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The barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in infants, children and young people at end-of-life: a mixed methods systematic review protocol

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ABSTRACT

Introduction. This protocol describes the objective and methods of a systematic review of barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in infants, children and young people (ICYP) at end-of-life.

Methods and analysis. The Cochrane Library, PROSPERO, CINAHAL, MEDLINE, PsycINFO, Web of Science Core Collection, ProQuest Dissertations & Theses Database, Evidence Search and OpenGrey will be electronically searched. Reference screening of relevant reviews and inquiries to researchers in the field will be undertaken. Studies will be selected if they apply qualitative, quantitative or mixed-methods designs to explore barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in ICYP at end-of-life. Articles will be screened by title and abstract by one reviewer with a second reviewer assessing 10% of the articles. Both reviewers will read and screen all remaining potentially relevant articles. For included articles, one reviewer will extract study characteristics and one will check this.
Both reviewers will undertake independent quality assessments of included studies using established and appropriate checklists including The Critical Appraisal Skills Programme Qualitative Checklist; The evaluative criteria of credibility, transferability, dependability and confirmability; The Quality Assessment Tool for Quantitative Studies, and The Mixed Methods Appraisal Tool. Data synthesis methods will be decided after data extraction and assessment.

Ethics and dissemination. This review will inform our understanding of symptom management in ICYP at end-of-life. The findings will be reported in a peer-reviewed journal and presented at conferences. The study raises no ethical issues.

Trial registration number CRD42019124797.

ARTICLE SUMMARY

Strengths and Limitations Of This Study

- This systematic review can give us a greater understanding of pain management in palliative care - highlighted as a research priority by NICE - and could inform the design of evidence-based interventions to support more effective medicine management
- The systematic review will follow robust guidelines and the quality of included articles will be assessed using validated tools
- The heterogeneity of the included studies, which may use qualitative, quantitative or mixed-methods approaches, could limit the overall data synthesis

KEYWORDS

Paediatric Palliative Care
Pain Management
Qualitative Research

INTRODUCTION

Approximately 49,000 infants, children and young people (ICYP) are living with a life-threatening or life-limiting condition in the UK [1]. These include congenital anomalies; cancer; and neurological, haematological, respiratory, genitourinary, perinatal, metabolic, circulatory and gastrointestinal conditions.
There were nearly 3000 child deaths due to medical conditions in England in 2017, of which over 2350 were due to a known life-limiting condition or neonatal death [2].

ICYP's palliative care needs often differ to those of adults and the diversity of conditions in this population means that practitioners must manage a wide range of complex symptoms [3]. A particular challenge is managing continuous 'background' pain as well as bouts of severe, sudden-onset 'breakthrough pain', both of which are common in ICYP with a terminal illness [4] and are known to be under-assessed and undertreated [5].

Family carers play a vital role in supporting ICYP with a terminal illness, allowing patients to be cared for and die at home where possible. However, there is little research on carers' experiences of administering medicines for symptom relief to ICYP receiving palliative care. Managing symptoms such as pain is potentially difficult for carers of children at home. They may lack the necessary skills and confidence required to balance symptom relief and side-effects while fear of errors can lead to insufficient or inappropriate doses of analgesics. Families will move ICYP away from their preferred place of care if symptoms, including pain, are not managed effectively [6].

Community nurses and doctors may also lack the skills and experience required to support carers. A systematic review found that GPs experience anxiety regarding their competency to deliver appropriate palliative care [7] while healthcare support workers providing end-of-life care in the community require training in palliative care to cope with emotionally demanding situations [8].

The recent National Institute for Health and Care Excellence (NICE) guideline [9] is based on evidence from 20 systematic reviews investigating different aspects of planning and management of end-of-life care for ICYP with life-limiting conditions. These include reviews on what information is perceived as helpful and what social and practical support is effective for ICYP and their caregivers. The findings indicate that timely, honest and consistent information that meets individuals' needs (e.g. developmentally appropriate for patients) is beneficial, including information about access to services, community and medical resources. One study also found that parents wanted information on how to use equipment that a child/ young person required [10]. However, symptom management was not identified as a major theme in these reviews.
Four other reviews looked at the effectiveness of pharmacological and non-pharmacological interventions for pain management, agitation, respiratory distress and seizures. Only the pain management review found any studies that met the inclusion criteria and all of these involved pharmacological interventions only.

Although these reviews provide essential guidance in managing end-of-life care for ICYP, to our knowledge no systematic review has examined the barriers and facilitators to symptom management in ICYP at end-of-life for healthcare professionals, caregivers and patients. NICE highlights pain management in palliative care as a research priority [9] and a greater understanding of this could inform the design of evidence-based interventions to support more effective medicine management.

Objectives
The main objective of this systematic review is to identify and synthesise the existing literature that explores the barriers and facilitators experienced by patients (CYP), carers and healthcare professionals when managing symptoms in ICYP at end-of-life.

METHODS

This protocol follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) [11] guidelines (online Supplementary File 1—PRISMA-P checklist) and is registered (ID CRD42019124797) on PROSPERO, an international register of systematic reviews [12]. Any changes to the protocol will be recorded on PROSPERO.

The reporting of the systematic review will be informed by the Centre for Reviews and Dissemination [13] and the Cochrane Qualitative Research Methods Group guidelines [14] and will follow the Enhancing Transparency in Reporting the Synthesis of Qualitative Research (ENTREQ) [15] and the PRISMA statements [11] for reporting systematic reviews (see online Supplementary File 2). In the case of sections applicable to qualitative systematic reviews that are included in PRISMA, but are not covered by ENTREQ, these will also be reported.

Eligibility Criteria
The criteria outlined below will be used for study selection. Following the recommendations of the Cochrane Qualitative and Implementation Methods Group Guidance (Harris et al., 2018), we have used STARLITE (Sampling Strategy, Type of study, Approaches, Range of years, Limits, Inclusions and exclusions, Terms used, Electronic sources [16] to report our search methods.

Sampling strategy: This review will consider all studies carried out worldwide that involve carers, healthcare professionals or patients' views on symptom management in ICYP up to the age of 24 years at end-of-life care. A cut-off age of 24 years will be used since this corresponds to adolescent growth and current understandings of this stage in life [17].

Type of study: The review will consider qualitative, quantitative and mixed-method studies including questionnaires, surveys, interviews, focus groups, case studies, and observations. Trials, cohort and intervention studies that assess barriers and facilitators to symptom management will all be considered.

Approaches: In addition to searching electronic databases, the search strategy will include hand searching of reference lists of identified eligible studies. Finally, active researchers in the field who have contributed to this literature will be contacted.

Range of Years: Studies published from the inception of each database will be included.

Limits: Articles written in any language other than English due to a lack of funding for adequate translation; masters theses; conference abstracts; reviews.

Inclusions: Barriers and facilitators experienced by carers, healthcare professionals, and the patients themselves, when managing symptoms in ICYP with terminal illnesses receiving palliative care and/or at end-of-life. All definitions of 'end-of-life' will be included since there are a wide variety of definitions and there is a paucity of research in ICYP symptom management in

this area. Data on carers; healthcare professionals; and patients' views, attitudes, opinions, perceptions, beliefs or feelings will be included.

Exclusions: Studies that focus only on the effectiveness of pharmacological treatments for symptom management will be excluded.

Searches

Electronic sources: The Cochrane Library and PROSPERO will be searched initially to check for any existing systematic reviews on this topic. As recommended by the Cochrane Qualitative and Implementation Methods Group [14], CINAHAL (Cumulative Index of Nursing and Allied Health Literature) via Ebsco and Ovid MEDLINE will be searched, as well as PsycINFO via Ebsco and the Web of Science Core Collection. To identify any additional unpublished work, the ProQuest Dissertations & Theses Database; Evidence Search; and OpenGrey will also be searched. The search strategy will include hand searching of reference lists of eligible studies for additional records. All searches will be run during February 2019.

Search terms used: A search strategy was developed based on the 'Managing Pain' search strategy used in the NICE guideline 'End-of-life Care for Infants, Children and Young people with Life-limiting Conditions: Planning and Management (NG61) [9]. The strategy incorporated search terms in four blocks: 1. 'Patient Population'; 2. 'Caregivers and Patients'; 3. 'End-of-life'; and 4. 'Pain and Symptoms.' Additional searches used in the Palliative Care Search Filter [18] were also incorporated into Block 3 for each database.

Combinations of keywords, text words, Medical Subject Headings (MeSH) and other terms relevant to the four blocks were selected for each database to optimise the search sensitivity and specificity. The search strategy was piloted and adapted for each database. A professional healthcare research librarian assisted in the development of the strategy. Please see Supplementary File 3 for the full search strategy for each database.

Data Management

All records and data will be saved to Endnote X8 [19]. This software will be used to identify potential duplicates. The researcher will check this and remove all confirmed duplicated.

Selection Process

Articles will first be screened by title and abstract by one reviewer (KG) and judged as either a) 'not relevant' or b) 'potentially relevant'. A second reviewer (SH) will assess a random sample of 10% of the articles. The reviewers will independently apply the criteria at all stages of the selection process. Inter-coder agreement will be evaluated using Cohen's kappa coefficient. A minimum kappa value of 0.75 will be taken to represent high agreement [20].

