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Symptoms and concerns among children and young people with life-limiting and life-threatening conditions: A systematic review highlighting meaningful health outcomes

Namisango E[1], Bristowe K[1], Allsop MJ[2], Murtagh FEM[3,4,] Abas M[5], Higginson IJ[1], Downing J[7], Harding R[1].

Author affiliations:

1 Cicely Saunders Institute, King's College London, London, UK.

2 Academic Unit of Palliative Care, Leeds Institute of Health Sciences, University of Leeds, Leeds, UK.

3 Cicely Saunders Institute of Palliative Care, Policy & Rehabilitation, King's College London, London, UK.

4 Wolfson Palliative Care Research Center, Hull York Medical School, Hull, UK.

5 Health Services and Population Research Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK.

6 International Children's Palliative Care Network, Bloemfontein, South Africa.

7 Palliative Care Unit, Makerere University, Kampala, Uganda.

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Declaration of conflict of interests

Eve Namisango, Matthew J Allsop, Katherine Bristowe, Fliss E M Murtagh, Melanie Abas, Irene J Higginson, Julia Downing and Richard Harding have no conflicts of interest.

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Abstract

Background: The design and provision of quality paediatric palliative care should prioritize issues that matter to children and their families, for optimal outcomes.

Aim: This review aims to identify symptoms concerns and outcomes, that matter to children and young people ("young people") with terminal illnesses and their families; it also aims to encourage the development of a relevant framework of health outcomes.

Study Design: This is a systematic literature review across multiple databases for identification of eligible primary evidence.

Data sources: Data sources such as PsychINFO, Medline, EMBASE, CINAHL, OpenGrey, and Science Direct Journals have been searched from 1 August 2016 to 30th July 2017. The study also incorporates consultations with experts in the field, citation searchers via Scopus, and a hand search for reference lists of included studies.

Results: Out of the 13,567 articles that have been evaluated, 81 studies were included. Of these, (n=68) are from high-income countries and (n=58) are cancer patients studies. A total of 3,236 young people, 2,103 family carers, 108 families, and 901 healthcare providers are included in the studies. Young people have not contributed to data in 30% of studies. Themes on priority concerns are presented by domain and health outcome; for example, 1) Physical (n=62 studies); e.g. physical symptoms, 2) psychological (n=65); e.g. worry 3) psycho-social (n=31); e.g. relationships, 4) existential (n=37); e.g. existential loss, and 5) "other" (n=39); e.g. information access.

Conclusion: Burdensome symptoms and concerns affect young people with malignant and non-malignant conditions and occur across the disease trajectory, so paediatric palliative care should not be limited to the end of life phase. A child-family centred framework of health outcomes, spanning the patient, family, and quality of service levels is proposed to inform service development. Future

research should address gaps identified; the involvement of the young people in research, evidence for developing countries, and for non-malignant conditions.

Keywords: person-centred outcomes; paediatrics; palliative care; young people; terminal illness

Key findings and implications of this manuscript

- An overarching theme identified in young people with malignant and non-malignant illnesses is the issue of multi-dimensional, complex symptoms and concerns which interact and occur across the disease trajectory.
- Our findings demonstrate considerable overlap in themes of illness experiences across diagnostic groups, settings of care and geographical location, alongside identifying common behaviours.
- This review presents an evidence-based child/family framework of symptoms, concerns and health outcomes. These span three levels; child, family, quality of services. This framework can encourage the development of paediatric palliative care outcome measures, to inform service audits, research, and evaluations.
- There is evidence that young people aged 6+ can self-report on symptoms, concerns and health outcomes, but reduced communication and cognitive abilities also remain a challenge. Developing person-centred child appropriate information and communication tools, which are, more inclusive of patients with special needs, should thus be prioritised.
- We highlight limited involvement of young people in research, a disparity in evidence coverage for developing countries, and a lack of evidence for non-malignant conditions.

1 Background

The number of children and young people ("young people") (aged 0-23 years) living with Life-limiting and Life-threatening Conditions (LLC) is increasing worldwide.[1-3] A crucial component of care for young people with LLC is palliative care, which seeks to improve the quality of life of patients and their families facing problems associated with life-threatening illness. Recent global estimates have set the annual number of young people that need palliative care at any point during their disease trajectory at 21 million, with 8 million requiring some form of specialist palliative care.[4] For high income countries, such as the UK and America, prevalence of LLC in young people is increasing[5] with most deaths caused by trauma, congenital conditions, extreme prematurity, and other acquired illness.[6] In resource-limited settings, the case mix of young people with LLC also includes conditions such as HIV which continues to pose a public health concern and is typically accompanied by a high symptom burden (e.g. pain, weight loss, lack of appetite, feeling sad and difficulty sleeping). According to the Joint United Nations Programme, between 2.9-3.5 million children are living with HIV infection, with sub-Saharan Africa shouldering 91% of the global burden.[7] The situation is further exacerbated due to the increasing incidence and prevalence of various types of cancer among young people, with over 80% of deaths occurring in resource-limited settings.[8] Besides HIV and cancer, complex chronic, neonatal, and other non-communicable diseases contribute to mortality and morbidity among the children in resource-limited settings.[9] The high mortality in resource-limited settings is largely attributed to health system challenges, such as late diagnosis, which limits curative treatment options,[10] and the poor coverage of supportive care services.[11] However, independent of context-specific case mix and health system challenges, there are key priorities that need to be addressed to develop provision of palliative care services for young people with LLC.

The current delivery of palliative care for young people typically runs parallel to existing health care systems, without integration of the existing and speciality services.[4] The provision of quality care to young people with LLC requires the critical establishment of robust evidence on the symptoms and

concerns that matter to the patients and their families.[12] Despite the need for this evidence, there is currently limited information on meaningful outcomes for young people with LLC.[12,13] This need for patient-level data is more pressing than ever amidst the worldwide demand to address the absence of person-centred outcome measures in the measurement of the quality of paediatric care.[13,14] Generating population-specific measures of Health-Related Quality of Life (HRQOL) is the key to developing palliative care for young people. Measurement of HRQOL will enable those developing and evaluating services to determine their effectiveness.[15] Furthermore, it can enable improvements in clinical care, research, and informed decision making.[16] Currently, there is no appropriate outcome assessment measure for use in paediatric palliative care.[15] In order to develop outcome assessment measures it is essential to understand the perspectives of the population in which they will be used.[17] At present, there is limited reporting on the needs and experiences of young people with LLC. In those cases where reviews of existing literature have been completed, they have been limited by inclusion of evidence from the North America alone[18] or focused solely on cancer and neuro-disability, neglecting other types of LLC.[18,19]

Research with young people with LLC is hampered by several methodological challenges. These include clinical considerations such as participants being very ill,[20] limited access to potential participants,[21] and limited capacity to generate self-reports due to the less developed (or impaired) verbal and cognitive skills of this population.[22] As symptoms and concerns affect children's beliefs, expectations, and perceptions, it becomes important for self-reports from young people to be prioritized wherever possible.[23] The inclusion of the perspectives of young people and their families is critical to ensure that outcome measures are meaningful to them and their families.[24] Regrettably, the level of young people's involvement in research remains limited and self-reports of their outcomes and experiences are not commonly reported.[25] Therefore, innovative and feasible approaches for engagement of young people in research that will shape their care should be prioritized.

This review aims to appraise the global evidence on symptoms and concerns that matter to young people and their families to identify meaningful core person-centred health outcomes in young people with LLC and their families. The objectives of this review are to: i) appraise the methodological quality and extent of research literature, detailing patient, caregiver, family, and health provider reports of symptoms and concerns across disease trajectories for young people living with LLC and their families; ii) identify the gaps that exist in the research literature (e.g. study design, countries, and conditions), and; iii) synthesise reports of symptoms and concerns, using a conceptual framework to identify the domains of importance in the development of outcome assessment measures for young people with LLC. These findings are utilised to discuss the implications for paediatric palliative care service development and outcome measurement.

2 Methods

This review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[26]

2.1 Search strategy

The databases searched were: MEDLINE via OVID (1946 –February week 4 2016), PsychINFO (1806 – February week 4 2016), EMBASE (1947 -2016 week 8 2016), CINAHL, Scopus (Elsevier) (1969 – 2016 week 8 2016), Science Direct Journals (Elsevier). Google Scholar and the OpenGrey website www.opengrey.eu/ [27] were used to identify relevant citations. Apart from the reference and citation searches, experts in the field were consulted to identify relevant literature. The search strategy was developed by the lead reviewer (EN) and a palliative care information scientist, after which it was reviewed by co-authors. The electronic search terms included combinations of Medical Subject Headings (MESH) and plain language words to capture the elements of the population (any life-limiting or life-threatening condition), intervention (palliative/ chronic, end of life etc.), and the phenomenon of interest (symptoms, concerns, outcomes etc.). The detailed search strategy is presented in Table 1. The search was undertaken between January and August 2016, and was updated on 31st July, 2017. Inclusion and exclusion criteria are presented in Table 1.

Table 1: Description of the search strategy

Focus of term	Search term used	Free text terms used
Population: Identify research that focuses on children and young people	Exp child/ Exp infant/ Exp p?diatrics	(Child* or infant* or newborn* or baby or babies or neonat* or perinatal or adolescen* or youth* or juvenile* or teen* or young people or p#diatric).tw.
Intervention: To identify conditions that require palliative care [150]	exp palliative care/ exp hospice care/ exp hospices/ exp terminal care.af/ exp terminally ill/ exp "death and dying"/	(End of life care.tw. Or EOL care.tw. Palliative care nursing.tw. Or palliative medicine.tw. or life-limiting condition* or incurable disease* or life-limiting condition* or progressive disease*).tw
Phenomenon of Interest/outcome: To identify literature on symptoms and concerns to children and young people living with life limiting and life threatening conditions.		(Need* or concern* or problem* or suffering or symptom* or perception* or outcome* or quality of life or health-related quality of life or perspective or meaning or symptom distress or what matters or consequence* or psychosocial or lived experience* or illness experience*). tw

2.2 Compliance with Ethical Standards

This study is funded through an unrestricted grant provided by the Open Society Foundations. There were no additional ethical concerns, and all authors have no conflicts of interest to declare.

2.3 Data collection

The lead reviewer (EN) screened the titles and abstracts of all articles that have been identified through the search for relevance and has exported all such relevant articles to Endnote reference software version 7. The full texts of the articles have been obtained in cases where the abstracts did not contain sufficient information for determining the relevance of an article. Any duplicate references were removed. Two independent reviewers (EN, MA) reviewed the titles and abstracts of the remaining references against the following criteria:

Inclusion criteria:

i. Focus on life-limiting and life-threatening conditions as defined by the WHO

ii. Focus on meaningful health outcomes in children and young people with life-limiting and life-threatening conditions and their families

iii. Mixed age groups studies that provide age-stratified results

iv. Case studies of at least three participants

v. Qualitative, quantitative, and mixed method studies

Exclusion criteria:

i. Case studies of just one or two patients

ii. No report on symptoms/concerns and preferences for children living with life-limiting and life-threatening conditions

iii. Focus on the needs of the family alone (i.e. excluding the child)

iv. No empirical data (editorials, reports, letters, reviews, discussion papers, commentaries and case histories)

v. Insufficient information to judge inclusion eligibility

vi. The full paper could not be obtained

Articles not meeting the inclusion criteria were discarded. Relevant studies were subsequently reviewed based on the following characteristics: (i) source of study, (ii) year of publication, (iii) study aims as reported, (iv) age range or mean age, (v) primary diagnosis as reported, (vi) study design, (vii) sampling approach, (viii) number and type of study participants, (ix) data collection methods, (x) setting, and (xi) key findings related to phenomenon of interest. Disagreements were resolved through consultation with senior researchers.

