoms measured by Pediatric Quality of Life™ inventory Cancer Module Scale focused (PedsQL™ Cancer Module).[15,16,18–20,23] The other instruments focused solely on single symptom, that is, procedure pain (DOLLS[21] and Wong-Baker FACES[21]), nausea (six-faced "happy face" analog scale[13] and PeNAT four-face scale[6]), fatigue (PedsQL Multidimensional Fatigue Scale[15,17] and Proxy report Childhood Cancer Fatigue Scale[14]), and sleep (Proxy report Children's Sleep Habits Questionnaire[14]).

Eleven studies described the time interval for symptom reports. Seven of the studies measured symptoms in the past month.[15–20,23] The other four studies included one study measuring symptoms throughout different time points during port-a-cath access,[21] another study measuring delayed nausea daily,[13] a third study collecting nausea reports four to 24 hours

after chemotherapy,[6] and a fourth study assessing sleep disturbance and fatigue in the past week.[14]

Symptom Profile: Intensity, Timing, Quality, and Distress

Most of the studies found that children with cancer under the age of eight years experienced substantial physical and psychological symptoms, especially as related to the intensity dimension. Although various instruments with different operational definitions were used to determine the level of intensity of symptoms, there were a considerable number of this age group children experienced moderate to severe intensity of symptoms, which included pain,[15,16,18–21] worry,[15,16,18–20,23] and anxiety.[15,16,18–20,23] However, the discordance between age and symptom intensity was noted. In Meeske's study, there was a trend that younger children and their proxy reported less total and intense symptoms among the four age groups (two to four, five to seven, eight to 12, and 13–18 years).[15] In Dupuis' study, compared with the older children, younger children (aged less than five years) who received antineoplastic presented a lower daily nausea score.[13] Similarly, in Hermont's study, the result of the comparison between the three age groups (five to seven, eight to 12, and 13–18 years) showed a tendency that children reported increasing feelings of worry as they got older.[23] Nevertheless, Meeske's study also reported that the fatigue intensive scores were higher in children aged two to four years than children aged five to seven years.[15] Badr's study showed that younger children (four years of age to 5 years, 11 months) reported more intense pain than their older counterparts (aged six to 10 years).[21]

Two studies examined the timing dimension of the symptoms.[13,22] Compared with their old counterparts, younger children (aged less than five years) vomited more frequently but reported no more frequent moderate to severe nausea on any day during the delayed phase. Only one study reported the coexisting phenomena between emetic episodes and nausea.[6] The relationship of the first nausea score and number of emetic episodes was much stronger in children aged four to eight years than in older children.

One qualitative study explored the distress dimension of the symptoms.[22] Reported by parents, younger children (aged less than five years) were more concerned about procedural pain and cancer pain as physical symptoms than older children. They missed their everyday life and felt different and left aside related to psychological symptoms.

This qualitative study also described how parents of children with cancer under eight described their symptoms' quality verbally.[22] However, it only provided examples of symptoms for age group zero to three years and four to seven years, with little descriptions of each specific symptom.

Factors Associated With Symptoms

Seven studies compared the concordance between children and their proxy symptom reports, revealing inconstant results. Two studies measured the intraclass correlation coefficient values (consistency between the patient and parent versions) for the five- to seven-year age group[19,20] and found high and moderate intraclass correlation coefficient in nausea, procedural anxiety, treatment anxiety, perceived physical appearance, pain and hurt, low consistency in communication, worry, and cognitive problems. This was consistent with Hermont's study that there was no statistically significant difference between the age group five to seven years and the proxy-reported scores in procedure anxiety, treatment anxiety, and worry.[23] However, in Zhou's study, children reported more distress and burden on procedural anxiety and worry than their parents ($P < 0.05$).[18] Parents showed more concerns about burden on cognitive problems than their children. Meanwhile, Pu et al.[17] found that although parents' total fatigue score is related to the score reported by children aged five to seven years, parents reported more severe levels of general fatigue.

Four studies reported the relationship between children's age and symptom scores (as described previously). There was discordance between a child's age and symptom intensity. Younger children reported lower total symptom,[15] nausea,[13] and worry[23] scores but higher fatigue[15] and pain[21] scores.

Discussion

The purpose of this review was to synthesize current evidence regarding symptom experience of children with cancer younger than eight years of age. Often these younger children were included in studies of children in a wide age range; this review suggests that there were limited studies describing symptoms has specifically targeted children less than eight years of age.