The full text of all remaining potentially relevant articles will then be obtained. If the relevance of a study cannot be ascertained from the abstract, then the full article will be obtained. The full articles will be read by two reviewers independently (KG and SH) to make the final decision about whether they should be chosen for inclusion in the review. A third reviewer (CL) will resolve any uncertainties. Additional information will be sought from authors if necessary at the stage of full-text assessment.

Data Collection Process and Items

The following information will be extracted into a piloted data collection form for all included studies: Study aims; patient population (infant/child/adolescent);

participant population (patient/caregiver/healthcare professional); inclusion and exclusion criteria; sample size; recruitment; design; intervention and comparator group (where applicable); date and duration of data collection; setting; country; data collection; analysis methods; data describing the participants' views/experiences of barriers and facilitators to symptom management. For qualitative data, the authors' interpretations (presented through themes and categories) will represent this data [21]. KG will extract this information and SH will check it, with any disagreements resolved through discussion with CL.

Quality assessment (including risk of bias)

A quality appraisal of included studies will be conducted independently by two reviewers (KG and SH). Disagreements will be resolved by discussion between KG and SH, and CL if required.

Three checklists will be used depending on each study's design. These were chosen since they are all validated and have been used in published systematic reviews within healthcare research. For each study type, Cohen's kappa coefficient will be used to measure inter-rater agreement between the two reviewers. A minimum kappa value of 0.75 will be taken to represent high agreement with disagreements resolved via discussion with CL.

As recommended by the Cochrane Qualitative and Implementation Methods Group [14], we will not calculate total quality scores across domains since domains of quality are not equal. Instead, KG, SH and CL will determine how each study's methodological limitations affect confidence in the findings via discussion. We will not exclude studies based on poor quality but will record and highlight methodological issues.

Qualitative studies will be quality appraised using the *Critical Appraisal Skills Programme for qualitative studies* [22]. The CASP assesses clarity of research aims; research design; recruitment methods; data collection; relationships between participants and researchers; ethical issues, analyses; description of findings; and valuableness of the research. It is comprised of nine closed questions (e.g. "Was there a clear statement of the aims of the research?" Yes/Can't tell/No) and one open-ended question ("How valuable is the research?"). For each question, there is the option to add comments to explain the reasoning for each rating. Currently, the CASP is the most frequently used qualitative research synthesis tool in the Cochrane Library and World Health Organisation guideline research [23] and has been used in similar systematic reviews assessing barriers and facilitators within healthcare e.g.[24 25]. However, because the CASP tool does not address aspects of the research validity and can favour papers that are less insightful as long as they comply with 'expectations of research practice' [26], in addition, the evaluative criteria of credibility, transferability, dependability and confirmability [27] will be applied. Included studies will be assessed as to whether they apply the techniques suggested for ensuring study quality according to Guba and Lincoln's [27] criteria i.e. prolonged engagement, persistent observation, peer review, triangulation, negative case analysis, referential adequacy and member checking to ensure credibility; thick description for transferability; inquiry audit for dependability; confirmability audit, audit trail, triangulation and reflexivity to ensure confirmability. Studies will be rated as 'high quality' if they meet at least three of the four criteria, 'medium quality' if they meet two of the criteria and 'low quality' if they meet one or none.

The Quality Assessment Tool for Quantitative Studies (QATQS) will be used to assess all clinical studies with or without randomisation and control groups, including quasi-experimental and before-and-after studies [28]. The QATQS is comprised of 22 closed questions and an overall rating of strong, moderate or

weak in eight sections: selection bias; study design; confounders; blinding; data collection; withdrawals and dropouts; intervention integrity; analysis. It has been shown to be a valid tool for assessing quality; comparing studies and addressing threats to validity of findings [29].

The Mixed Methods Appraisal Tool (MMAT-Version 11) will be used to assess the quality of any mixed methods studies [30]. This tool consists of five closed questions assessing the research question; research design; integration of qualitative and quantitative methods; integration of qualitative and quantitative data; and consideration of methodological limitations in mixed methods studies. As reported by the Cochrane Qualitative and Implementation Methods Group, this tool has been used widely in systematic reviews and has the advantage of being able to assess interdependent qualitative and quantitative elements of mixed-methods research [23].

Outcomes and Prioritisation

The main outcomes sought are carers'; healthcare professionals'; and patients' (CYP) views on the barriers and facilitators to effective symptom management in ICYP at end-of-life.

Data Synthesis

Although it is unlikely that the majority of included studies will be quantitative, if this is the case then random-effects meta-analysis will be conducted to synthesise group means and standard deviation from individual studies using Comprehensive Meta-Analysis (CMA) version 3 [31].

For meta-analysis to be conducted, data must be available from two or more eligible studies reporting similar barriers or facilitators. The studies must report the number of participants reporting that barrier/facilitator and the total number of valid participant responses for that survey item. A random-effects model will be used for all analyses since, unlike a fixed-effects model, this can be used when statistical heterogeneity ($\tau 2$) is present in the results of the included studies [32]. Where evidence of statistically significant heterogeneity is present, sensitivity analyses will be conducted where possible to verify the robustness of the study conclusions, assessing the impact of methodological quality, study design, sample size and the potential effects of missing data. We will use funnel plots to detect potential reporting biases and small-study effects where data is available from 10 or more studies [33].

If the included studies are all qualitative or a combination of quantitative and qualitative, there are several approaches that could be taken for data synthesis. Some of the most commonly used methods to synthesise qualitative health research include thematic analysis [34]; grounded theory [35] and meta-ethnography [36 37]. However, there is no consensus on the best approach, which will depend on the type and number of included studies [38] and the form and nature of the research question [37]. As such, we will make a final decision on the most appropriate method after selecting and quality assessing the included articles, as recommended by the Cochrane Qualitative and Implementation Methods Group [38].

We will first analyse and synthesise data related to the experience of patients, care providers and healthcare professionals separately before deciding whether it is appropriate to aggregate data between these groups. This data will likely include themes, concepts and categories of information. If it is relatively 'thin' then we will consider using thematic synthesis to undertake line-by-line coding and development of descriptive and analytic themes. If the included articles include sufficient 'thick' data (e.g. enough detail about the context of the study to

infer whether the findings can be generalised to other situations and/or populations [39]), we will consider a more interpretative approach such as meta-ethnography. This method goes beyond aggregating data to generate new interpretations of the findings.

As recommended by the Cochrane Qualitative and Implementation Methods Group [23] the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative research [40]) will be used to summarise our confidence in synthesised qualitative findings (e.g. in the themes that we identify). The CERQual is made up of four key components i.e., methodological limitations of included studies, coherence of the review finding; adequacy of the data contributing to a review finding; relevance of the included studies to the review question. After assessing each of the four components, overall confidence will be graded as high, moderate, low, or very low. The barriers and facilitators to symptom management will be divided into overarching themes for each group (patients; healthcare professionals; carers); and presented in a matrix along with our CERQual assessment of confidence in the evidence of each theme and an explanation of this assessment.

The GRADE guidelines [41] will be used to appraise the quality of any quantitative findings. The GRADE guidelines include four elements for which quantitative findings will be rated against: risk of bias ('Study limitations'), inconsistency, indirectness, imprecision, publication bias.

Patient and public involvement
Consultation with young people, parents and health care professionals has been used to determine their perception of the barriers and facilitators they experience when managing symptoms in ICYP at end-of-life. It is based on their perspectives that this systematic review was deemed to be timely and crucial to conduct to inform further research work. Moreover, patient and public involvement is represented in the authorship (MJ) of this manuscript.

DISCUSSION

This systematic review will be the first to synthesise and report barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in ICYP at end-of-life**.** The review findings will be used to inform our ongoing work to develop a structured educational tool to support carers and healthcare professionals to administer pain and symptom relief to ICYP at the end-of-life.

Ethics and dissemination
As this is a systematic review of published literature, ethical approval will not be sought. We will publish the protocol and our findings in peer-reviewed journals aimed at paediatric palliative care clinicians and researchers as well as health commissioners. We will present our work at the growing numbers of national and international meetings focused on paediatric palliative care and pain.

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Author Contributions
EH, RH, MJ, IW and CL conceived the idea, planned and designed the study protocol. KG, SM, DS planned the data extraction and statistical analysis and wrote the first draft; JB and LB provided critical insights. All authors have approved and contributed to the final written manuscript.

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Competing Interests
None declared.

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PRISMA Statement: Recommended items to address in Systematic Reviews and Meta-Analyses

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	

Section/topic	#	Checklist item	Reported on page #
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and	

Section/topic	#	Checklist item	Reported on page #
		confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

ENTREQ Statement: Recommended items to address in a synthesis of qualitative research.