2.4 Assessment of methodological quality of studies

All studies have been assessed for methodological quality using the Hawker checklist for reviewing disparate data systematically.[28] Ten components have been assessed for methodological rigour with a possible range of scores (good=4, fair =3, poor =2, and very poor =1). No studies have been eliminated based on quality criteria. The STROBE checklist was referred to assess comprehensiveness of reporting for observational studies.[29] Two authors have independently assessed and rated the included studies for rigour and methodological quality. The independent scores by the two authors have been compared for consistency. Any inconsistencies have been resolved through consultation with experts (RH, FM, and KB). The inter-rater agreement was computed using the Intraclass Correlation Coefficients (ICC) and Cohen's Kappa statistic for the methodological and grading datasets. Decisions on acceptable levels of agreement were based on the following cut-offs: poor <0, slight (0.0-0.2.), fair (0.21-0.40), moderate (0.41-0.60), substantial (0.61-0.80), and almost perfect (0.81-1.00).

2.5 Analysis

2.5.1 Data extraction

Data from studies that met the inclusion criteria were extracted into a Microsoft Excel spreadsheet which had been piloted by the lead reviewer (see Appendix 1). Quotes to support reported themes and original author notes have been extracted for qualitative studies. The identified outcome measures have also been extracted into a pre-designed Microsoft Excel template and assessed for quality of measurement properties using the COSMIN checklist.[30]

2.5.2 Data synthesis

The data has been synthesised using a systematic review and integrative design.[31,32] Both qualitative and quantitative narrative syntheses approaches have been used. Descriptive statistics have also been used to summarize the studies under selected subheadings such as country, setting, focus, diagnosis, characteristics of respondents, and the main themes identified. Descriptive themes, encompassing the themes or codes of the primary studies, have been developed with attention to similarities and differences across and between studies, and then grouped by phenomenon/themes. Disagreements have been resolved through discussions, guided by references to results, discussion, and conclusions sections of included studies and through consultation of content experts. Data has been assessed for contrasting themes within different diagnostic groups and by developmental age, grouped as follows: (0-5 years, 6-9, 10-14, 15+); it has been based on guidance on feasibility as informed by included studies, best practices[33,34] and expert guidance.

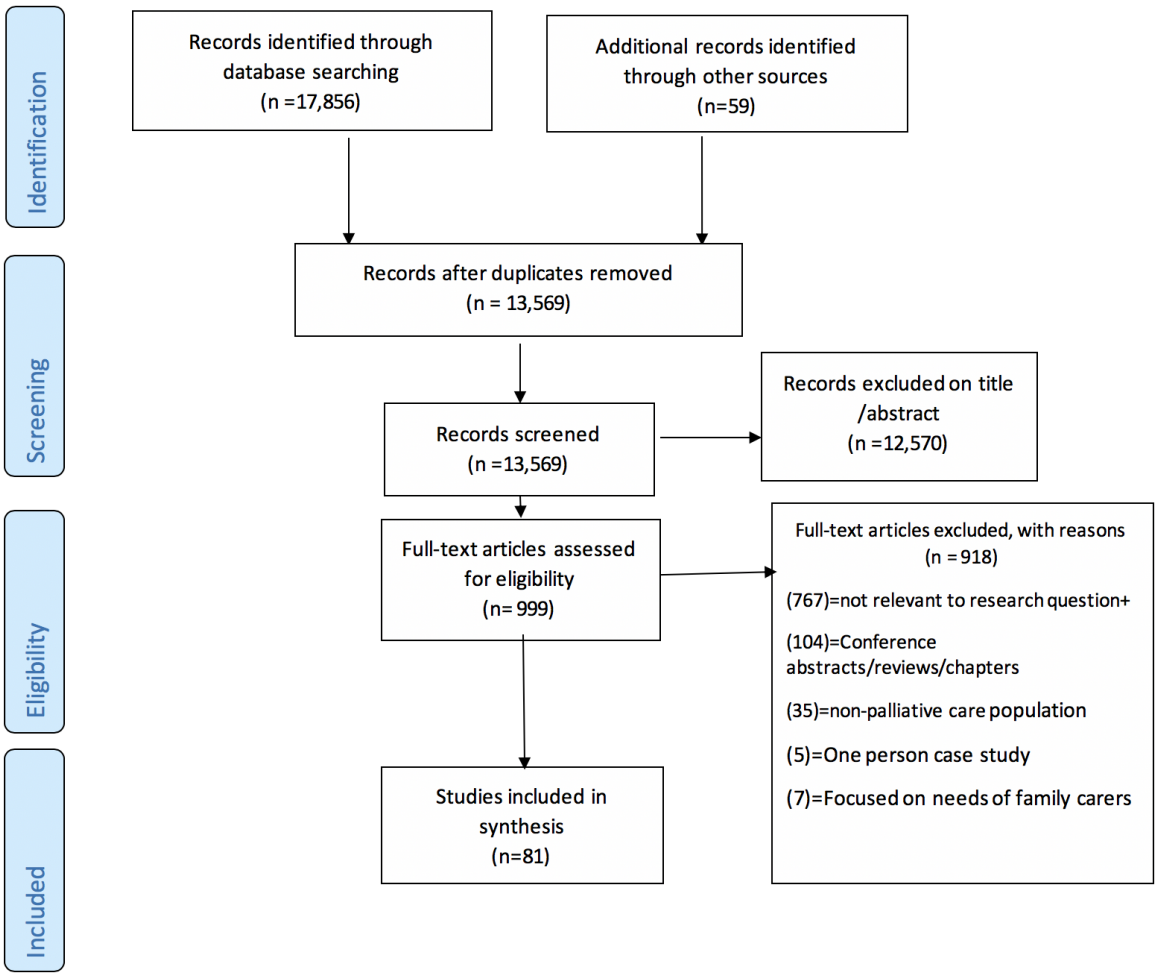
Subsequently, a conceptual framework of domains underlying the concept of health outcomes has been developed. A reference has been made to the WHO definition for paediatric palliative care and the core domains have been mapped out; physical, psychological, social, and spiritual/existential.[35] A fifth domain, “other”, was adopted to accommodate any themes and sub-themes that did not seem to fit into the existing four domains. References have been made to WHO definitions for health,[36] the Patient-Reported Outcomes Measurement Information Systems (PROMIS) framework,[37] and related literature,[18,19,38,39] to aid the labelling of themes and sub-themes, while seeking expert guidance (FM, KB, RH) where necessary. The lead reviewer has further coded the data by domain, themes, and sub-themes, documenting illustrative examples of the outcomes. Two content experts (RH, SE) have verified that the coding and areas of disagreement have been resolved through discussion and consultation of experts.

3 Results

3.1 Study selection process

A total of 13,569 articles were identified, after eliminating the duplicates. These were assessed for eligibility, after which 81 have been included in this review; of these 81, 79 were original studies, published between 1996 and 2017 (see Figure 1).

Figure 1: PRISMA flow chart of study selection and inclusion



3.2 Characteristics of included studies

Of the 81 included papers, 68 (84%) are from high income countries [USA (n=22), Canada (n=15), Sweden (n=9), UK (n=9), Australia (n=3), Japan (n=2), Netherlands (n=2), Germany (n=1), Hong Kong (n=1) , New Zealand (n=1), Spain (n=1), Switzerland (n=1), 1 multi-country [UK and Australia n=1], and 13 (16%) from low-middle income countries [Lebanon (n=1), Malaysia (n=1), Taiwan (n=1), Thailand (n=1), Jamaica (n=1), Brazil (n=1), South Africa (n=2), Uganda (n=1), Malawi (n=1), Nigeria (n=1), Zimbabwe (n=1), multi-national Uganda and South Africa (n=1)].

A total of 2,951 young people, 545 parents/family carers, and 401 professionals are represented by the included studies. Respondents, as reported by studies, are as follows; young people (n=29), parents (n=14), health workers (n=6), parents/young people and siblings (n=21), young people/parents/health workers (n=7), and clinical file reviews (n=4). Forty-five (55.6%) of the studies are qualitative, 27 (33.3%) are quantitative (of which four were clinical file reviews), and 9 (11.1%) are mixed methods. As presented in Appendix 1, a range of approaches for data collection and analysis have been adopted. The focus of the papers varies, including a focus on symptom experiences (n=42; 51.9%), outcomes (n=20; 24.3%), friendship dynamics (n=1; 1%), scale development (n=4; 4.9%). and end-of-life care experiences (n=14; 17.3%).

Most of the studies (n=58; 71.6%) involve cancer patients; of these, 46 studies provided details on types of cancer, with treatment status reported in all studies (Table 2).

Table 2: Overview of participant characteristics

Characteristics of study participants in the included studies		***Number of*** **participants (*n*) across included studies**
Children and young people *Age range 0-23 years old*		*n* = 3,236 (sample range = 3 – 385)
Participating, number of parents		*n* = 2,103 (sample range = 5-449)
Participating, number of health workers		*n* = 901 (sample range = 7-276)
Families		*n* = 108
Diagnoses of young people as presented in included studies		***Number of*** **studies (*n*)**
Condition of children and young people in studies (where single condition)	*Cancer (*leukaemia (n=37), brain tumours (n=24), lymphomas (n=19), solid tumours (n=24), sarcomas (n=16), neuro-oncology (n=2), other(n=17), diffuse intrinsic pontine glioma, malignant melanoma, neuroblastoma, retinoblastoma, liver cancer, medulloblastoma, langerhans cell histiocytosis, wilms, head and neck cancer, bone cancer, acute myeloid leukaemia, and acute lymphoblastic leukaemia	*n* = 58 (73.4%)
	Epilepsy	2[40,41]
	HIV	5[42-46]
	Sickle cell disease	1[47]
	Liver disease	2[48,49]
	Advanced heart disease	1[50]
	Neural disability	3[19,27,51]
	Brain tumours, leukaemia, bone tumour, congenital heart defect, renal disease, cystic fibrosis, congenital syndrome	1[52]
	Asthma, arthritis, epilepsy, diabetes	1[53]
Mixed diagnoses	Renal disease, cystic fibrosis and congenital syndrome asthma, arthritis, epilepsy, cerebral palsy, diabetes mellitus, atopic dermatitis, or cystic fibrosis	1[54]
	Gastro intestinal, paediatric oncology and cardiology	1[23]
	Cancer, cardiac, neurological; and gastroenterological problems	1[55]
	Paediatric neuro-disability; cerebral palsy, autism, epilepsy, learning difficulties, acquired brain injury	1[19]
	Terminal illnesses	1[56]
	Life limiting conditions	1[39]
	Cancer and HIV	1[57]

3.3 Quality of included studies

The level of agreement on the quality of study appraisal scores is good (ICC=0.80.). Hawker's quality scores range from 20 to 38, out of a possible score of 40. The mean and range scores for qualitative studies was 31 (range 21-38), 29 for mixed method studies (range 21-36) and 31.2 for quantitative studies (range 20-38). These studies are mainly descriptive, non-experimental, and cross-sectional, with some of them using convenience samples; one randomized controlled trial is included[58] (see Appendix 1 for details). The quality of included studies is poor in the following domains: ethics, bias, sampling, and limited articulation of the generalisability of the findings. In most instances, the discussion of ethics has been limited to seeking approval from ethics review boards; assent and consent processes have rarely been explained in detail. It is found that only two papers have mentioned the use of child-appropriate information sheets.[59] Very few studies have mentioned the consideration of respondent age in questionnaire development as a way of ensuring age-appropriateness of the questions.[54,59-65] The process surrounding data collection with young people has rarely been explained in detail.

For 12 qualitative studies, the setting of the interviews and discussions has been provided, including quiet locales and open areas.[41,66-76] A majority of qualitative studies fail to account for potential bias from researchers. Only three qualitative studies validated the findings, using focus group interviews [41,71] or documentary analysis for triangulation.[59]

3.4 Aspects of the health of young people with life-limiting illness and their families

The full thematic of findings are presented in Appendix 1 and key findings are explained in the following section by domain.