Based on the 12 reviewed studies, our main findings are young children are a particularly disadvantaged group in terms of symptom reports as there are very few instruments that span this age range. In this study, PedsQL Cancer Modules (for age five to seven years) were the most frequently used instruments for evaluating self- and proxy-reported multiple symptoms, with pain, worry, and anxiety as the most commonly reported intense symptoms.

Characteristics of children's symptom reports are closely related to their cognitive development.

Although children as young as five years of age can provide a self-report of their symptoms, variability of responses and difficulty were reported by previous studies when obtaining responses with younger children.[1,24] According to Piaget's theory of cognitive development,[25] children under the age of eight are still in the process of reaching concrete operational stage, as exemplified in one of the included studies, these children would believe that they were nauseous because they vomited instead of making an independent assessment of the severity of their nausea.[6] In this study, we also found that these younger children reported more physical symptoms but less psychological symptoms. This was consistent with the evidence that younger children were more concerned with pain as they lack the cognitive maturity to develop autonomous strategies and therefore might be less able to cope with it.[22,26] Meanwhile, previous researchers also suggested that cognitive development could affect precision in measuring and interpreting the symptom experience, as most self-report measures have higher accuracy with older children.[27] This further leads to the discussion about the suitable way to collect symptom reports for this age group of children.

In this study, three categories of symptom reporters existed, including children reporters alone (usually aged over five years), children and parent reports, and parents alone. Parent proxy symptom report was commonly used for this age group. However, as shown in our results, there existed inconsistent concordance between children's and parents' reports.[17–20,23] Although parents were more concerned about the impact of cancer on children's cognitive abilities, children at this age were more sensitive about the direct and apparent symptoms such as treatment anxiety. Meanwhile, some symptoms (such as nausea) were proved to be unreliable to use proxy reporters.[6] Therefore, to understand the entire symptom experience of this age group, it is necessary to get children's self-reports. Given these children's cognitive maturity, most of the studies that used child reporters employed expressive visualized instruments with face scales for response options (such as PeNAT and DOLLS). Previous studies also suggested that modern electronic and computer technologies (e.g., virtual reality, computer games) helped elicit children's self-report symptoms, as used in the older children.[28,29] Furthermore, influenced by their family environment and cognitive development level, children's symptom vocabulary may vary across ages and families. Ruland et al. conducted a review listing the terms or expressions children with cancer use to describe their symptoms.[30] It concluded that more research were needed to better understand differences in symptom experiences among different age groups and that it would be imperative to ascertain these children's own age-specific symptom expressions. In response to this calling, a recent published article described the development of a new self-report symptom screening tool (mini-SSPedi) for children aged four to seven years receiving cancer treatments.[31] The authors proposed a stepwise approach incorporating three phases, that is, establishing an appropriate instrument structure, evaluating understanding of each symptom, and testing the entire instrument. The result showed this instrument was understandable and easy to complete among cancer and pediatric hematopoietic stem cell transplantation recipients between four and seven years of age.

During the literature search, two qualitative studies, which recruited children with cancer less than eight years of age, were identified as they explored children's own symptom expressions.[32,33] However, we were unable to include them in this review, as results for this particular age group were not reported separately. Nevertheless, findings from the two studies provided insightful implications for future symptom studies on the younger children. Particularly, these authors found that children experienced symptoms as feeling states and that cancer symptoms were viewed in the context of assigned meanings. Obviously, there is a need for more qualitative studies to fully understand these children's symptom experience.

This integrative review has some limitations. First, the included articles were limited to Chinese and English in light of the authors' language competency. Second, in spite of the fact that search strategies were developed by agreement of all the authors, there are still potential eligible studies on this particular age group that may have been missed for inclusion. Third, the main keyword search term "symptoms" might possibly bias the findings, as most subheadings under the MeSH term "signs and symptoms" were related to the physical domain, which could be the narrow scope of all the symptoms experienced by children aged under eight years. Fourth, some qualitative data of the included studies did not describe the symptom profiles extensively, which implies the possibility of certain biases being introduced by the interpretation of the reviewers, although discussions were held before agreement was finally reached.

Conclusion

High-quality supportive care is based on a comprehensive assessment of symptom experience. This integrative review symptom identified the current evidence on the symptom experience of children with cancer younger than eight years of age in terms of symptom quality, symptom intensity, timing, and the distress dimension. Future studies are suggested

to continue investigating the four dimensions of symptom profiles in consideration of their developmental nuances and examining the concordance among different symptom reporters (children, parents, and heath care professionals). In the meantime, more qualitative studies on this age group will facilitate a better understanding of young children's overall symptom experience.

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