No	Item	Guide and description
1	Aim	State the research question the synthesis addresses.
2	Synthesis methodology	Identify the synthesis methodology or theoretical framework which underpins the synthesis, and describe the rationale for choice of methodology.
3	Approach to searching	Indicate whether the search was pre-planned or iterative.
4	Inclusion criteria	Specify the inclusion/exclusion criteria.
5	Data sources	Describe the information sources used and when the searches conducted; provide the rationale for using the data sources.
6	Electronic Search strategy	Describe the literature search.
7	Study screening methods	Describe the process of study screening and sifting.
8	Study characteristics	Present the characteristics of the included studies
9	Study selection results	Identify the number of studies screened and provide reasons for study exclusion.
10	Rationale for appraisal	Describe the rationale and approach used to appraise the included studies or selected findings.
11	Appraisal items	State the tools, frameworks and criteria used to appraise the studies or selected findings.
12	Appraisal process	Indicate whether the appraisal was conducted independently by more than one reviewer and if consensus was required.
13	Appraisal results	Present results of the quality assessment and indicate which articles, if any, were weighted/excluded based on the assessment and give the rationale.
14	Data extraction	Indicate which sections of the primary studies were analysed and how were the data extracted from the primary studies.

15	Software	State the computer software used, if any.
16	Number of reviewers	Identify who was involved in coding and analysis.
17	Coding	Describe the process for coding of data.
18	Study comparison	Describe how were comparisons made within and across studies.
19	Derivation of themes	Explain whether the process of deriving the themes or constructs was inductive or deductive.
20	Quotations	Provide quotations from the primary studies to illustrate themes/constructs, and identify whether the quotations were participant quotations of the author's interpretation.
21	Synthesis output	Present rich, compelling and useful results that go beyond a summary of the primary studies.

From: Tong A, Flemming K, McInnes E, Oliver S, Craig .(2012). Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. BMC Medical Research Methodology, 12(1):181.

The barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in infants, children and young people at end-of-life: a mixed methods systematic review protocol

Search Strategy (Searched February 2019)

Database: The Cochrane Library

ID	Search
#1	MeSH descriptor: [Infant] explode all trees
#2	MeSH descriptor: [Child] explode all trees
#3	MeSH descriptor: [Adolescent] explode all trees
#4	MeSH descriptor: [Pediatrics] explode all trees
#5	MeSH descriptor: [Puberty] explode all trees
#6	(Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy* OR Girl* OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid* OR Kindergartan* OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* or Prepubescen* OR Paediatric* OR Pediatric*):ti,ab,kw (Word variations have been searched)
#7	MeSH descriptor: [Caregivers] explode all trees
#8	(Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*):ti,ab,kw (Word variations have been searched)
#9	MeSH descriptor: [Palliative Care] explode all trees
#10	MeSH descriptor: [Terminal Care] explode all trees
#11	MeSH descriptor: [Advance Care Planning] explode all trees
#12	MeSH descriptor: [Attitude to Death] explode all trees
#13	MeSH descriptor: [Bereavement] explode all trees
#14	("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR "Life-limit*" OR Termina* OR "Life-threatening" OR Deathbed* OR "Death Bed*" OR "Passing Away" OR "Passing On" OR Expiring OR Expiration OR Hospice):ti,ab,kw (Word variations have been searched)
#15	((Final OR Advance* OR Incurable) NEXT (ill* OR disease? OR condition?)):ti,ab,kw (Word variations have been searched)
#16	((Approach* OR Close* OR Near* or Imminent* or Impending) NEAR/3 (death)):ti,ab,kw (Word variations have been searched)
#17	((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase? OR Stage?)):ti,ab,kw (Word variations have been searched)

#18 MeSH descriptor: [Death] this term only

#19 MeSH descriptor: [Hospices] this term only

#20 MeSH descriptor: [Life Support Care] this term only

#21 MeSH descriptor: [Terminally Ill] this term only

#22 palliat*

#23 hospice*

#24 terminal care

#25 MeSH descriptor: [Pain] explode all trees

#26 MeSH descriptor: [Signs and Symptoms] explode all trees

#27 MeSH descriptor: [Disease Management] explode all trees

#28 (Pain OR Symptom OR Medicine Management):ti,ab,kw (Word variations have been searched)

#29 #1 OR #2 OR #3 OR #4 OR #5 OR #6

#30 #7 OR #8

#31 #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24

#32 #25 OR #26 OR #27 OR #28

#33 #29 AND #30 AND #31 AND #32 (Word variations have been searched)

Database: PROSPERO

Line Search for

1. MeSH DESCRIPTOR Infant EXPLODE ALL TREES
2. MeSH DESCRIPTOR Child EXPLODE ALL TREES
3. MeSH DESCRIPTOR Adolescent EXPLODE ALL TREES
4. MeSH DESCRIPTOR Pediatrics EXPLODE ALL TREES
5. MeSH DESCRIPTOR Puberty EXPLODE ALL TREES
6. MeSH DESCRIPTOR Caregivers EXPLODE ALL TREES
7. MeSH DESCRIPTOR Terminal Care EXPLODE ALL TREES
8. MeSH DESCRIPTOR Palliative Care EXPLODE ALL TREES
9. MeSH DESCRIPTOR Attitude to Death EXPLODE ALL TREES
10. MeSH DESCRIPTOR Hospice Care EXPLODE ALL TREES
11. MeSH DESCRIPTOR Bereavement EXPLODE ALL TREES
12. MeSH DESCRIPTOR Hospices EXPLODE ALL TREES
13. MeSH DESCRIPTOR Death EXPLODE ALL TREES
14. MeSH DESCRIPTOR Life Support Care EXPLODE ALL TREES
15. MeSH DESCRIPTOR Terminally Ill EXPLODE ALL TREES
16. MeSH DESCRIPTOR Pain EXPLODE ALL TREES
17. MeSH DESCRIPTOR Signs and Symptoms EXPLODE ALL TREES
18. MeSH DESCRIPTOR Disease Management EXPLODE ALL TREES
19. MeSH DESCRIPTOR Pain Management EXPLODE ALL TREES
20. #1 OR #2 OR 3 OR #4 OR #5
21. #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
22. #16 OR #17 OR #18 OR#19
23. #6 AND #18 AND #19 AND #20
24. #18 AND #19 AND #20

Database: CINAHAL via EBSCOhost

#	Query	Limiters/Expanders
S16	S4 AND S7 AND S12 AND S15	
S15	S13 OR S14	
S14	(MH "Pain+") OR (MH "Pain Management") OR (MH "Medication Management") OR (MH Symptoms)	
S13	TI ((Pain* OR Symptom* OR "Medic* management")) OR AB ((Pain* OR Symptom* OR "Medic* management"))	
S12	S8 OR S9 OR S10 OR S11	
S11	SO ("Journal of palliative care" OR "Journal of palliative medicine" OR "Hospice journal physical psychosocial & pastoral care of the dying" OR "Supportive care in cancer" OR "Palliative medicine" OR "Palliative & supportive care" OR "Journal of supportive oncology" OR "Journal of social work in end of life & palliative care" OR "Journal of pain and symptom management" OR "Journal of pain & palliative care pharmacotherapy" OR "International journal of palliative nursing" OR "Death studies" OR "Death education" OR "American journal of hospice care" OR "American journal of hospice & palliative medicine" OR "Omega journal of death & dying")	
S10	palliat* OR hospice* OR "terminal care"	
S9	(MH "Palliative Care") OR (MH "Life Support Care") OR (MH "Hospices") OR (MH "Death") OR (MH "Bereavement+") OR (MH "Attitude to Death+") OR (MH "Advance Care Planning+") OR (MH "Terminal Care+") OR (MH "Terminally Ill")	
S8	AB (("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR "((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* or Imminent* or Impending) N3 (Death)) OR Deathbed* OR "Death Bed*" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration) OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice)) OR TI (("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR "((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* or Imminent* or Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration) OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice))	
S7	S5 OR S6	
S6	AB ((Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner*" OR Psychologist*)) OR TI ((Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner*" OR Psychologist*))	

S5 (MH Caregivers) OR (MH Physicians) OR (MH "Home Health Care") OR (MH" Health Personnel")

S4 S1 OR S2 OR S3

S3 (TI (Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool* OR Youth? OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* or Prepubescen* OR Paediatric* OR Pediatric*)) OR (AB (Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool# OR Youth# OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*))

S2 (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") OR (MH "Infant+") OR (MH "Infant, Newborn") OR (MH Pediatrics+) OR (MH Puberty)

S1 AG (child* or school* or preschool* or adolescen* or infant* or neonat*)

Database: MEDLINE via OVID

1. exp advance care planning/
2. exp attitude to death/
3. exp bereavement/
4. Death/
5. Hospices/
6. Life Support Care/
7. Palliative Care/
8. exp terminal care/
9. Terminally Ill/
10. palliat$.af.
11. hospice$.af.
12. terminal care.af.
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. journal of palliative care.jn.
15. journal of palliative medicine.jn.
16. hospice journal physical psychosocial & pastoral care of the dying.jn.
17. supportive care in cancer.jn.
18. palliative medicine.jn.
19. palliative & supportive care.jn.
20. journal of supportive oncology.jn.
21. journal of social work in end of life & palliative care.jn.
22. journal of pain & symptom management.jn.
23. journal of pain & palliative care pharmacotherapy.jn.
24. international journal of palliative nursing.jn.
25. death studies.jn.
26. death education.jn.
27. american journal of hospice care.jn.
28. american journal of hospice & palliative medicine.jn.
29. omega journal of death & dying.jn.
30. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. 13 or 30
32. Child, Preschool/
33. exp child/
34. exp adolescence/
35. exp infant/