3.5 Physical (n=62 studies; 77%)

3.5.1 Physical symptoms and concerns

Disease and procedure-related pain has emerged as a major concern across the disease trajectory, and during the end of life stage; the pain is often reported as 'intolerable', or 'out of control', with procedure-related pain being associated with fear, anxiety, and suffering.[77,48,52,55,63,78-87] For this reason, the need for parental protection and assistance during treatment is stressed upon in cases of young children with cancer.[63,88] Two studies have found such pain to be more prevalent in children with solid tumours.[89,90] Inadequate treatment of pain, side effects of opioids, and treatment of non-pain related symptoms have also been mentioned as concerns by paediatric oncology patients.[77,83] Concept elicitation and illness experience studies highlight pain control as a priority in cancer and non-cancer disease groups.[19,27,45,51,74,76,91,92]

Other commonly reported physical symptoms are lack of energy, nausea, vomiting, dry mouth, weight loss, and drowsiness[78,85,93-95 27,43,52,85,93,94,96-98]. Symptoms associated with severe distress during cancer treatment include difficulty in swallowing and shortness of breath.[78,99] Symptoms associated with severe distress include shortness of breath, feeding difficulties, fatigue, drowsiness, nausea, loss of motor function, pain, reduced mobility, decreased appetite, respiratory failure, and lack of energy.[50,52,55,63,79,100] Difficulty in breathing/shortness of breath, fatigue, drowsiness, and nausea is a common concern at the end of life, in both cancer and non-cancer patients.[52,55,79,82,89,100,101,50] Providing support with eating, sleeping problems, and minimizing symptom distress are commonly expressed as the end of life care priorities.[76,102,103] In two studies, neurological deterioration, loss of the ability to communicate, and decreased physical activity have been associated with impending death.[72,104]

On-going seizures are a major concern among epilepsy patients.[40] Weight loss, fever, mouth sores, stunted growth, diarrhoea, wasting, lymphadenopathy, oral candida, acute malnutrition, pneumonia, and respiratory tract infections are common in paediatric patients with HIV.[43,46,57] One study conducted among HIV positive children, aged 6-15 years, reported a high prevalence of other morbidities such as hearing impairment, visual impairment, gingivitis, speech impairment, and gross motor deficits.[46] The end-stage renal failure patients have also reported physical needs of post-renal transplant adjustment and coping;[105] their dependence on and need for a wheelchair compromises their function and has been associated with negative emotions.[105]

Studies that address concerns in neuro-disability and, particularly, the one on the development of the suffering scale in adolescents with cancer, prioritised physical symptoms and associated distress as core domains, which should be included in outcome measures for young people with LLC.[27,74] It is noticed that children tend to use unique language to describe their symptoms and, at times, have difficulty explaining their feelings.[106 62,107] The 'no symptom' syndrome is also reported in one study and has been interpreted as a form of denial, lack of specific symptoms, or unchanged health status.[52]

Young people express the need to be normal with full ability to perform age-appropriate functions such as self-care, mobility, and physical activity.[93,94 53,68,70,104,105,108-112] Symptoms become more of a concern when they lead to physical and mental changes or affect the ability of young people to engage in daily activities.[47,54,63,66,81,104,108,109,113]

3.6 Psychological (n=65 studies, 80%)

The psychological consequences of living with LLC span a spectrum of sub-domains including emotional, mood-related, cognitive, behavioural change, and isolation. Based on observations,

children aged 0-6 years express a need for emotional satisfaction and expression of their own will.[88] Mood-related symptoms include emotional instability[27], feeling shy about living with the disease,[51] feeling horrible, furious, upset, and disappointed[105], angry, scared, bored, sad, nervous, and crying. 62,66,67,74,100,109 51,97

Across literature specific to children receiving cancer treatment, commonly experienced psychological symptoms persisted, including mood swings, feeling sad, and worry, alongside a lack of concentration.[63,78,85,114] At the end of life, psychosocial symptoms of cancer patients include fear of going to sleep and dying, displaying a distance from family, confusion, anxiety and depression, irritability, inability to laugh or smile, insecurity, and mood swings.[52,60,63,89,93] One study has found emotional concerns to be more dominant in older age groups (12 and above).[94] Palliative care professionals mention the need for alleviation of psychological suffering as an important domain of quality of life in paediatric palliative care.[112]

Cognitive changes that have been identified include disturbance of consciousness, declining attention and concentration orientation, social skills, cognition, energy, and drive.[51,73,89,92,95] Other concerns include the need for a sense of self-worth,[115] resilience, coping with illness, accepting the present pain for potential gain in future, and the desire to protect other people from similar illness experiences. Children have sometimes reported psychological growth; for example, on achieving milestones like treatment completion, they reflect on the whole experience cognitively; “they either felt the same as old- not having noted any changes on outlook to life, completely different, or not normal.”[116] School-going children have also reported poorer performance at school.[74,114]

Parents of young people report a common range of behaviours in their children: anti-social, disobedient, unwilling to take medication, creating difficulties in incorporating daily medication into their routine schedules, and pill burden associated distress.[40,44,53,86,105,108,117] Adolescents (aged 12-18 years) are concerned that isolation or being like a "prisoner" has radically altered their lives and made it alien to them; some have cited memories of fear that could not be forgotten.[63] Hospitalisation, for treatment, is associated with isolation, affecting opportunities for interaction with friends and siblings, and invoking emotions of sadness, and homesickness.[47,109] The impact of living with LLC on social and physical functioning leads to feelings of frustration regarding a strong wish for 'normalcy'.[63,72,108,113]

3.7 Psychosocial (n=31 studies; 38%)

Young people and their families perceive living with LLC as a stressful life experience, irrespective of the type of diagnosis. Some concerns reveal a social and physical health overlap (e.g. young people with epilepsy who "felt different" due to their need for medication[40]). For paediatric HIV patients, disease-related features such as skin rash and facial lipodystrophy have been found to be associated with stigma.[42] Paediatric cancer patients are more concerned about hair loss and skin changes, which affect their body image.[104,118] The experiences of becoming the centre of attention to peers, being bullied at school, and isolation, have been prominently expressed.[40,41,44,48,49,53,118] Young people who have received liver transplants cite the plight of post-treatment features such as large scars, clubbed fingers, and short stature.[48]

Hospitalisation is a particularly undesirable experience associated with disruption of school schedule and social interaction, and resulting in isolation.[23,48,54,66,67,70,74,93,105,111,113,118] Young people generally value social relations where they feel comfortable talking, being listened to, share secrets, and are treated with respect.[23,39,40,48,76,112,113,119] Young people, health professionals, and families express the

need for children to experience fun, humour, laughter, recreation, and leisure alongside treatment.[23,27,68,76,104,112,113]

Family relation concerns have been highlighted in 20 studies.[19,39-42,47,48,54,59,63,74,86,88,108,120-126] Young people value support from their families as it is a structure that helps them feel comfortable and secure. Concerns regarding lack of family support have also been reported; children report discomfort in having to deal with expressions of anger, shock and sorrow from their parents/caregivers, which engenders a sense of being a burden.[63,125,126] Young people are worried about their family carers/parents' emotions of fear, hopelessness, depression, and anxiety.[40-42,48,104,120]

Older children have raised concerns regarding receipt of information about their diagnosis directly from the right people, rather than by overhearing parents and physicians.[44,47,108,127] Some young people prefer to keep their diagnosis a secret from peers for fear of social stigma.[40,44,47,108] In three studies, adolescents have reported concerns relating to sexuality. These concerns include initiating and maintaining romantic relationships, painful sex, and fertility concerns after treatment.[47,98,108]

3.7.1 Existential/spiritual/religious (n=37;46%)

The concerns under this category include existential loss, existential vacuum, worry about death, not being at peace, uncertainty arising from inability to anticipate situations, a need to be remembered, hopes, and finding meaning in life in situations, especially when young people feel that their dreams and hopes for the future are being ruined due to terminal illness. [39,45,49,70,74,81,91,104,113,114,128,129] In one study, health professionals have noted that the "life goes on" ideology is important.[112] It is common for the young people, including three-year-olds, to end their narratives with concerns about impending death.[130] Young people and families have also expressed the construct of connection to

something larger than the self. These beliefs seem to help them build resilience.[64,101,104] The desire for religious prayers has been mentioned in several instances as a priority.[75,113] The young people have also reported a sense of spiritual growth in maturity and some are thankful for the "gift of life" and wish to protect others from similar experiences.[102,131]

3.8 Other concerns (n=39; 48%)

Besides physical, psychological, psychosocial, and spiritual/existential concerns, additional pressing problems have also been found; they include communication and information, decision making, and care provision concerns (see Table 3 for details).

Table 3: Other concerns outlined within the literature

Communication and information needs/concerns/problems (n=18)	Communication difficulties in children with neuro-disabilities and brain tumors.[19,51,72,79,92] Sensitivity and honesty in breaking bad news, general access to information and how it is delivered. [49,59,63,76,88,94,104,109,129,132,133] Preference for regulating the amount of information given and provision in child friendly formats.[59,134]
Decision making (n=9)	'The right to be heard and listened to', informed decision making.[45,59,94,112] Advance care planning, end of life care priorities.[44,45,75,109]
Care provision concerns (n=10)	Meaningful relationships with health care providers was found useful for coping and resilience.[63,70,88] Insufficient time with doctors' lack of initiatives to make treatment fun for paediatric palliative care patients were mentioned as unpleasant experiences of care.[53,59,109] Problems with transitioning care.[42,129,135,136]
Financial costs (n=2)	Carers giving up work to care of ill children and catastrophic financial expenditures.[72,108]

3.9 Sub-group analysis by age group and type of diagnosis

The differences in symptoms and concerns that matter to young people, with respect to age and type of diagnosis, are noted in this study; these are presented in Table 4. For example, treatment procedural pain and alienation are more dominant in younger children (0-5 years), while an existential loss, self-image, and need for access to information are more dominant in older children (6-9, 10-14, 15+) years.[137]

Table 4: Differences in symptoms and concerns that matter to young people, with respect to age and type of diagnosis

Age group / disease group	Themes
0-5 years	Profound procedural/treatment related pain concerns[77,120,138] Feeding138 Physical and emotional satisfaction88 Strange environments, alienation88 Play facilities and toys134 Spiritual concerns122
6-9 years	Shared feelings[81] Play facilities and toys[134] Limited reporting of feeling and emotion concerns[139] Concerns about being different[48] Connectedness to a super natural being, prayer[113] Information and communication through play[59]
10-14 years	Pain and fatigue[140,141] Having energy and not being sick make a good day[102] Self-image[120] Concerns about being different[48] fear of death[81] Guilt81 More psychosocial morbidity[79,81,140] Disclosure[49] Feelings and emotions more common[139] Teenage friendly facilities[134] Connectedness to a super natural being, prayer[113] Information and communication[59,134] Quality of interaction with care providers[49] Maintenance of childhood friends and involvement of peers[72]
15+ years	Pain and fatigue[140] Having energy and not being sick, make a good day[102] Self-image[120] Concerns about being different[48] Adolescent friendly facilities[49,134] More psychosocial morbidity[79,140-142] Feelings and emotions more common[139] Disclosure[49] Connectedness to a super natural being, prayer[113] Information and communication[134] Quality of interaction with care providers[49] Maintenance of childhood friends and involvement of peers[72]
Neuro-disabilities	Mobility, communication problems, cognitive deficits, toileting and safety[19,51,92]
HIV, epilepsy, sickle cell, end stage liver disease and renal failure	Non-disclosure/keeping diagnosis a secret[40,42,47,49,105]

Symptoms and concerns that have been identified for young people with LLC and their families are mapped in a summary diagram, alongside illustrative examples of useful health outcomes, in Figure 2.