36. Infant, Newborn/
37. exp pediatrics/
38. Puberty/
39. (Infant* or Neonat* or Newborn or New born or Perinatal or Babies or Baby or Toddler* or Child* or Boy* or Girl* or Schoolchild* or School age* or School-age* Preschool* or Pre-school* or Kid* or Kindergartan* or Highschool* or Youth* or Young adult* or Young person or Young people or Preteen* or Teen* or Adolescen* or Juvenile* or Minor* or Puberty or Prepuberty or Pubescen* or Prepubescen* or Paediatric* or Pediatric*).ti.
40. (Infant* or Neonat* or Newborn or New born or Perinatal or Babies or Baby or Toddler* or Child* or Boy* or Girl* or Schoolchild* or School age* or School-age* or Preschool* or Pre-school* or Kid* or Kindergartan* or Highschool* or Youth* or Young adult* or Young person or Young people or Preteen* or Teen* or Adolescen* or Juvenile* or Minor* or Puberty or Prepuberty or Pubescen* or Prepubescen* or Paediatric* or Pediatric*).ab.
41. 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40
42. Caregivers/
43. Physicians/
44. Home Care Services/
45. Health Personnel/
46. (Carer* or Caregiver* or Parent* or Mother* or Father* or Famil* or Guardian* or Healthcare Professional* or Health care professional* or Health care support worker* or Healthcare Support Worker* or Doctor* or Nurse* or Consultant* or GP or General Practitioner* or Patient* or Pharmacist* or Hospice Staff or Practitioner* or Psychologist*).ti. or (Carer* or Caregiver* or Parent* or Mother* or Father* or Famil* or Guardian* or Healthcare Professional* or Health care professiona*l or Health care support worker* or Healthcare Support Worker* or Doctor* or Nurse* or Consultant* or GP or General Practitioner* or Patient* or Pharmacist* or Hospice Staff or Practitioner* or Psychologist*).ab.
47. 42 or 43 or 44 or 45 or 46
48. (End-of-life or End of Life or EOL or Palliat* or Dying or Life-limit* or Termina* or Life-threatening or ((Final or Advance* or Incurable) adj3 (ill* or disease* or condition*)) or ((Approach* or Close or Near* or Imminent* or Impending) adj3 Death) or Deathbed* or Death Bed* or Passing Away or Passing On or Expiring or Expiration or ((Advanced or Late or Last or End or Final or Terminal) adj1 (Phase* or Stage*)) or Hospice).ab.
49. (End-of-life or End of Life or EOL or Palliat* or Dying or Life-limit* or Termina* or Life-threatening or ((Final or Advance* or Incurable) adj3 (ill* or disease* or

condition*)) or ((Approach* or Close or Near* or Imminent* or Impending) adj3 Death) or Deathbed* or Death Bed* or Passing Away or Passing On or Expiring or Expiration or ((Advanced or Late or Last or End or Final or Terminal) adj1 (Phase* or Stage*)) or Hospice).ti.

50. 31 or 48 or 49
51. Pain/
52. Pain Management/
53. Medication Therapy Management/
54. (Pain* or Symptom* or Medic* management).ti. or (Pain* or Symptom* or Medic* management).ab.
55. 51 or 52 or 53 or 54
56. 41 and 47 and 50 and 55

Database: PsycINFO via EBSCOhost

#	Query	Limiters/Expanders
S15	S4 AND S7 AND S11 AND S14	
S14	S12 OR S13	
S13	TI (Pain* OR Symptom* OR "Medic* management") OR AB (Pain* OR Symptom* OR "Medic* management")	
S12	DE "Pain" OR "Pain Management" OR "Symptoms"	
S11	S8 OR S9 OR S10	
S10	TI (("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR "((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* or Imminent* or Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration) OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice OR "Life Support Care" OR "Advanced Care Planning")) OR AB (("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR "((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* or Imminent* or Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR Passing On" OR "Expiring" OR Expiration) OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice OR "Life Support Care" OR "Advanced Care Planning"))	
S9	SO ("Journal of palliative care" OR "Journal of palliative medicine" OR "Hospice journal physical psychosocial & pastoral care of the dying" OR "Supportive care in medicine" OR "Palliative medicine" OR "Palliative & supportive care" OR "Journal of supportive oncology" OR "Journal of social work in end of life & palliative care" OR "Journal of pain and symptom management" OR "Journal of pain & palliative care pharmacotherapy" OR "International journal of palliative nursing" OR "Death studies" OR "Death education" OR "American journal of hospice care" OR "American journal of hospice & palliative medicine" OR "Omega journal of death & dying")	
S8	DE ("Death Attitudes" OR "Bereavement" OR "Hospice" OR "Palliative Care" OR "Terminally Ill Patients")	
S7	S5 OR S6	
S6	TI ((Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner*" OR Psychologist*)) OR AB ((Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner*" OR Psychologist*))	
S5	DE ("Caregivers") OR ("Physicians") OR ("Home Care") OR ("Health Personnel")	

S4 S1 OR S2 OR S3

S3 KW (Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool* OR Youth# OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*)

S2 TI ((Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool* OR Youth# OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*)) OR AB ((Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool# OR Youth# OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*))

S1 AG (child* or school* or preschool* or adolescen* or infant* or neonat*)

Database: Web of Science Core Collection

#5. (#4 AND #3 AND #2 AND #1) AND LANGUAGE: (English) Indexes=SCI-EXPANDED, SSCI, A&HCI, BKCI-S, BKCI-SSH, ESCI Timespan=All years

#4. TS=(Pain* OR Symptom* OR "Medic* management") Indexes=SCI-EXPANDED, SSCI, A&HCI, BKCI-S, BKCI-SSH, ESCI Timespan=All years

#3. SO=(AMERICAN JOURNAL OF HOSPICE PALLIATIVE MEDICINE OR JOURNAL OF PALLIATIVE CARE OR JOURNAL OF PALLIATIVE MEDICINE OR PALLIATIVE MEDICINE OR PALLIATIVE SUPPORTIVE CARE OR JOURNAL OF PAIN PALLIATIVE CARE PHARMACOTHERAPY OR SUPPORTIVE CARE IN CANCER OR THE JOURNAL OF SUPPORTIVE ONCOLOGY OR DEATH EDUCATION OR DEATH STUDIES OR AMERICAN JOURNAL OF HOSPICE CARE) OR TS=(End-of-life OR End of Life OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR Life-threatening OR ((Final OR Advance* OR Incurable) NEAR/3 (ill* OR disease$ OR condition$)) OR ((Approach* OR Close* OR Near* or Imminent* or Impending) NEAR/3 (Death)) OR Deathbed* OR Death Bed OR Passing Away OR Passing On OR Expiring OR Expiration OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEAR/1 (Phase$ OR Stage$)) OR Hospice* OR Advanced Care Planning OR Life support care OR bereave*)

#2. TS=(Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*) Indexes=SCI-EXPANDED, SSCI, A&HCI, BKCI-S, BKCI-SSH, ESCI Timespan=All years

#1. TS=(Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy$ OR Girl$ OR Schoolchild* OR "School age$" OR School-age$ OR Preschool* OR Pre-school* OR Kid$ OR Kindergartan$ OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*) Indexes=SCI-EXPANDED, SSCI, A&HCI, BKCI-S, BKCI-SSH, ESCI Timespan=All years

Database: ProQuest Dissertations & Theses Database

1. mainsubject.Exact("children & youth") OR ab(Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy* OR Girl* OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid? OR Kindergartan* OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor? OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*) OR ti(Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler OR Child* OR Boy* OR Girl* OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR "Pre-school" OR Kid? OR Kindergartan* OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor? OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR OR Paediatric* OR Pediatric*)

2. mainsubject.Exact("caregivers") OR ab(Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*) OR ti(Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*)

3. mainsubject.Exact("palliative care") OR ti(End-of-life OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR ((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* OR Imminent* OR Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice OR "Advanced Care Planning" OR "Bereav* OR " Life Support Care") OR ab(End-of-life OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR ((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* OR Imminent* OR Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice OR "Advanced

Care Planning" OR "Bereav* OR " Life Support Care")

4. mainsubject.Exact("pain") OR ab(pain* OR symptom* OR "Medic* management) OR ti(pain* OR symptom* OR "Medic* management)

5. #1 OR #2 OR #3 OR #4 Limit to English language

Database: OpenGrey

#1 lang:"en" (Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy* OR Girl* OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid? OR Kindergartan* OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor? OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*) **AND** (Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*) **AND** (End-of-life OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR ((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* OR Imminent* OR Impending) N3 (Death)) OR Deathbed* OR "Death Bed*" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEAR/1 (Phase# OR Stage#)) OR Hospice OR "Advanced Care Planning" OR "Bereav* OR "Life Support Care") **AND** (Pain* OR Symptom* OR "Medic* management")

Database: Evidence Search Health and Social Care (NICE)

S1 Infant* Caregiver* "End of Life" Pain*

S2 Infant* "End of Life" Pain*

S3 "End of Life" Pain*

S4 "End of Life" Symptom*

Key:
Ab = abstract
DE = subjects [exact]
Diskw = Index term (key term)
Mainsubject Exact = Subject Heading
MH = Subject Heading
MeSH = Medical Subject Heading
MA = Medical Subject Heading
SO = Journal title
TS; TI = Title

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Reported (Section)
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Yes (Title)
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Yes (Abstract, registration number)
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Yes (Title page)
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Yes (Contributions)
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	Yes (Amendments)
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Yes (Funding statement)
Sponsor	5b	Provide name for the review funder and/or sponsor	Yes (Funding statement)
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Yes (Introduction, Rationale)
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Yes (Introduction, Objectives)
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Yes (Methods, Eligibility criteria)
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Yes (Methods, Information sources)
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Yes (Methods, Search)
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Yes (Methods, Study records)
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Yes (Methods, Study records)

Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Yes (Methods, Study records)
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Yes (Methods, data items)
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Phenomenon of interest is defined. (Outcomes and prioritisation, Phenomenon of interest)
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Appraisal of study quality is described. (Outcomes and prioritisation, Appraisal of study quality)
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	Thematic synthesis will be applied. (Outcomes and prioritisation, Data synthesis)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	Data synthesis
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	Data synthesis
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	The ConQual approach will be adopted. (Outcomes and prioritisation, Confidence in the synthesised qualitative findings)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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BMJ Open

The barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in infants, children and young people at end-of-life: a mixed methods systematic review protocol

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The barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in infants, children and young people at end-of-life: a mixed methods systematic review protocol

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ABSTRACT

Introduction. This protocol describes the objective and methods of a systematic review of barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in infants, children and young people (ICYP) at end-of-life.

Methods and analysis. The Cochrane Library, PROSPERO, CINAHL, MEDLINE, PsycINFO, Web of Science Core Collection, ProQuest Dissertations & Theses Database, Evidence Search and OpenGrey will be electronically searched. Reference screening of relevant reviews and inquiries to researchers in the field will be undertaken. Studies will be selected if they apply qualitative, quantitative or mixed-methods designs to explore barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in ICYP at end-of-life.

Articles will be screened by title and abstract by one reviewer with a second reviewer assessing 10% of the articles. Both reviewers will read and screen all remaining potentially relevant articles. For included articles, one reviewer will extract study characteristics and one will check this.

Both reviewers will undertake independent quality assessments of included studies using established and appropriate checklists including The Critical Appraisal Skills Programme Qualitative Checklist; The evaluative criteria of credibility, transferability, dependability and confirmability; The Quality Assessment Tool for Quantitative Studies, and The Mixed Methods Appraisal Tool. Data synthesis methods will be decided after data extraction and assessment.

Ethics and dissemination. This review will inform our understanding of symptom management in ICYP at end-of-life. The findings will be reported in a peer-reviewed journal and presented at conferences. The study raises no ethical issues.

Trial registration number CRD42019124797.

ARTICLE SUMMARY

Strengths and Limitations Of This Study

- This systematic review can give us a greater understanding of symptom management in paediatric palliative care - highlighted as a research priority by the National Institute for Health and Care Excellence (NICE) and could inform the design of evidence-based interventions to support more effective medicine management
- The systematic review will follow robust guidelines and the quality of included articles will be assessed using validated tools
- The heterogeneity of the included studies, which may use qualitative, quantitative or mixed-methods approaches, could limit the overall data synthesis

KEYWORDS

Paediatric Palliative Care
Pain Management
Qualitative Research
Symptom management
End of life care

INTRODUCTION

Approximately 49,000 infants, children and young people (ICYP) are living with a life-threatening or life-limiting condition in the UK [1]. These include congenital anomalies; cancer; and neurological, haematological, respiratory, genitourinary, perinatal, metabolic, circulatory and gastrointestinal conditions. There were nearly 3000 child deaths due to medical conditions in England in 2017, of which over 2350 were due to a known life-limiting condition or neonatal death [2].

ICYP's palliative care needs often differ to those of adults, and the diversity of conditions in this population means that practitioners must manage a wide range of complex symptoms [3]. A particular challenge is managing continuous 'background' pain as well as bouts of severe, sudden-onset 'breakthrough pain', both of which are common in ICYP with a terminal illness [4] and are known to be under-assessed and undertreated [5].

Family carers play a vital role in supporting ICYP with a terminal illness, allowing patients to be cared for and die at home where possible. However, there is little research on carers' experiences of administering medicines for symptom relief to ICYP receiving palliative care. Managing symptoms such as pain is potentially difficult for carers of children at home. They may lack the necessary skills and confidence required to balance symptom relief and side-effects while fear of errors can lead to insufficient or inappropriate doses of analgesics. Families will move ICYP away from their preferred place of care if symptoms, including pain, are not managed effectively [6].

Community nurses and doctors may also lack the skills and experience required to support carers. A systematic review found that GPs experience anxiety regarding their competency to deliver appropriate palliative care [7] while healthcare support workers providing end-of-life care in the community require training in palliative care to cope with emotionally demanding situations [8].

The recent National Institute for Health and Care Excellence (NICE) guideline [9] is based on evidence from 20 systematic reviews investigating different aspects of planning and management of end-of-life care for ICYP with life-limiting conditions. These include reviews on what information is perceived as helpful and what social and practical support is effective for ICYP and their caregivers. The findings indicate that timely, honest and consistent information that meets individuals' needs (e.g. developmentally appropriate for patients) is beneficial, including information about access to services, community and medical resources. One study also found that parents wanted information on how to use equipment that a child/ young person required [10]. However, symptom management was not identified as a major theme in these reviews [9].
Four other reviews looked at the effectiveness of pharmacological and non-pharmacological interventions for pain management, agitation, respiratory distress and seizures [9]. Only the pain management review found any studies that met the inclusion criteria and all of these involved pharmacological interventions only.

Although these reviews provide essential guidance in managing end-of-life care for ICYP, to our knowledge no systematic review has examined the barriers and facilitators to symptom management in ICYP at end-of-life for healthcare professionals, caregivers and patients. NICE highlights pain management in palliative care as a research priority [9] and a greater understanding of this could inform the design of evidence-based interventions to support more effective medicine management.

Objectives

The main objective of this systematic review is to identify and synthesise the existing literature that explores the barriers and facilitators experienced by children and young people themselves and their carers and healthcare professionals when managing symptoms in ICYP at end-of-life.

METHODS

This protocol follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) [11] guidelines (online Supplementary File 1—PRISMA-P checklist) and is registered (ID CRD42019124797)[12] on PROSPERO, an international register of systematic reviews [13]. Any changes to the protocol will be recorded on PROSPERO.

The reporting of the systematic review will be informed by the Centre for Reviews and Dissemination [14] and the Cochrane Qualitative Research Methods Group guidelines [15] and will follow the Enhancing Transparency in Reporting the Synthesis of Qualitative Research (ENTREQ) [16] and the PRISMA statements [11] for reporting systematic reviews (see online Supplementary File 2). In the case of sections applicable to qualitative systematic reviews that are included in PRISMA, but are not covered by ENTREQ, these will also be reported.

Eligibility Criteria

The criteria outlined below will be used for study selection. Following the recommendations of the Cochrane Qualitative and Implementation Methods Group Guidance [15], we have used STARLITE (Sampling Strategy, Type of study, Approaches, Range of years, Limits, Inclusions and exclusions, Terms used, Electronic sources [17]) to report our search methods.

Sampling strategy: This review will consider all studies carried out worldwide that involve carers, healthcare professionals or patients' views on symptom management in ICYP up to the age of 24 years at end-of-life care. A cut-off age of 24 years will be used since this corresponds to adolescent growth and current understandings of this stage in life [18].

Type of study: The review will consider qualitative, quantitative and mixed-method studies including questionnaires, surveys, interviews, focus groups, case studies, and observations. Trials, cohort and intervention studies that assess barriers and facilitators to symptom management will all be considered.

Approaches: In addition to searching electronic databases, the search strategy will include hand searching of reference lists of identified eligible studies. Finally, active researchers in the field who have contributed to this literature will be contacted.

Range of Years: Studies published from the inception of each database will be included.

Limits: Articles written in any language other than English due to a lack of funding for adequate translation; masters theses; conference abstracts; reviews.

Inclusions: Barriers and facilitators experienced by carers, healthcare professionals, and the patients themselves, when managing symptoms in ICYP with terminal illnesses receiving palliative care and/or at end-of-life. All definitions of 'end-of-life' will be included since there are a wide variety of definitions and there is a paucity of research in ICYP symptom management in this area. Data on carers; healthcare professionals; and patients' views, attitudes, opinions, perceptions, beliefs or feelings will be included.

Exclusions: Studies that focus only on the effectiveness of pharmacological treatments for symptom management will be excluded.