Figure 2: A framework of domains on symptoms, concerns health outcomes in young people with life limiting and life-threatening illnesses

MAIN DOMAINS				
 **Physical**	 **Psychological**	 **Social**	 **Existential/Spiritual**	 **Quality of care and practical concerns**
Impecable identification assessment and management of symptoms and the associated distress .	**Identify and address child and family fears and concerns. Provide intervetions that enhance positive coping, reslinece and self efficacy**	**Provide support for relationship building and management. Provide avenues for children to engage in age. appropriate social activities across the socio-ecological layer . Provide teenage and adolscent friendly social services .**	**Assess spiritual wellbeing (consider meaning issues , relationships with supernatural power, beliefs and practices, outlook on self and death, look out for indicators of spiritual wellbeing) Refer child and family to their preferred spiritual care provider**	**Establish appropriate means of providing information and communication. Mainstreatm coordination with the care team. Avail useful information in appropriate formats. Provide care in preferred child/family environment Link child and family to social support services available**
THEMES				
▪ Physical symptoms ▪ Symptom distress ▪ Physical Function ▪ Treatment-related concerns ▪ Procedural-related pain ▪ Physical needs ▪ Normalcy	▪ Emotional positive and negative ▪ Behavioral ▪ Cognitive	▪ Relationships ▪ Perspective of others ▪ Social function ▪ Life values ▪ Sexuality*	▪ Worry about death ▪ Existential loss* ▪ Meaning of illness ▪ Connectedness ▪ Spiritual growth	▪ Communication and information* ▪ Decision-making* ▪ Care provision* ▪ Financial concerns* ▪ Care environment that is strange to home
Illustrative examples [**Were more dominant in 10-14,15-17 year age group; **More dominant in children of school-going age]*				
Physical symptoms: Pain, nausea, vomiting, fatigue **Symptom distress**: Suffering, wiped out, crying due to pain **Function**: Self-care, mobility, doing usual things, normalcy **Treatment related concerns**: Procedural/treatment associated pain, effects of opioids, fertility concerns after cancer treatment, treatment related pain, anxiety and worry	**Emotional**: Fear, worry, sadness, anxiety, happiness **Cognitive**: Declining in performance at school**, feeling stupid,orientation skills,reduced concentration lack of self-worth **Behaviour**: Aggression, adherence/ non-adherence **Self-image**: Impact of loss of hair, changes in skin, or facial lipodystrophy on self-image **Illness experience**: Hard; illness is tough	**Relationships**: Family, friends, community, others, teasing, bullying, stigma **Perspective of others**: Concerns about family, Being a burden to family **Activities of daily living**: School**, feel joy, feel happy, have fun, play, be with friends **Life values**: Equal opportunities like normal children*, achieve life goals*, live as normal **Sexuality**: Initiate and maintain sexual relationships **Perspective of others:** Wish to protect others from bad experiences being a burden to others	**Worry about death**: Worried about death, will I be remembered after death? am I dying? **Existential concerns:** Loss of future, threat to values, life devoid of meaning, suffering as educator **Meaning of illness**: Illness is tough, horrible experience, personal experience of discovering diagnosis **Connectedness**: Connection with God or something larger than self **spiritual growth:** Appreciate life as a gift, **Resilience and coping**: Keeping the Spirit alive must survive the hard bits of illness	**Information and communication**: Lack of access to information on disease and treatment, breaking bad news **Decision-making**: Advance care planning, shared decision-making **Care provision**: Availability of doctors, point of contact care provision, help with care transition, transitioning into adult care **Financial concerns**: Foregoing leisure, can't afford medication **Strange hospital environment:** Hospitalization is seen as imprisonment, missing home, longing for play during hospitalization to cope with strange environment

4 Discussion

Through the process of drawing together a comprehensive body of literature across global regions and different conditions, this paper identifies the symptoms and other concerns faced by young people with LLC and their families. Previous reviews have focused solely on cancer and neuro-disability.[18,19,143] This synthesis and presentation of symptoms and concerns across core health domains can be used to guide the development of outcome assessment measures for paediatric palliative care. While the studies are of intermediate methodological quality, it has been possible to extract data on what young people with LLC consider as important, to inform the development of the child/family centred conceptual framework. Studies in this review recruited patients at various stages of the disease trajectory, but multi-dimensional burdensome symptoms and concerns were found across studies. This finding informs debate around the appropriate timing of referral to, and the initiation of, paediatric palliative care (i.e. soon after diagnosis vs. later in the disease trajectory and towards the end of life). The key message is that, for optimal outcomes, paediatric palliative care should be provided from the time of diagnosis and through to death and bereavement, as is recommended by the World Health Assembly.[35] This approach would align with recent evidence demonstrating the benefits of providing early integrated palliative care in adult populations.[144]

The themes concerning symptoms and concerns identified in this review are multidimensional and can be aligned to three domains; child (i.e. Physical, Psychological, Existential/Spiritual), carer / family (i.e. social) and quality of services (Quality of care and practical concerns). Incorporating these three domains into outcome assessment has been previously proposed when evaluating models of palliative care. .[145] Given the task at hand - that of meeting such multi-dimensional concerns - paediatric palliative care models of care may benefit from key elements that have been proposed for person-centred care, which include respect, coordination and integration, physical comfort and emotional support, involvement and support for carers/family, information and education, continuity, and transition.[146] Person-centred care also proposes key activities such as personalised care, self-

management support, and shared decision making.[147] This ethos embraces the core child/family concerns that have been identified in this review. The review findings also demonstrate the intrinsic link between child and carer/family, and care provider interactions, as reflected under the quality of services domain. Positive engagement through information, education, and communication has the potential to enhance child/carer/family self-efficacy and self-management, which can have an impact on outcomes of care. Positive provider interactions may explain the way system process related concerns link to the optimal goals of care and the reasons for their importance. An important consideration for development of services for young people with LLC is the development indicators that can be used to assess the structure, process, and outcomes aspects of health services. This review makes an important contribution by putting forward an evidence-based child/family framework of domains, from which such indicators could be selected. This makes it easier for care providers to gather more information about the relevant domains some of the constructs and symptoms to facilitate prompt action.

The information and communication theme identified in this review warrants further exploration in young people with LLC. Young people are a unique population with varying symptoms and concerns which occur alongside continuing physical, emotional and cognitive development, and a dynamic socio-ecological environment.[33] Indeed, several studies have highlighted the uniqueness of the language that children use to describe their symptoms and concerns.[18,107] Furthermore, paediatric palliative care patients may also have reduced communication and cognitive abilities.[15] This review highlights the ability of young people (6+ years) to self-report on symptoms and health outcomes. As such, young people should be central to and involved in the elicitation of preferences and development of outcome measures. Such an approach should be aligned with simultaneous investment in appropriate information and communication tools and strategies. It is time to prioritise the provision of self/proxy reporting options for outcome measures in paediatric palliative care to make self-report a preferred option for subjective outcomes, whenever possible.[34,148,149]

This review identifies differences in the way health concerns, such as social and psychological well-being, are expressed based on developmental age. With age, the cognitive, emotional, and socio-ecological aspects of children undergo change. For example, an advanced understanding of illness emerges in adolescents[150] alongside a shift towards a preference for self-efficacy and shared decision-making models.[94] Although the core domains of health remain robust across adult and paediatric populations, the developmental age of young people needs to be considered. Differences across cognitive, emotional and socio-ecological facets render the use of adult-based measures inappropriate, even with adolescents.[148]

It is observed that young people have not been interviewed in 30% of the studies, and 35% are mixed samples of young people and proxies, suggesting a low level of involvement of young people in the research that aims to inform the direction of their care. The findings echo previous reports about children with cancer.[25] Involving young people in research that informs their care is the first step to allowing their experiences to update the models of care; this is far from commonplace across the literature. In order to guide best practices on research involving young people, methodological concerns regarding the following need to be addressed: the use of age-appropriate methods of data collection; question wording; duration of interviews; processes of data collection; the manner in which challenging issues of interviewing ill children are dealt with; provision of sufficient details on recruitment strategies, and; informed consent processes.[12,33]

The review observes considerable overlap across themes related to the subjective experiences of illness across diagnostic groups, study locations, and age groups of children. For example, there are parallels in themes identified across previous reports in paediatric cancer,[18,143] paediatric HIV,[151] and paediatric neuro-disability.[19] Furthermore, similar indicators have been found that are useful for comparing models of care across different settings.[146] This enhances the feasibility of multi-setting comparisons.[152] It also lends credibility to the use of generic palliative care outcome measures in children with LLC, with minor adaptations wherever necessary, for aspects such as health status, the

process of care, or socio-cultural concerns.[153] There are over 300 LLC conditions experienced by young people that may require palliative care; the development of disease-specific outcome measures across all conditions may not be appropriate or feasible, moreover users want fewer tools.[154 155,156] Overlap in the conceptualisation of health outcomes in paediatric palliative care can support the growth of the research field.[148]

5 Strengths and limitations

To reduce bias, the review adopted a broad and comprehensive search strategy across multiple databases, did not limit article inclusion by language, and involved field experts to identify any additional relevant literature. The search has been conducted following PRISMA guidelines. The quality of studies was also assessed, although not used as a basis for article exclusion. This is the first review to comprehensively appraise the state of evidence on symptoms and concerns in young people with a broad range of life-limiting and life-threatening conditions, across the disease trajectory. This is also the most comprehensive framework of meaningful outcomes for young people with LLC.

This review has some limitations. Data from a disparate evidence base has been compiled, which utilises a wide range of methods to understand the symptoms and concerns of young people. The variety of approaches meant that it was not possible to assess the extent or magnitude of identified symptoms and concerns among study participants. The inclusion of studies, with both qualitative and quantitative approaches, led the team to adopt narrative methods of synthesis, with efforts made to be transparent about how this was undertaken. Furthermore, some studies did not report the recruitment strategies and as such potential bias could not be assessed, compromising our judgement regarding the methodological quality of the studies included.[157] Many conditions require palliative care and different terminologies are used in different settings and consequently relevant articles may not have been identified.[154]

6 Implications for research and practice

There is a high burden of interacting and multidimensional symptoms and concerns in paediatric palliative care populations. These occur across the disease trajectory, in both malignant and non-malignant conditions. Therefore, early integration of paediatric palliative care into care plans to address these issues is recommended.

A skilled multi-professional team will be needed to address the symptoms and concerns raised, given they are so wide-ranging. This study challenges the unidimensional or typical biomedical models of care for children with LLC, which fail to comprehensively address their multi-dimensional symptoms and concerns. This child/family centred framework of child/family domains, grounded in their illness, mirrors the structure, process, and outcomes domains of health service improvement, and can guide the development of appropriate outcome measures to assess existing services and support their development.[15] The measures will inform service audits, research, and evaluations to stimulate service development. Developmental age will be important to consider when developing paediatric palliative care outcome measures, with differences across young people identified across the emotional, cognitive, and socio-ecological levels in this review. The developmental age categorizations that have been used to explore these variations in this review were broad and future studies should explore this further, using narrower categories or those that have been recommended for paediatric palliative care.[150] Our findings indicate commonality in the illness experience, suggesting that unified person-centred outcome measures for children across different diseases are feasible. It is instead developmental age which may determine variations in the domains (content) and form of a measure.[158]

Internationally, the state of science remains poor for aspects of care for young people with LLC, including spiritual/existential concerns, patient-reported experiences of care, service delivery, decision-making information, and approaches to communication.[143] Future studies should further explore these areas, alongside addressing gaps in evidence on symptoms and concerns for young

people with LLC with non-malignant conditions, those in developing countries and those from different social-cultural settings.