Searches

Electronic sources: The Cochrane Library and PROSPERO will be searched initially to check for any existing systematic reviews on this topic. As recommended by the Cochrane Qualitative and Implementation Methods Group [15], CINAHL (Cumulative Index of Nursing and Allied Health Literature) via Ebsco and Ovid MEDLINE will be searched, as well as PsycINFO via Ebsco and the Web of Science Core Collection. To identify any additional unpublished work, the ProQuest Dissertations & Theses Database; Evidence Search; and OpenGrey will also be searched. The search strategy will include hand searching of reference lists of eligible studies for additional records. All searches will be run during February 2019.

Search terms used: A search strategy was developed based on the 'Managing Pain' search strategy used in the NICE guideline 'End-of-life Care for Infants, Children and Young people with Life-limiting Conditions: Planning and Management (NG61) [9]. The strategy incorporated search terms in four blocks: 1. 'Patient Population'; 2. 'Caregivers and Patients'; 3. 'End-of-life'; and 4. 'Pain and Symptoms.' Additional searches used in the Palliative Care Search Filter [19] were also incorporated into Block 3 for each database.

Combinations of keywords, text words, Medical Subject Headings (MeSH) and other terms relevant to the four blocks were selected for each database to optimise the search sensitivity and specificity. The search strategy was piloted and adapted for each database. A professional healthcare research librarian assisted in the development of the strategy. Please see Supplementary File 3 for the full search strategy for each database.

Data Management

All records and data will be saved to Endnote X8 [20]. This software will be used to identify potential duplicates. The researchers will check this and remove all confirmed duplicated.

Selection Process

Articles will be screened by title and abstract by one reviewer (KG) with a second reviewer (SH) assessing 10% of the articles, randomly selected. At this stage, articles will be judged as either a) 'not relevant' or b) 'potentially relevant'. Both reviewers will read and screen all remaining potentially relevant articles. The reviewers will independently apply the criteria at all stages of the selection process. Inter-coder agreement will be evaluated using Cohen's kappa coefficient. A minimum kappa value of 0.75 will be taken to represent high agreement [21].

The full text of all remaining potentially relevant articles will then be obtained. If the relevance of a study cannot be ascertained from the abstract, then the full

article will be obtained. The full articles will be read by two reviewers independently (KG and SH) to make the final decision about whether they should be chosen for inclusion in the review. A third reviewer (CL) will resolve any uncertainties. Additional information will be sought from authors if necessary at the stage of full-text assessment.

Data Collection Process and Items

The following information will be extracted into a piloted data collection form for all included studies: Study aims; patient population (infant/child/adolescent); participant population (patient/caregiver/healthcare professional); inclusion and exclusion criteria; sample size; recruitment; design; intervention and comparator group (where applicable); date and duration of data collection; setting; country; data collection; analysis methods; data describing the participants' views/experiences of barriers and facilitators to symptom management. For qualitative data, the authors' interpretations (presented through themes and categories) will represent these data [22]. KG will extract this information and SH will check it, with any disagreements resolved through discussion with CL.

Quality assessment (including risk of bias)

A quality appraisal of included studies will be conducted independently by two reviewers (KG and SH). Disagreements will be resolved by discussion between KG and SH, with CL if required.

Three checklists will be used depending on each study's design. These were chosen since they are all validated and have been used in published systematic reviews within healthcare research. For each study type, Cohen's kappa coefficient will be used to measure inter-rater agreement between the two reviewers. A minimum kappa value of 0.75 will be taken to represent high agreement with disagreements resolved via discussion with CL.

As recommended by the Cochrane Qualitative and Implementation Methods Group [15], we will not calculate total quality scores across domains since domains of quality are not equal. Instead, KG, SH and CL will determine how each study's methodological limitations affect confidence in the findings via discussion. We will not exclude studies based on poor quality but will record and highlight methodological issues.

Qualitative studies will be quality appraised using the *Critical Appraisal Skills Programme for Qualitative Studies (CASP)* [23]. The CASP assesses clarity of research aims; research design; recruitment methods; data collection; relationships between participants and researchers; ethical issues, analyses; description of findings; and valuableness of the research. It is comprised of nine closed questions (e.g. "Was there a clear statement of the aims of the research?" Yes/Can't tell/No) and one open-ended question ("How valuable is the research?"). For each question, there is the option to add comments to explain the reasoning for each rating. Currently, the CASP is the most frequently used qualitative research synthesis tool in the Cochrane Library and World Health Organisation guideline research [24] and has been used in similar systematic reviews assessing barriers and facilitators within healthcare e.g.[25 26]. However, because the CASP tool does not address aspects of the research validity and can favour papers that are less insightful as long as they comply with 'expectations of research practice' [27], in addition, the evaluative criteria of credibility, transferability, dependability and confirmability [28] will be applied. Included studies will be assessed as to whether they apply the techniques suggested for ensuring study quality according to Guba and Lincoln's [28] criteria i.e. prolonged engagement, persistent observation, peer review, triangulation, negative case analysis, referential adequacy and member checking to ensure credibility; thick

description for transferability; inquiry audit for dependability; confirmability audit, audit trail, triangulation and reflexivity to ensure confirmability. Studies will be rated as 'high quality' if they meet at least three of the four criteria, 'medium quality' if they meet two of the criteria and 'low quality' if they meet one or none.

The Quality Assessment Tool for Quantitative Studies (QATQS) will be used to assess all clinical studies with or without randomisation and control groups, including quasi-experimental and before-and-after studies [29]. The QATQS is comprised of 22 closed questions and an overall rating of strong, moderate or weak in eight sections: selection bias; study design; confounders; blinding; data collection; withdrawals and dropouts; intervention integrity; analysis. It has been shown to be a valid tool for assessing quality; comparing studies and addressing threats to validity of findings [30].

The Mixed Methods Appraisal Tool (MMAT-Version 11) will be used to assess the quality of any mixed methods studies [31]. This tool consists of five closed questions assessing the research question; research design; integration of qualitative and quantitative methods; integration of qualitative and quantitative data; and consideration of methodological limitations in mixed methods studies. As reported by the Cochrane Qualitative and Implementation Methods Group, this tool has been used widely in systematic reviews and has the advantage of being able to assess interdependent qualitative and quantitative elements of mixed-methods research [24].

Outcomes and Prioritisation

The main outcomes sought are carers'; healthcare professionals'; and patients' (CYP) views on the barriers and facilitators to effective symptom management in ICYP at end-of-life.

Data Synthesis

Although it is unlikely that the majority of included studies will be quantitative, if this is the case then random-effects meta-analysis will be conducted to synthesise group means and standard deviation from individual studies using Comprehensive Meta-Analysis (CMA) version 3 [32].

For meta-analysis to be conducted, data must be available from two or more eligible studies reporting similar barriers or facilitators. The studies must report the number of participants reporting that barrier/facilitator and the total number of valid participant responses for that survey item. A random-effects model will be used for all analyses since, unlike a fixed-effects model, this can be used when statistical heterogeneity (I^2) is present in the results of the included studies [33]. Where evidence of statistically significant heterogeneity is present, sensitivity analyses will be conducted where possible to verify the robustness of the study conclusions, assessing the impact of methodological quality, study design, sample size and the potential effects of missing data. We will use funnel plots to detect potential reporting biases and small-study effects where data is available from 10 or more studies [34].

If the included studies are all qualitative or a combination of quantitative and qualitative, there are several approaches that could be taken for data synthesis. Some of the most commonly used methods to synthesise qualitative health research include thematic analysis [35]; grounded theory [36] and meta-ethnography [37 38]. However, there is no consensus on the best approach, which will depend on the type and number of included studies [39] and the form and nature of the research question [38]. As such, we will make a final decision on the most appropriate method after selecting and quality assessing the included articles, as

recommended by the Cochrane Qualitative and Implementation Methods Group [39].

We will first analyse and synthesise data related to the experience of patients, care providers and healthcare professionals separately before deciding whether it is appropriate to aggregate data between these groups. These data will likely include themes, concepts and categories of information. If data are relatively 'thin' then we will consider using thematic synthesis to undertake line-by-line coding and development of descriptive and analytic themes. If the included articles include sufficient 'thick' data (e.g. details about the context and background of the studies and participants [40]), we will consider a more interpretative approach such as meta-ethnography [37]. This method goes beyond aggregating data to generate new interpretations of the findings.

As recommended by the Cochrane Qualitative and Implementation Methods Group [24] the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative research [41]) will be used to summarise our confidence in synthesised qualitative findings (e.g. in the themes that we identify). The CERQual is made up of four key components i.e., methodological limitations of included studies, coherence of the review finding; adequacy of the data contributing to a review finding; relevance of the included studies to the review question. After assessing each of the four components, overall confidence will be graded as high, moderate, low, or very low. The barriers and facilitators to symptom management will be divided into overarching themes for each group (patients; healthcare professionals; carers); and presented in a matrix along with our CERQual assessment of confidence in the evidence of each theme and an explanation of this assessment.

The GRADE guidelines [42] will be used to appraise the quality of any quantitative findings. The GRADE guidelines include four elements for which quantitative findings will be rated against: risk of bias ('Study limitations'), inconsistency, indirectness, imprecision, publication bias.