7 Conclusion

Burdensome symptoms and concerns affect young people with malignant and non-malignant conditions and occur across the disease trajectory, so paediatric palliative care should not be limited to the end of life phase. A child-family centred framework of health outcomes, spanning the patient, family, and quality of service levels is proposed to inform service development. Future research should address gaps identified; the involvement of the young people in research, evidence for developing countries, and for non-malignant conditions.

Data Availability Statement

The data extraction table used to compile all details from included studies accompanies this article as a supplementary file. EndNote files used for compiling articles during searching and reviewing can be requested from the corresponding author with a reasonable request outlining intention for their use.

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Contributors' Statements

Eve Namisango conceptualised and designed the study, reviewed literature, abstracted and analysed the data, and drafted the initial manuscript.

Professor Richard Harding, Professor Fliss Murtagh, and Dr Katherine Bristowe reviewed the protocol, data abstraction tools, data analysis framework, and the results.

Professor Irene Higginson and Dr Melanie Abas reviewed the research questions, search strategy, and review findings.

Dr Matthew Allsop reviewed the protocol, abstracted data, and carried out data analysis in association with the lead reviewer.

Professor Julia Downing reviewed the analysis framework and appraised the interpretation of the review findings.

All authors have contributed to the final manuscript.

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Table 2: Characteristics of studies included in the review (N=81)

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
Qualitative research design										
Allard et al (2014), UK	To identify key health outcomes, beyond morbidity and mortality, regarded as important in children and young people with neuro-disability, and their parents	i) Children with neuro-disability and parents of children with neuro-disability. ii) Participants were identified through the Council for disabled children. The children and parents were recruited separately.	Range 8-25 years	Neuro-disability	Qualitative Content analysis	Purposive	54 Children and young people with neuro-disability and parents of children with neuro disability.	i) Structured interviews and focus group discussions. Used talking mat board to help young people with communication problems express their views ii) Children were interviewed separately except in two instances iv) Not stated	Community	35:B3
Avoine-Blondin et al (2017), Canada	Describe domains of quality of life in the context of pediatric palliative care in oncology according to perceptions of professional caregivers	i) Health professionals who had been active in the hematology/oncology department, have cared for at least one child with advanced cancer and treated in palliative care. ii) Selected from a comprehensive list of the members of the department	Child defined as less than 18 years	Cancer	Qualitative Thematic analysis	Maximum variation sampling strategy	20 health professionals	i) Individual semi-structured Interviews ii) Not applicable iii) Interviews recorded	Hospital	32:B3
Barrera et al (2005), Canada	To investigate health-related quality of life in children eligible for Phase 1 trials and why families consider participating in these trials	i) Children with recurrent disease treated in the hematology /oncology unit of a large eligible for phase 1 trial. ii) Identified from the oncology unit in the hospital	Range 7 -15 years	Cancer	Qualitative Not stated	Not stated	9 children and 9 parents	i) Semi structured long interviews ii) It's not stated if children were interviewed separately ii) Interviews were recorded	Hospital and home	31:C1

[1] Hawker et al, 2002 quality score

[2] National Service Frameworks level of evidence grading (UK Department of Health, 2001)

Authors (year), country	**Study aim as reported**	**i) Population ii) Recruitment**	**Age of child**	**Primary Diagnosis as reported**	**Research design Methodology**	**Sampling approach**	**Participants**	**i) Data collection method ii) Presence/absence of parents at interview iii) Recording**	**setting**	**Quality score [1]/level of evidence[2]**
Bjork et al (2006), Sweden	To describe children's needs as expressed by their behaviour, body language and verbal expression through observation	i) Children newly diagnosed with cancer initiated in care within one month of diagnosis and family spoke Swedish. ii) Identified through the hospital clinic	Range --7 months – 6.5 years	Cancer	Qualitative, longitudinal, observational narratives Manifest content analysis and latent content analysis	Purposive	12 children	i) Non- structured observations using a mobile positioning method. ii) Children had least one parent present during the observation. Some had a grandparent and sibling present. iii) Field notes were recorded after each observation	Hospital ward	36:C1
Cataudella et al (2012), Canada	To explore the psychological experiences of children with brain tumours at the end of life	i) Bereaved parents of children diagnosed at less than 18 years of age with a brain tumour, and who died between 2 and 12 years prior to the study. ii) Identified through a patient registry. Health workers contacted eligible potential participants via email	Range 1-19 years	Brain tumours	Qualitative, retrospective study nested in a larger qualitative study Thematic analysis	Purposive	24 bereaved parents	i) Focus group discussions ii) N/A no children involved iii) Not stated	Hospital outpatient	31:C1
Darcy et al (2014), Sweden	Explore young children's and their parent's perceptions of how cancer affects the child's health and everyday life shortly after diagnosis	i) Children were aged 1-6 years when receiving a cancer diagnosis and the family could communicate in Swedish. (3-9 weeks after diagnosis). ii) Approached by study nurses who provided information about the study	Range 1-5 years	Cancer	Qualitative, longitudinal study Inductive approach	Purposive	13 children and 23 Parents	i) Semi-structured interviews Child interviews were child led and involved playing with toys, sessions and use of smiley faces. ii) Parents were present during child interview sessions. iii) Interviews were recorded	Home and hospital	34:B3
de Aquino et al (2014), Brazil	Construction of meaning about illness and death in the narratives of children with cancer at different stages of cancer treatment	i) Children were undergoing treatment Children (had been less than one month to 2 years of treatment. ii) Identified from the outpatient clinic	Range 7-9 years	Cancer	Qualitative Narrative and thematic analysis	Purposive	6 children	i) Play sessions with each child. ii) Parents were allowed in the observation room iii) Sessions were recorded.	Outpatient	29:C1

Authors (year), country	**Study aim as reported**	**i) Population ii) Recruitment**	**Age of child**	**Primary Diagnosis as reported**	**Research design Methodology**	**Sampling approach**	**Participants**	**i) Data collection method ii) Presence/absence of parents at interview iii) Recording**	**setting**	**Quality score [1]/level of evidence[2]**
Einberg et al (2015), Sweden	Describe perceptions of friendship from the perspective of children undergoing cancer treatment	i) Children with experience of cancer treatment (undergoing or have undergone treatment for cancer). ii) Selected by nurses using inclusion criteria.	Range 8 -12 years	Cancer	Qualitative Inductive approach	Purposive	15 children	i) Focus group discussion including icebreaking sessions, theme and concluding phases ii) Not stated iii) Not stated	Hospital	33:B3
Enskar K et al (1997), Sweden	To identify children's experiences of problems related to their cancer and the disease –effect on the child's life situations.	i) Children with cancer and on treatment with their parents. ii) Identified by facility staff.	Range 6.5 - 12.5 years	Cancer	Qualitative Comparative thematic analysis	Purposive	5 children and 5 parents	i) Semi-structured interviews Children begun with drawing a picture of a situation they had experienced in hospital and explaining it. ii) Parents and children were interviewed separately. iii) Not stated	Hospital and home	29: C1
Evan et al (2012), USA	Determine what is quality of life from the perspective of paediatric patients with advanced disease	i) Parents and their children, years, with physician-determined life-limiting conditions (having a, 20% chance of survival beyond3 years.) ii) Participants were identified through referrals	Range 9-21 years	Advanced Cancer Advanced heart disease	Qualitative secondary analysis Grounded theory approach	Purposive	29 children	i) Semi-structured interviews ii) Children interviewed without their parents. iii) Interviews videotaped and audiotaped	Hospital, In-home children's hospice	34:B3
Fraser DF (2003), New Zealand	How children's peer relationships and friendship appear to be affected by cancer	i) Primary school age children with cancer undergoing treatment. Their parents and siblings. ii) Not stated	Range 4-15 years	Cancer	Qualitative Not stated	Purposive	12 families (children Parents Siblings)	i) In-depth interviews ii) Not stated iii) Not stated	Family home	22:C1
Forrester et al (2015), Jamaica	To explore the lived experiences of adolescents aged 18_19 years with Sicke-cell disease	i) Adolescents with Sicke-cell disease who were knowledgeable about the phenomenon; diagnosed over 10 years ago. ii) Identified by triage nurse at the clinic	Range 18-19 years	Sickle cell	Qualitative Inductive and interpretive	Purposive	6 adolescents	i) In-depth interviews ii) Not stated iii) All interviews were audiotaped	Outpatient	33:C1

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
Griffiths et al (2011), Australia	To explore the experiences of children with a recent diagnosis of cancer	i) English speaking children diagnosed with cancer and were receiving care from the study hospital. ii) Identified from hospital cancer unit Clinical staff sent out letters to families that met the inclusion criteria.	Range 8-16 years	Cancer	Qualitative, longitudinal design Phenomenological approach and idiographic analysis	Not stated	9 families (child responses only reported)	i) Structured interviews at two time points ii) Not stated iii) Interviews were digital recorded	Home and hospital	32:C1
Hendricks-Ferguson (2008), USA	To identify symptoms of greatest parental concern on the last day and during the last week of their children's lives, the five most common symptoms of parental concern, and symptom-management strategies used during the last week of the children's lives.	i) English-speaking bereaved parents whose children had died 6–36 months prior to the study, and had received care by the hospice program during the last week of life, and were present with the child during the last week of the life Had telephone access. ii) Contacted by post to brief them about the study, those interested were recruited.	Range 1 week – 19 years	Cancer Renal disease Congenital heart defects Congenital syndrome Cystic syndrome	Qualitative, descriptive, exploratory, and retrospective The Krippendorff method for semantical content analysis	Convenience	28 bereaved parents	i) Semi-structured interviews ii) N/A- no children iii) Interviews audio-taped	Tele-based	31:C1
Hedstrom et al (2003), Sweden	What aspects of disease and treatment are perceived as especially distressing for children with cancer?	i) Swedish-speaking Children/adolescents aged 8-19 years, diagnosed with a malignancy at least 1 month before potential inclusion, and spent enough time at the ward at the time of data collection. Parents of children less than 8 years. Respective nurses for the children. ii) Eligible participants received an information sheet from the hospital one week to the hospital visit,	Range 0 - 19 years	Cancer	Qualitative descriptive design nested in a larger study Content analysis	Not stated but referenced	50 children and adolescents, their parents, and 118 nurses	i) Semi-structured interviews using one question ii) Not stated iii) Interviews were audio-taped	Inpatient	37:B3

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
		recruited during hospitalisation.								
Hinds et al (2004), USA	To solicit quality of life perspectives of children and adolescents receiving cancer treatment	i) English-speaking Paediatric oncology patients, mainly on late phase of treatment. ii) Not stated.	Range 8-18 years	Cancer	Qualitative, cross sectional and longitudinal Comparative semantic content analysis	Referenced	i) Phase 1: 23 children and adolescent (8-15 years) ii) Phase 2: 13 children adolescents (10-18 years)	i) Interviews ii)Not stated iii) Not stated	Outpatient and Inpatient	33:B3
Hsioa et al (2007), USA	To identify the aspects of physician communication that children with life-limiting illnesses and their parents perceived to be facilitative or obstructive in paediatric palliative care	i) English children with physician-determined life-limiting conditions and a 20% chance of survival beyond 3 years and their respective parents ii) Identified from referrals by health providers	Range 7-22 years	Oncology Cardiology	Qualitative Grounded theory and content analysis	Consecutive	20 parent-child dyads	i) Semi-structured interviews ii) Not stated iii) Interviews audiotaped and video taped	Hospital, In home children's hospice	34:B3
Ito et al (2015), Japan	To explore the characteristics of a good death for children with cancer	i) Japanese-speaking children 18 years of age or older, diagnosed with cancer at age 15 or younger, at 5 years post 5 cancer treatment Bereaved parents who had lost a child ≤ 16 years to cancer in the previous 6 months and Survivors ii) Identified through medical records. Survivors were recruited through outpatient clinics	Median age 23.5 years	Cancer	Qualitative Content analysis	consecutive	10 paediatric cancer survivors, 10 bereaved family members and 20 medical professionals	i) In-depth and semi-structured interviews ii) Not stated iii) Interviews audiotaped	Hospital	29: C1
Kamper R and Savedra (2010), USA	To describe the responses of children with advanced cancer	i) English or Spanish speaking Children with advanced cancer. (leukaemia, nonresponsive	Range 6 - 17 years	Cancer	Qualitative multi-centre longitudinal study	Not stated but referenced	60 children	i) Semi-structured interviews using the Spiritual Quality of Life (SQL) questionnaire	Hospital, clinic and home	31:B3