Patient and public involvement

Consultation with young people, parents and health care professionals has been used to determine their perception of the barriers and facilitators they experience when managing symptoms in ICYP at end-of-life. It is based on their perspectives that this systematic review was deemed to be timely and crucial to conduct to inform further research work. Moreover, patient and public involvement (PPI) is represented in the authorship (MJ) of this manuscript. MJ is the PPI representative at the UK National Institute for Health Research (NIHR) Pain and Palliative Care Clinical Studies Group-Children. MJ is a parent of four children, one of whom died from T-cell acute lymphoblastic leukaemia at the age of 12. She has supported many families of children with cancer including those receiving palliative and end-of-life care.

DISCUSSION

This systematic review will be the first to synthesise and report barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in ICYP at end-of-life**.** The dearth and heterogeneity of the included studies, which may use qualitative, quantitative or mixed-methods approaches, could limit the overall data synthesis we are able to conduct. As we expect there to be a lack of suitable studies, they will not be excluded on the basis of quality, which may limit the confidence in our findings. The review findings will be used to inform our ongoing work to develop a structured

educational tool to support carers and healthcare professionals to administer pain and symptom relief to ICYP at the end-of-life.

Ethics and dissemination
As this is a systematic review of published literature, ethical approval will not be sought. We will publish the protocol and our findings in peer-reviewed journals aimed at paediatric palliative care clinicians and researchers as well as health commissioners. We will present our work at the growing numbers of national and international meetings focused on paediatric palliative care and pain.

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Author Contributions
EH, RH, MJ, IW and CL conceived the idea, planned and designed the study protocol. KG, SH, DES planned the data extraction and statistical analysis and wrote the first draft; JB, LB and SJ provided critical insights. All authors have approved and contributed to the final written manuscript.

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Competing Interests
None declared.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Reported (Section)
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Yes (Title)
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Yes (Abstract, registration number)
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Yes (Title page)
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Yes (Contributions)
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	Yes (Amendments)
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Yes (Funding statement)
Sponsor	5b	Provide name for the review funder and/or sponsor	Yes (Funding statement)
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Yes (Introduction, Rationale)
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Yes (Introduction, Objectives)
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Yes (Methods, Eligibility criteria)
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Yes (Methods, Information sources)
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Yes (Methods, Search)
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Yes (Methods, Study records)
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Yes (Methods, Study records)

Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Yes (Methods, Study records)
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Yes (Methods, data items)
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Phenomenon of interest is defined. (Outcomes and prioritisation, Phenomenon of interest)
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Appraisal of study quality is described. (Outcomes and prioritisation, Appraisal of study quality)
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	Thematic synthesis will be applied. (Outcomes and prioritisation, Data synthesis)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	Data synthesis
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	Data synthesis
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	The ConQual approach will be adopted. (Outcomes and prioritisation, Confidence in the synthesised qualitative findings)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

PRISMA Statement: Recommended items to address in Systematic Reviews and Meta-Analyses

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	

Section/topic	#	Checklist item	Reported on page #
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and	

Section/topic	#	Checklist item	Reported on page #
		confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

ENTREQ Statement: Recommended items to address in a synthesis of qualitative research.

No	Item	Guide and description
1	Aim	State the research question the synthesis addresses.
2	Synthesis methodology	Identify the synthesis methodology or theoretical framework which underpins the synthesis, and describe the rationale for choice of methodology.
3	Approach to searching	Indicate whether the search was pre-planned or iterative.
4	Inclusion criteria	Specify the inclusion/exclusion criteria.
5	Data sources	Describe the information sources used and when the searches conducted; provide the rationale for using the data sources.
6	Electronic Search strategy	Describe the literature search.
7	Study screening methods	Describe the process of study screening and sifting.
8	Study characteristics	Present the characteristics of the included studies
9	Study selection results	Identify the number of studies screened and provide reasons for study exclusion.
10	Rationale for appraisal	Describe the rationale and approach used to appraise the included studies or selected findings.
11	Appraisal items	State the tools, frameworks and criteria used to appraise the studies or selected findings.
12	Appraisal process	Indicate whether the appraisal was conducted independently by more than one reviewer and if consensus was required.
13	Appraisal results	Present results of the quality assessment and indicate which articles, if any, were weighted/excluded based on the assessment and give the rationale.
14	Data extraction	Indicate which sections of the primary studies were analysed and how were the data extracted from the primary studies.

15	Software	State the computer software used, if any.
16	Number of reviewers	Identify who was involved in coding and analysis.
17	Coding	Describe the process for coding of data.
18	Study comparison	Describe how were comparisons made within and across studies.
19	Derivation of themes	Explain whether the process of deriving the themes or constructs was inductive or deductive.
20	Quotations	Provide quotations from the primary studies to illustrate themes/constructs, and identify whether the quotations were participant quotations of the author's interpretation.
21	Synthesis output	Present rich, compelling and useful results that go beyond a summary of the primary studies.

From: Tong A, Flemming K, McInnes E, Oliver S, Craig .(2012). Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. BMC Medical Research Methodology, 12(1):181.

The barriers and facilitators experienced by patients, carers and healthcare professionals when managing symptoms in infants, children and young people at end-of-life: a mixed methods systematic review protocol

Search Strategy (Searched February 2019)

Database: The Cochrane Library

ID	Search
#1	MeSH descriptor: [Infant] explode all trees
#2	MeSH descriptor: [Child] explode all trees
#3	MeSH descriptor: [Adolescent] explode all trees
#4	MeSH descriptor: [Pediatrics] explode all trees
#5	MeSH descriptor: [Puberty] explode all trees
#6	(Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy* OR Girl* OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid* OR Kindergartan* OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* or Prepubescen* OR Paediatric* OR Pediatric*):ti,ab,kw (Word variations have been searched)
#7	MeSH descriptor: [Caregivers] explode all trees
#8	(Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*):ti,ab,kw (Word variations have been searched)
#9	MeSH descriptor: [Palliative Care] explode all trees
#10	MeSH descriptor: [Terminal Care] explode all trees
#11	MeSH descriptor: [Advance Care Planning] explode all trees
#12	MeSH descriptor: [Attitude to Death] explode all trees
#13	MeSH descriptor: [Bereavement] explode all trees
#14	("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR "Life-limit*" OR Termina* OR "Life-threatening" OR Deathbed* OR "Death Bed*" OR "Passing Away" OR "Passing On" OR Expiring OR Expiration OR Hospice):ti,ab,kw (Word variations have been searched)
#15	((Final OR Advance* OR Incurable) NEXT (ill* OR disease? OR condition?)):ti,ab,kw (Word variations have been searched)
#16	((Approach* OR Close* OR Near* or Imminent* or Impending) NEAR/3 (death)):ti,ab,kw (Word variations have been searched)
#17	((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase? OR Stage?)):ti,ab,kw (Word variations have been searched)

#18 MeSH descriptor: [Death] this term only

#19 MeSH descriptor: [Hospices] this term only

#20 MeSH descriptor: [Life Support Care] this term only

#21 MeSH descriptor: [Terminally Ill] this term only

#22 palliat*

#23 hospice*

#24 terminal care

#25 MeSH descriptor: [Pain] explode all trees

#26 MeSH descriptor: [Signs and Symptoms] explode all trees

#27 MeSH descriptor: [Disease Management] explode all trees

#28 (Pain OR Symptom OR Medicine Management):ti,ab,kw (Word variations have been searched)

#29 #1 OR #2 OR #3 OR #4 OR #5 OR #6

#30 #7 OR #8

#31 #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24

#32 #25 OR #26 OR #27 OR #28

#33 #29 AND #30 AND #31 AND #32 (Word variations have been searched)

Database: PROSPERO

Line Search for

1. MeSH DESCRIPTOR Infant EXPLODE ALL TREES
2. MeSH DESCRIPTOR Child EXPLODE ALL TREES
3. MeSH DESCRIPTOR Adolescent EXPLODE ALL TREES
4. MeSH DESCRIPTOR Pediatrics EXPLODE ALL TREES
5. MeSH DESCRIPTOR Puberty EXPLODE ALL TREES
6. MeSH DESCRIPTOR Caregivers EXPLODE ALL TREES
7. MeSH DESCRIPTOR Terminal Care EXPLODE ALL TREES
8. MeSH DESCRIPTOR Palliative Care EXPLODE ALL TREES
9. MeSH DESCRIPTOR Attitude to Death EXPLODE ALL TREES
10. MeSH DESCRIPTOR Hospice Care EXPLODE ALL TREES
11. MeSH DESCRIPTOR Bereavement EXPLODE ALL TREES
12. MeSH DESCRIPTOR Hospices EXPLODE ALL TREES
13. MeSH DESCRIPTOR Death EXPLODE ALL TREES
14. MeSH DESCRIPTOR Life Support Care EXPLODE ALL TREES
15. MeSH DESCRIPTOR Terminally Ill EXPLODE ALL TREES
16. MeSH DESCRIPTOR Pain EXPLODE ALL TREES
17. MeSH DESCRIPTOR Signs and Symptoms EXPLODE ALL TREES
18. MeSH DESCRIPTOR Disease Management EXPLODE ALL TREES
19. MeSH DESCRIPTOR Pain Management EXPLODE ALL TREES
20. #1 OR #2 OR 3 OR #4 OR #5
21. #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
22. #16 OR #17 OR #18 OR#19
23. #6 AND #18 AND #19 AND #20
24. #18 AND #19 AND #20