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
	to a spiritual quality of life (SQL) interview.	to treatment or relapsed, or Stage IV solid tumour that had recurred or progressed Potential participants were ii) Identified by facility staff			Content analysis			conducted every two to five weeks ii) Parents allowed to present but children's responses were taken. iii) Not stated		
Lan et al (2015), Malaysia	To gather parents' experiences in the end of life (EOL) care of their children, and gather their parents' views, needs and concerns of the level of support given to them.	i) Bereaved parents of children <18 years who died of life limiting and life threatening conditions in the previous two years. ii) Information leaflets were provided to eligible participants and those interested were recruited.	Range 3-10 years	Life limiting and life threatening conditions	Qualitative Not stated	Purposive	11 bereaved parents	i) Focus group discussions and in-depth interviews. ii) N/A no children iii) Not stated	Not stated	29:C1
Ljungman et al (1999), Sweden	Evaluate care, support and information given to children and parents	i) Children were previously admitted to the study hospital ward and were 1 month after diagnosis to 3 months post-treatment. ii) Recruited through clinic	Range 0-19.2 years	Cancer	Qualitative Multi-centre descriptive	Not clear	55 children and 54 parents	i) Semi-structured interviews ii) Children under 10 were interviewed concurrently with their parents. Those above 10 were interviewed independently iii) Not stated	Inpatient	27:C1
McCleary - Sills et al (2013), Uganda and South Africa	determine the psychosocial needs of children with HIV	i) HIV positive children and their family care givers /staff providing care to HIV positive children. ii) Identified and recruited by facility staff	Range 15-18 years	HIV/AIDS	Qualitative Thematic analysis	Purposive	49 children, 39 carers and 22 service staff	i) Focus group discussions In-depth Interviews ii) Not stated iii) Not stated	Outpatient	29:C1
Momani et al (2015), USA	To describe health-related quality of life (HRQOL) reported by children and adolescents in responses to two	i) English-speaking children aged 8-18 years enrolled in an ongoing study. ii) Details on how patients were recruited are referenced as this was part of a bigger study	Range 8-18 years	Cancer	Qualitative, longitudinal Content analysis	Not stated but referenced	150 children and adolescents	i) Interviews ii) It's not stated of children were interviewed with or without their parents/carers iii) Not stated	Not stated	29: B3

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
	interview questions during treatment for acute lymphoblastic leukaemia (ALL) and compare their responses by age, gender, risk group, and time in treatment through a quantitative content analysis approach.									
Montonya-Juarez et al (2013), Spain	1)To determine the elements parents identify as suffering in their hospitalised children, 2)To establish observational indicators for the detection and the interpretation of suffering in children necessary for the evaluation and the personalised intervention from the professionals	i) Parents of hospitalised children with an advanced and/or terminal illness. ii) Recruited from paediatric units at a hospital	Range 0-16 years	Stated as terminal illness	Qualitative Content analysis	Purposive	13 parents	i)Semi structured interviews ii) N/A –no children iii) Interviews were digital recorded	Inpatient	31:C1
Nicholas et al (2011), Canada	To understand how children and adolescents perceive and manage end stage renal disease	i) Children under going ESRD treatment. ii) Identified through a facility health care provider	Range 7-18 years	End-stage renal disease	Qualitative Ethnographic approach and content analysis	Not clear	25 children and adolescents	i) Interviews ii) It's not stated of children were interviewed with or without their parents/carers iii) Interviews audiotaped	Hospital and home	28:C1

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
Pritchard et al (2008), USA	To identify the cancer-related symptoms that most concerned parents during the last days of their child's life and the strategies parents identified as helpful with their child's care.	i) English speaking Bereaved parents of children who had died a cancer-related death within the previous 6 to 10 months prior to the survey. ii) Participants were identified through the hospital	Range 0-21 years	Cancer	Qualitative Content analysis	Not stated	65 bereaved parents	i) Interviews ii) N/A –no children iii) Not stated	Tele-based	28:C1
Punpanich et al (2008), Thailand	To develop an understanding of the current psychosocial needs, experiences, and perceptions of their current life situations among HIV infected children and their caregivers	i) Children living with HIV/AIDS receiving care from the hospital in which the study was conducted. ii) Recruited through their care providers	Range 8-16 years	HIV/AIDS	Qualitative Thematic analysis	Not stated	34 children and 35 family caregivers	i) Interviews were conducted using ii) Not stated parents/carers iii) Interviews were tape recorded	Hospital	24:C1
Ronen et al (1999), Canada	establish the different elements of HRQOL in childhood epilepsy	i) Children with epilepsy, defined as recurrent, unprovoked seizures, within preceding 24 months. ii) Participants who met the inclusion criteria were invited a letter to participate in the study	Range 6 years - 12 years 11 months	Epilepsy	Qualitative Textual analysis	Stratified purposeful sampling	29 children and 42 parents	i) Focus group discussions Involved use of drawing of maps of important places in the daily life of the child and paly dough to trigger discussions and dialogue. ii) Children interviewed separately iii) Interviews and focus group discussions were audiotaped	Outpatient	36:B3
Ronen et al (2001), Canada	To develop a child-centred qualitative research methodology to facilitate direct exploration of health-related	i)Children with active epilepsy ii) Through hospital care centre	Range 6-12 years	Epilepsy	Qualitative Textual analysis of the raw data, utilizing ethnography	Purposeful stratified sampling	29 children and their parents	i) Focus group discussion Groups Drawing environmental maps and using playdough ii) Not stated iii) Not stated	Outpatient	33:B1

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
	quality of life (HRQL) issues To identify the quality of life elements in pre-adolescent children with a chronic medical condition.									
Ruhe et al (2015), Switzerland	To explore patient's perspective in paediatric oncology on participation in discussions and decision making surrounding their cancer diagnosis	i) Children receiving cancer treatment in cancer care centres. Interviews conducted three weeks after diagnosis. ii) Recruitment was done by physicians based on willingness to participate.	Range 9-17 years	Cancer	Qualitative Thematic analysis	Purposive	17 children	i) Semi-structured interviews ii) Not stated iii) Interviews were audio-taped	Hospital and home	30:C1
Soanes et al (2009), UK	To map needs of children with brain tumour and their parents from diagnosis to end of treatment	i) Children commencing treatment for brain or spinal cord tumour ii) Identified through the cancer clinic	Range 4-16 years	Brain tumours	Qualitative, longitudinal exploratory and descriptive case study Thematic analysis framework, indexing and charting, mapping and interpretation	Convenience	18 parents and 10 children	i) A modified Mosaic Approach for children 4–6 years; plus use of photography The 'draw and write technique' with children aged 6–12 year olds, children Semi-structured interviews ii) Not stated iii) No mention of interview recording	Hospital and home	34:C1
Stegenga (2009), USA	To explore the lived experience of receiving the diagnosis of cancer from the perspective of the adolescent	i) English-speaking children diagnosed within 4 to 6 months ii) Identified by health professionals	Range 13-17 years	Cancer	Qualitative Phenomenological	Purposive	10 children	i) Semi-structured interviews – ii) Not stated iii) Interviews were audiotaped	Not stated	29:C1
Taylor et al (2010), UK	To explore, in their own words, young people's lived experience	i) Young people who had received organ transplants for chronic liver disease, acute liver failure, and metabolic liver disease.	Range 12-18 years	Chronic, acute, and metabolic liver diseases	Qualitative Framework analysis	Purposive	14 young people	i) Semi-structured interviews ii) Not stated iii) Interviews were tape recorded	Hospital, outpatient and home	29:C1

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
	of life after transplantation	ii) Recruited from tertiary liver care centre								
Weaver et al (2015), USA	To identify meaningful symptoms to shape the paediatric PRO-OCTAE instrument's accuracy , development applicability and terminology	i) English-speaking children and adolescents with cancer between the ages of 7 and 20 years undergoing chemotherapy. ii) Identified through chart reviews and referrals from primary teams	Range 7-20 years	Cancer	Qualitative Phrase semantics	Purposive	96 children	i) Interviews Interviews ii) Children were interviewed without parents iii) Interviews were tape recorded	Hospital	37:B3
Weaver et al (2015), USA	To investigate medical decision-making preferences of adolescent oncology patients and the parental and clinician behaviours that adolescents report to be supportive of their preferred level of decision-making involvement	i) English-speaking children diagnosed with cancer or a with relapse in the prior 6 months ii) Participants were identified through facility medical records and referrals from clinic services	Range 12-18 years	Cancer	Qualitative Content analysis	Purposive	40 children	i) Interviews using ii) Children and adolescents were interviewed alone 57% of the time and with parents for 43% of the time iii) Interviews were video recorded	Hospital	30:B3
Wise (2002), South Africa	What is the lived experience of paediatric recipients Undergoing liver transplantation?	i) English-speaking children who were one year post-liver transplantation ii) Participants approached through the hospital	Range 7 -15 years	End stage Liver disease	Qualitative Interpretive phenomenological approach	Purposive	9 children	i) In-depth interviews. ii) Not stated iii) Not stated	Hospital and home	21:C1

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
Woodgate et al (2014), Canada	To Provide a deeper understanding of the existential challenges faced by children living with cancer	i) English-speaking Children undergoing treatment for cancer, and were 3 months post cancer diagnosis. ii) For recruitment, participants were approached by a designated intermediary.	Range 8-17 years	Cancer	Qualitative Interpretive and descriptive approach	Purposive	13 children	i) Children kept a log of their feeling states associated with cancer via a computer diary. The computer diary had a drawing tool to help children express existential challenges. Interviews. ii) Not stated iii) Interviews digitally recorded	Home and inpatient	38: C1
Woodgate (2008), Canada	Description of children's and adolescents' perspectives about their cancer symptoms	i) English-speaking children and adolescents with a history of cancer, at least 3 months post cancer diagnosis ii) Recruited from outpatient cancer unit and were approached by a designated nurse	Range 9-17 years	Cancer	Qualitative Interpretive, descriptive constant comparative method	Theoretical purposive sampling	13 children	i) Interviews using author developed Verbal and non-verbal behaviour was also documented and analysed ii) Not stated iii) Interviews were tape recorded	Home	34:C1
Woodgate (2005), Canada	To understand how adolescents see themselves through the cancer trajectory	i) Adolescents who had received chemotherapy participants were recruited from inpatient and outpatient units of the care centre ii) Participants were approached by a designated intermediary.	Range 12 to 18 years	Cancer	Qualitative-longitudinal nested study Interpretive interactionism	Purposive	15 adolescents	i) Individual and group interviews Observation of non-verbal behaviour ii) Not stated iii) Interviews were audiotaped	Inpatient and outpatient	35: B3
Woodgate et al (2003), Canada	To explore and describe the childhood cancer symptom course from the perspectives of children and their families	i) Children receiving chemotherapy alone or combination with surgery, radiation or bone marrow transplant. Captures diagnosis, treatment and illness phases. ii) Recruited by designated facility using the study criteria	Range 4.5-18 years	Cancer	Qualitative and longitudinal Constant comparative method of analysis	Purposive	39 children, their parents and siblings	i) Semi-structured interviews Participant observation for verbal and non-verbal behaviour Focus group interviews Reflexive journal ii) Not stated iii) Interviews were audiotaped	Homes, inpatient and outpatient	37:B3

Authors (year), country	**Study aim as reported**	**i) Population ii) Recruitment**	**Age of child**	**Primary Diagnosis as reported**	**Research design Methodology**	**Sampling approach**	**Participants**	**i) Data collection method ii) Presence/absence of parents at interview iii) Recording**	**setting**	**Quality score [1]/level of evidence[2]**
Woodgate et al (2003), Canada	To discover meaningful descriptions and interpretations of families' experiences with childhood cancer	i) Children receiving chemotherapy alone or combination with surgery, radiation or bone marrow transplant. Captures diagnosis, treatment and illness phases ii) Participants were identified through affiliated clinics	Range 4.5-18 years	Cancer	Qualitative and longitudinal Interpretive interaction constant comparative method of analysis	Purposive	39 children, their parents and siblings	i) Interviews Participant observation for verbal and non-verbal behaviour ii) Not stated iii) Interviews were audiotaped	Inpatient and outpatient	37:B3
Zelecer et al (2010), Canada	To explore the end-of-life experience of children with brain tumours and their families.	i) Bereaved parents of children who died of a brain tumour while under the care of the Children's Hospital, in the previous ten years prior to the study. iii) Identified by facility health workers	Range 1-19 years	Brain tumours	Qualitative Thematic analysis	Not stated	25 bereaved parents	i) Focus groups discussions ii) It's not stated of children were interviewed with or without their parents/carers iii) Interviews were audiotaped and video taped	Away from hospital setting	30:C1
Mixed methods research design										
Donnelly et al (2005), USA	To develop an empirically based conceptual model of the needs of children with life-limiting conditions	i) Professionals with expertise in paediatric palliative care and hospice ii) Identified through a professional body and colleagues	Not applicable	Life limiting conditions	Mixed methods Multi-dimensional scaling and cluster analysis	Purposive snowball	Experts (nurses, social workers, physicians) Stage 1 *n*=50 Stage 2 *n*=32	i) Concept mapping methodology Stage 1:Web based brain storming Stage 2:Sorting and rating the needs statements ii) Not applicable iii) Not applicable	Not reported	35:B3
Enskar et al (1996), Sweden	To document the physical, psychological, social, and existential problems; symptoms and inconvenience caused by the disease, and treatment or hospitalization perceived by Swedish health care personnel to be the most	i) Health care professionals ii) Selected from a list of staff from 4 oncology centres	Not applicable	Cancer	Mixed methods Delphi technique with three inquiries, alongside content analysis and ranking	Random	**First inquiry** 24 health care personnel **Second inquiry** 18 health workers **Third inquiry** 22 health care workers	i) The Delphi technique ii) Not applicable iii) Not applicable	Clinic	33:B3

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
	troublesome for children with cancer and their families.									
Freeman et al (2003), USA	To identify commonly reported problems and helpful resources important to children with brain or spinal cord tumours and siblings during phases of illness.	i) Affected children and siblings whose diagnosis occurred within the prior 10 years and the family had received care or lived in the north-eastern region of the United States. ii) Identified through facility staff, local advocacy and support groups, community resource organisations, newsletters, websites, and list servers	Range 9 -23 years	Cancer specifically Brain tumours	Mixed methods Thematic and descriptive analysis	Not stated	40 affected children and siblings	i) Focus group discussions ii) Not stated iii) Not stated	Not stated	36:C1
Jones et al (2006), USA	To Identify the social work perception of the psychosocial needs of dying children and adolescents needs of children and their families	i) Paediatric oncology social workers, 80% practiced in hospital settings. ii) Recruited from regions of the Association of paediatric oncology social workers	Range 0-14 years Range 15-21 years	Cancer	Mixed methods Exploratory (qualitative and quantitative)	Snow ball	131 social workers	i) Literature review Focus group discussions with paediatric oncology social workers and further review by content experts. ii) Not applicable iii) Not applicable	Not stated for focus group discussions Survey was mail-based	32:B3
Heath et al (2010), Australia	To examine the symptoms, level of suffering and care of Australian children with cancer at the end of life	i) Bereaved parents whose children died of cancer at least one year prior to the study. ii) Participants identified thorough primary health care providers and family social workers	Mean age at death 6.7 years	Cancer	Mixed methods Cross–sectional	Not stated	96 bereaved families	i) Semi-structured interviews and self-completed questionnaires ii) Not applicable iii) Not applicable	Hospital and outpatient	29:C1
Ho Cheung et al (2010), Hong Kong	To examine the impact of cancer on physical, emotional, and psychosocial well-being of Hong Kong Chinese children	i) Chinese or Cantonese speaking Children diagnosed with cancer within the previous 6 months and undergoing active treatment admitted for treatment of cancer.	Range 7 -15 years	Cancer	Mixed methods cross-sectional Content analysis	Not stated	98 children	i) Semi-structured interviews ii) Children separately iii) Interviews were audiotaped	Inpatient	32:B3

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
		ii) Recruited through the hospital inpatient unit								
Khadra et al (2015), Canada	To develop a scale to measure suffering in North American adolescents diagnosed with cancer.	i) French-speaking adolescents had been diagnosed with cancer; had previously completed four to six weeks of cancer therapy (to have experienced treatment and related side effects); were aware of their illness, treatment plan and side effects ii) Recruited from hospital clinics	Range 12-19 years	Cancer	Mixed methods Methodological design for instrument development and content analysis	convenience for adolescents purposive sampling for health professionals	19 adolescents and 16 health care profession	i) Semi-structured interviews ii) Not stated iii) Not stated	Hospital	33:B3
Morris et al (2015), UK	To seek a shared vision between families and clinicians regarding key aspects of health as outcomes, beyond mortality and morbidity, for children with neurodisability, and (ii) to appraise which multidimensional patient reported outcome measures (PROMs) could be used to assess salient health domains.	i) Health professions, young people and parent carers being in a nominal group ii) Not stated	Not stated	Neuro-disability	Mixed methods Q sorting	Purposive	3 young patients, 5 parents/carers, and 7 health professionals	i) Q-sorting of a list of health outcomes for paediatric neuro-disability ii) Not stated iii) Not stated	Not stated	29 : C1
Oberholzer et al (2011), South Africa	To identify the needs of children in a haematology-oncology unit and to identify and prioritise resources that could be mobilised	i) Children previously treated for an oncology or haematological disorder in a private hospital. (must have received the treatment before the age of 13) Admitted to the hospital during the previous six	Range 6-14 years	Cancer	Mixed methods Explorative, descriptive and contextual design Q-sort scaling method	Purposive	26 children	i) Literature review Child ranking of items for importance using the Q – sort method (pictorial cards). ii) Children interviewed separately iii) Not stated	Outside hospital	32:B3

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
	in order to meet the needs of these children.	months before the study for active or follow-up procedures. Children with brain tumours were excluded. ii) Register children contacted through facility staff								
Petersen et al (2005), UK	Develop , test and implement European instruments for the assessment of HRQOL of children and adolescents with disabilities and their families	i) Children and adolescents (8-12, 13-16 years) with chronic health conditions and their families. ii) Contacted during visits to clinics and in advance with an information sheet	4-7 years 8-12 years 13-16 years	Asthma Epilepsy Diabetes Arthritis Atopic dermatitis Cerebral palsy Cystic fibrosis	Mixed methods Thematic analysis for qualitative	Purposive	154 children and adolescents, 142 parents and 26 experts	i) Focus group discussions individual interviews as a second option. ii) Not stated iii) Not stated	Outpatient	25:c1
Ravens-Sieberer et al (1998), Germany	How do the KINDL results compare to qualitatively analysed answers to open questions regarding quality of life?	i) Children who were former outpatients of the hospital. ii) Participants were identified through hospital records	Range 10-16 years	Diabetes Asthma	Mixed methods Content analysis for qualitative	Not stated	45 children and 45 mothers	i) Self-administered questionnaire sent via mail ii) Not stated iii) Not applicable	Home and mail-based	21:C1
Tomlison et al (2014), Canada	To identify if any of the previously identified scales were suitable for use or adaptation as a paediatric self-report symptom screening tool	i) Healthcare professionals with expertise in symptom management as follows: four paediatric oncologists, four nurse practitioners, one pharmacist, and one neuropsychologist. And a patient advocate. ii) Invited based on targeted expertise	Not applicable	Cancer	Mixed methods Nominal group technique methods	Purposive	10 health care professionals and 1 patient representative	i) Focus group discussions Consensus via of the face-to-face discussion and email correspondence ii) Not applicable iii) Not applicable	Hospital	26: C1
Wilson et al (2011), USA	Illustrate the range of concerns children with life threatening cancer have	i) Children with advanced cancer ii) Study was nested in a larger survey	Range 6 -17 years	Cancer	Mixed methods Longitudinal study for qualitative	Not stated	3 children	i) Semi-structured interviews questionnaires ii) Not stated iii) Not stated	Not stated	26: C1
Quantitative research design										

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
Blume et al (2014), USA	To describe parent perspectives regarding the end-of-life experience of children with advanced heart disease	i) English speaking Bereaved parents of children who were less than 21 years at death from any type of heart disease at any of the participating study sites inpatient units (in the previous 9 months -4 years). ii) Hospital medical records	Range 3.6 days to 20.4 years	Advanced heart disease	Quantitative Cross sectional study	Not stated	50 bereaved parents	i) Survey/questionnaire – 'the survey about caring for children with Heart Disease at end –of –Life' ii) Not applicable iii) Not applicable	Outpatient	29: C1
Chao-Hsing et al (2009), Taiwan	To assess and describe the occurrence , frequency and severity and distress of symptoms reported by Taiwanese paediatric cancer patients aged 10-18 years	i) Chinese speaking families with a child diagnosed with cancer and attending care at the study hospital. ii) Participants were recruited through the hospital clinic	Range 10-18 years	Cancer	Quantitative Cross sectional – nested in a longitudinal study	Not reported but reference	144 children and their mothers	i) The MSAS (10-18) questionnaire , self-administered ii) Not stated iii) not applicable	Inpatient, outpatient and mail-based	28:B3
Cleve et al (2012), USA	To examine the common symptoms and to explore commonly occurring symptoms over time.	i)English or Spanish speaking diagnosed with leukaemia non-responsive to treatment or relapsed ii) Recruited through hospital or clinic	Range 6-17 years	Cancer	Quantitative Longitudinal study design	Not stated	60 children	i) The MSAS (10-18) questionnaire self /proxy MSAS (10-18). ii) Parents were allowed to be present if they wished iii) Reporting was audio taped.	Hospital, clinic and home	35:B3
Collins et al (2000), USA	To determine multi-dimensional symptoms in children with cancer	i) English speaking Paediatric cancer patients currently or previously had a cancer diagnosis. Patients were recruited through hospitals, identified through review of patient charts for eligibility. ii) Hospital outpatient review of charts used for identification	Range 10-18 years	Cancer	Quantitative Nested in a clinical trial	random	159 children	i) The MSAS (10-18) questionnaire self-completed by children with or without assistance Assistance involved the study administrator administering the questionnaire verbally. ii) Children interviewed independently iii) Not stated	Inpatient, outpatient and home	37:B3
Collins et al, (2002),	Evaluate the reliability and validity of a	i) Children with a Cancer diagnosis and were undergoing treatment, had	Range 7-12 years	Cancer	Quantitative	Random	90 children	i) The MSAS (10-18) questionnaire self-	Inpatient and outpatient	36:B3

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
UK and Australia	revised MSAS in patients aged 7-12 years	no indication of an organic brain syndrome or psychiatric disturbance severe enough to be unable to complete the questionnaire. ii) Hospital outpatient review of charts used for identification			Multicentre longitudinal			completed by children with or without assistance ii) Children interviewed independently iii) Not stated		
Drake et al (2003), Australia	To examine symptom prevalence, characteristics and distress of children dying in hospital	i) Nurse carers for Children >12 months who died at pain and palliative care service at a children's hospital and had been hospitalised for more than 24 hours ii) Medical records	Range 1-18.6 years	Cancer, cardiac, neurological gastrointestinal	Quantitative Retrospective record review	Census of all who met inclusion criteria	30 nurses who cared for the 30 children at end of life	i) Proxy nurse completed the memorial symptom assessment scale (MSAS) 10-18 Record review ii) Not applicable iii) Not applicable	Hospital	32:C1
Dupuis et al (2010), Canada	To develop an instrument to assess cancer-treatment-related adverse effects that parents believe children find most bothersome and use it to solicit the opinions of parents regarding this issue	i) Parents of a child who had been diagnosed with cancer at least 2 months prior to enrolment and had received intravenous antineoplastic therapy during the month prior to enrolment. ii) Provincial database and assessed for eligibility	Range 4-18 years	Cancer	Quantitative Multi-centre cross sectional	Random selection and consecutive proportional to size	158 parents	i) Questionnaire – Parents identified symptoms experienced by their children in the previous 30 days and these were ranked for severity and level of distress ii) Not applicable iii) Not applicable	Inpatient and outpatient	34:B3
Friedrichsdorf et al (2015), USA	To compare end-of-life pain and symptom management in children with advanced cancer who received care exclusively from a paediatric oncology service with that of those who received concurrent PPC	i) English-speaking bereaved parents who, had a child had cancer and received primary care from the study clinic at least 30 days following diagnosis, the child died in the previous seven years. ii) Administrative data and through their oncologists	Mean age at death 10 (sd=6.3)	Cancer	Quantitative Retrospective cross sectional	Not stated	60 bereaved parents	i) Survey using the ''Survey About Caring for Children with Cancer. ii) Not applicable iii) Not applicable	Outpatient, home and tele-based	30:C1

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
	home care services.									
Garvie et al (2012), USA	To understand the attitudes, beliefs, and preferences about death and dying held by adolescents with HIV and their families	i) English-speaking adolescents at least 14-21 years of age who had been diagnosed with HIV , knew their status and either their legal guardian(s), if they were younger than 18 years, or chosen family decision maker if age 18 years or older ii) Study nested in a larger survey	Range 14-21 years	HIV/AIDS	Quantitative Nested in a two centre randomised controlled trial	Random	24 adolescents and 24 families	i) Survey questionnaire : The 31-item Lyon ACP survey-adolescent version ii) Not stated iii) Not stated	Hospital and outpatient	36:B3
Goldman et al (2006), UK	Survey symptoms in children/young people with progressive cancer and identify which are the most important and which are the most difficult to treat effectively.	i) Study included Children in the palliative phase and died by study completion ii) Through their physicians	Range 4 months - 19 years	Cancer	Quantitative Multi-centre longitudinal study	Not stated	164 children and family where appropriate	i) Questionnaire –author developed ii) Children interviewed with family iii) Not applicable	Cancer care centres	33:B3
Heath et al (2010), Australia	To examine the symptoms, level of suffering and care of Australian children with cancer at the end of life	i) English-speaking bereaved parents of children who had died of cancer in the previous 8 years ii) Through their respective family oncologists and social workers	Mean age at death 9.4 years	Cancer	Quantitative Retrospective cross sectional	Census of parents of deceased children who met inclusion criteria	89 parents	i) Survey/questionnaire parents ii) Not applicable iii) Not applicable	Hospital	29:C1
Hongo et al (2003), Japan	This study analyses the signs and symptoms at the end of life in such children	Medical records of children who died of cancer during the specified time frame	Range 2.8 -22 years	Cancer	Quantitative Record review	Census of all children who died of cancer at study hospital	28 medical records of children	i) Review of medical records and records of daily documentations by staff ii) Not applicable iii) Not applicable	Hospital	31 :C1

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
Huda Abu-Saad Huijer et al (2013), Lebanon	To evaluate the quality of life, symptom prevalence and symptom management among a sample of paediatric oncology patients	i) Diagnosed with cancer for more than one month, aware of their diagnoses, currently receiving cancer treatments (like chemotherapy or radiation). ii) Identified by study staff using hospital appointment and admission lists	Range 7-18 years	Cancer	Quantitative Cross sectional	Convenience	85 children	i) Questionnaires: The MSAS (7-12, and 13-18 versions ii) Children were interviewed separately iii)Not applicable	Inpatient and outpatient	35 :C1
Jacobs et al (2015), USA	To examine the baseline congruence between the self-reported needs of adolescents with cancer for EOL care and their families' perception of those needs. To better understand how adolescents with cancer approach EOL issues	i) English-speaking adolescents diagnosed with cancer and were aware of the diagnosis in the intervention arm of the trial	Range 14-21 years	Cancer	Quantitative Randomised controlled trial	random	17 adolescents and 17 family carers	i) Questionnaire 'The Lyon Advance Care Planning Survey-Adolescent & Family Versions scale, adapted for context version. ii) children interviewed separately iii) Not stated	Hospital	32: B3
Jalmsell et al (2006), UK	Identify the symptoms that moderately or severely affect the sense of well-being of children with malignancies during the last month of their lives as reported by their parents.	i) Swedish-speaking bereaved parents of children who had died in the previous 6 years and had a non-confidential telephone number. ii) Deceased children were identified through the national death register which is linked to the cancer register	Range 9-15 years	Cancer	Quantitative Retrospective and descriptive analysis	Not stated	449 bereaved parents	i) Survey using author(s) developed questionnaire ii) Not applicable iii) Not applicable	Mail-based	28:B3
Janssens et al (2014), UK	To identify what aspects of health clinicians target when working with children with neuro-disability,	i) Health professionals ii) Recruited through child health development teams and professional societies in England.	Not stated	Neuro-disability	Quantitative Delphi methodology	Purposive	276 health professionals	i) Delphi process ii) Not applicable iii) Not applicable		30:B3

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
	and which might be appropriate to assess the performance of health services.									
Lavy et al (2007), Malawi	To determine the prevalence of different symptoms among children with incurable disease who are referred to the paediatric palliative care team at QECH, Malawi	i) All the children referred to the paediatric palliative care team was carried out during a 4-month period. ii) Admission for palliative care referrals	Range 4 months - 16 years	Cancer HIV	Quantitative Cross sectional	Consecutive	95 children	i) Questionnaire and observations. Children or carers responded to questionnaire based interviews on symptoms Observations for clinical signs ii) Not stated iii) Not applicable	Inpatient	20:C1
Macartney et al (2014), Canada	This study describes the symptom experience and health-related quality of life of children who had completed treatment 3 months before study	i) Children in surviving treatment for brain tumour. ii) Through neuro-oncology follow-up clinics	2-18 years	Cancer	Quantitative Observational cross sectional study	Convenience	50 children	i) Questionnaires : MSAS questionnaire versions 7-12 and 10-18 ii) Self-report as appropriate and child supported if younger iii) Not stated	Home and clinic	30:C1
McHugh et al (2016), Zimbabwe	Prevalence of chronic co-morbidity among children aged 6-15 years at diagnosis of HIV infection.	i) Children aged 6-15 years , tested HIV positive following provider initiated HIV testing and counselling. ii) Those that tested positive and met inclusion criteria	6-15 years	HIV	Quantitative Cross sectional study	Not stated	385 children	i) Interviewer administered questionnaire, physical examination data collected from paper forms through optic mark recognition ii) Not applicable iii) Optic mark recognition used	Hospital	30: B3
Mitchell et al (2006), UK	To provide an overview of parents' and children's views of psychosocial support they receive at different	i) Paediatric oncology patients who received treatment from paediatric oncology treatment centres in the UK. Children on (83%) and off treatment ii) Via treatment centres	Range 10-19 years	Cancer	Quantitative Multicentre cross sectional nested in a larger multi-centre postal survey	Purposive	112 children and 127 parents	i) Postal Survey /questionnaire – author developed ii) Not stated iii) Not stated	Home	28:C1

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
	stages of the illness									
Nakawesi et al (2014), Uganda	To determine the palliative care needs	i) HIV exposed and infected children admitted to inpatient paediatric unit ii) Hospital medical records	<5 years	HIV /AIDS	Quantitative Retrospective record review	Not applicable	243 records of children	i) Not applicable ii) Not applicable iii) Not applicable	Hospital	29:C1
Poder et al (2010), Sweden	To describe which problems that according to parents, cause most problems for children receiving cancer treatment.	i) Swedish and English speaking parents of diagnosed with cancer at least less than 14 days prior to the survey , scheduled for treatment and had access to a telephone ii) Through hospital clinic	0-18 years	Cancer	Quantitative Multi-centre prospective longitudinal	Not stated referenced	214 parents of 115 children	i) Questionnaire – MSAS 10-18 Tele-based Interviews ii) Not applicable iii) Not applicable	Paediatric Oncology centre	28 :B3
Theunissen et al (2007), Netherlands	To make a comprehensive inventory of the physical, psychological, and social symptoms of children with cancer and their parents during the palliative phase and the extent to which health professionals address those symptoms	i) Dutch-speaking Bereaved parents whose children received palliative care for terminal cancer care in the previous three years. ii) Hospital patient records.	Mean age at death 10.9 (standard deviation 4.9)	Cancer, end stage	Quantitative Retrospective Cross-sectional survey	Based on willingness to participate	32 bereaved parents	i) Survey /questionnaire: ‘‘The Problem Need Palliative Care’’ questionnaire adapted for the paediatric population. ii) Not applicable iii) Not applicable	Mail-based	28:C1
Olagunju et al (2016), Nigeria	To investigate if child symptom burden is related to depressive symptoms of caregivers	i) Children with cancer undergoing treatment in tertiary hospitals in Nigeria ii) Through hospital	Range 7-12 years	Cancer	Quantitative Multi-centre cross sectional	Consecutive	72 children and their care givers	i) Questionnaires: MSAS (7-12), Centre for epidemiologic studies depression ii) Not stated iii)Not applicable	Inpatient and outpatient	34:B3

Authors (year), country	Study aim as reported	i) Population ii) Recruitment	Age of child	Primary Diagnosis as reported	Research design Methodology	Sampling approach	Participants	i) Data collection method ii) Presence/absence of parents at interview iii) Recording	setting	Quality score [1]/level of evidence[2]
Van Zanten et al (2016), UK	To compile an inventory of symptoms experienced, interventions applied, and current service provision in end-of-life care for	i) Records of Children with diffuse intrinsic pontine glioma who received treatment from hospital 12 weeks before death ii) Medical records	Range 0-18 years	Cancer	Quantitative Retrospective cohort study design	Not stated	63 records	I) Record review ii) Not applicable iii) Not applicable	Hospital	28:C1
Wolfe et al (2015), USA	To describe symptom distress in children	i) Children at least 2 years of age, receiving care from any of the study sites With at least 14 day history of progressive ,recurrent or non-responsive cancer Decided not to pursue cancer directed therapy. Child and parent ii) Enrolled by their oncologists	Range 7-12 years	Cancer	Quantitative Randomised controlled trial	random	104 children	i) Questionnaire : the PEDIQUEST memorial symptom Assessment Scale (PQ-MSAS) ii) Parents were present where appropriate (for young children) iii) Not stated	Inpatient and outpatient	38:B1
Wolfe et al (2000), USA	To determine symptoms at end of life, effectiveness of treatment and factors related to suffering from pain at the end of life	i) English speaking Bereaved parents who had lost children about 3.1 years ago. ii) Identified through their physicians	Mean age 10.8 (standard deviation 6.7)	Cancer	Quantitative Retrospective	Not stated	103 bereaved parents	i) Questionnaire –author(s) developed ii) Not applicable iii) Not applicable	Tele-based	32:B3