Database: CINAHAL via EBSCOhost

#	Query	Limiters/Expanders
S16	S4 AND S7 AND S12 AND S15	
S15	S13 OR S14	
S14	(MH "Pain+") OR (MH "Pain Management") OR (MH "Medication Management") OR (MH Symptoms)	
S13	TI ((Pain* OR Symptom* OR "Medic* management")) OR AB ((Pain* OR Symptom* OR "Medic* management"))	
S12	S8 OR S9 OR S10 OR S11	
S11	SO ("Journal of palliative care" OR "Journal of palliative medicine" OR "Hospice journal physical psychosocial & pastoral care of the dying" OR "Supportive care in cancer" OR "Palliative medicine" OR "Palliative & supportive care" OR "Journal of supportive oncology" OR "Journal of social work in end of life & palliative care" OR "Journal of pain and symptom management" OR "Journal of pain & palliative care pharmacotherapy" OR "International journal of palliative nursing" OR "Death studies" OR "Death education" OR "American journal of hospice care" OR "American journal of hospice & palliative medicine" OR "Omega journal of death & dying")	
S10	palliat* OR hospice* OR "terminal care"	
S9	(MH "Palliative Care") OR (MH "Life Support Care") OR (MH "Hospices") OR (MH "Death") OR (MH "Bereavement+") OR (MH "Attitude to Death+") OR (MH "Advance Care Planning+") OR (MH "Terminal Care+") OR (MH "Terminally Ill")	
S8	AB (("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR "((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* or Imminent* or Impending) N3 (Death)) OR Deathbed* OR "Death Bed*" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration) OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice)) OR TI (("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR "((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* or Imminent* or Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration) OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice))	
S7	S5 OR S6	
S6	AB ((Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner*" OR Psychologist*)) OR TI ((Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner*" OR Psychologist*))	

S5 (MH Caregivers) OR (MH Physicians) OR (MH "Home Health Care") OR (MH" Health Personnel")

S4 S1 OR S2 OR S3

S3 (TI (Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool* OR Youth? OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* or Prepubescen* OR Paediatric* OR Pediatric*)) OR (AB (Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool# OR Youth# OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*))

S2 (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") OR (MH "Infant+") OR (MH "Infant, Newborn") OR (MH Pediatrics+) OR (MH Puberty)

S1 AG (child* or school* or preschool* or adolescen* or infant* or neonat*)

Database: MEDLINE via OVID

1. exp advance care planning/
2. exp attitude to death/
3. exp bereavement/
4. Death/
5. Hospices/
6. Life Support Care/
7. Palliative Care/
8. exp terminal care/
9. Terminally Ill/
10. palliat$.af.
11. hospice$.af.
12. terminal care.af.
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. journal of palliative care.jn.
15. journal of palliative medicine.jn.
16. hospice journal physical psychosocial & pastoral care of the dying.jn.
17. supportive care in cancer.jn.
18. palliative medicine.jn.
19. palliative & supportive care.jn.
20. journal of supportive oncology.jn.
21. journal of social work in end of life & palliative care.jn.
22. journal of pain & symptom management.jn.
23. journal of pain & palliative care pharmacotherapy.jn.
24. international journal of palliative nursing.jn.
25. death studies.jn.
26. death education.jn.
27. american journal of hospice care.jn.
28. american journal of hospice & palliative medicine.jn.
29. omega journal of death & dying.jn.
30. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. 13 or 30
32. Child, Preschool/
33. exp child/
34. exp adolescence/
35. exp infant/

36. Infant, Newborn/
37. exp pediatrics/
38. Puberty/
39. (Infant* or Neonat* or Newborn or New born or Perinatal or Babies or Baby or Toddler* or Child* or Boy* or Girl* or Schoolchild* or School age* or School-age* Preschool* or Pre-school* or Kid* or Kindergartan* or Highschool* or Youth* or Young adult* or Young person or Young people or Preteen* or Teen* or Adolescen* or Juvenile* or Minor* or Puberty or Prepuberty or Pubescen* or Prepubescen* or Paediatric* or Pediatric*).ti.
40. (Infant* or Neonat* or Newborn or New born or Perinatal or Babies or Baby or Toddler* or Child* or Boy* or Girl* or Schoolchild* or School age* or School-age* or Preschool* or Pre-school* or Kid* or Kindergartan* or Highschool* or Youth* or Young adult* or Young person or Young people or Preteen* or Teen* or Adolescen* or Juvenile* or Minor* or Puberty or Prepuberty or Pubescen* or Prepubescen* or Paediatric* or Pediatric*).ab.
41. 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40
42. Caregivers/
43. Physicians/
44. Home Care Services/
45. Health Personnel/
46. (Carer* or Caregiver* or Parent* or Mother* or Father* or Famil* or Guardian* or Healthcare Professional* or Health care professional* or Health care support worker* or Healthcare Support Worker* or Doctor* or Nurse* or Consultant* or GP or General Practitioner* or Patient* or Pharmacist* or Hospice Staff or Practitioner* or Psychologist*).ti. or (Carer* or Caregiver* or Parent* or Mother* or Father* or Famil* or Guardian* or Healthcare Professional* or Health care professiona*l or Health care support worker* or Healthcare Support Worker* or Doctor* or Nurse* or Consultant* or GP or General Practitioner* or Patient* or Pharmacist* or Hospice Staff or Practitioner* or Psychologist*).ab.
47. 42 or 43 or 44 or 45 or 46
48. (End-of-life or End of Life or EOL or Palliat* or Dying or Life-limit* or Termina* or Life-threatening or ((Final or Advance* or Incurable) adj3 (ill* or disease* or condition*)) or ((Approach* or Close or Near* or Imminent* or Impending) adj3 Death) or Deathbed* or Death Bed* or Passing Away or Passing On or Expiring or Expiration or ((Advanced or Late or Last or End or Final or Terminal) adj1 (Phase* or Stage*)) or Hospice).ab.
49. (End-of-life or End of Life or EOL or Palliat* or Dying or Life-limit* or Termina* or Life-threatening or ((Final or Advance* or Incurable) adj3 (ill* or disease* or

condition*)) or ((Approach* or Close or Near* or Imminent* or Impending) adj3 Death) or Deathbed* or Death Bed* or Passing Away or Passing On or Expiring or Expiration or ((Advanced or Late or Last or End or Final or Terminal) adj1 (Phase* or Stage*)) or Hospice).ti.

50. 31 or 48 or 49
51. Pain/
52. Pain Management/
53. Medication Therapy Management/
54. (Pain* or Symptom* or Medic* management).ti. or (Pain* or Symptom* or Medic* management).ab.
55. 51 or 52 or 53 or 54
56. 41 and 47 and 50 and 55

Database: PsycINFO via EBSCOhost

#	Query	Limiters/Expanders
S15	S4 AND S7 AND S11 AND S14	
S14	S12 OR S13	
S13	TI (Pain* OR Symptom* OR "Medic* management") OR AB (Pain* OR Symptom* OR "Medic* management")	
S12	DE "Pain" OR "Pain Management" OR "Symptoms"	
S11	S8 OR S9 OR S10	
S10	TI (("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR "((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* or Imminent* or Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration) OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice OR "Life Support Care" OR "Advanced Care Planning")) OR AB (("End-of-life" OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR "((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* or Imminent* or Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR Passing On" OR "Expiring" OR Expiration) OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice OR "Life Support Care" OR "Advanced Care Planning"))	
S9	SO ("Journal of palliative care" OR "Journal of palliative medicine" OR "Hospice journal physical psychosocial & pastoral care of the dying" OR "Supportive care in medicine" OR "Palliative medicine" OR "Palliative & supportive care" OR "Journal of supportive oncology" OR "Journal of social work in end of life & palliative care" OR "Journal of pain and symptom management" OR "Journal of pain & palliative care pharmacotherapy" OR "International journal of palliative nursing" OR "Death studies" OR "Death education" OR "American journal of hospice care" OR "American journal of hospice & palliative medicine" OR "Omega journal of death & dying")	
S8	DE ("Death Attitudes" OR "Bereavement" OR "Hospice" OR "Palliative Care" OR "Terminally Ill Patients")	
S7	S5 OR S6	
S6	TI ((Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner*" OR Psychologist*)) OR AB ((Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner*" OR Psychologist*))	
S5	DE ("Caregivers") OR ("Physicians") OR ("Home Care") OR ("Health Personnel")	

S4 S1 OR S2 OR S3

S3 KW (Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool* OR Youth# OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*)

S2 TI ((Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool* OR Youth# OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*)) OR AB ((Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy# OR Girl# OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid# OR Kindergartan# OR Highschool# OR Youth# OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty or Prepuberty or Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*))

S1 AG (child* or school* or preschool* or adolescen* or infant* or neonat*)

Database: Web of Science Core Collection

#5. (#4 AND #3 AND #2 AND #1) AND LANGUAGE: (English) Indexes=SCI-EXPANDED, SSCI, A&HCI, BKCI-S, BKCI-SSH, ESCI Timespan=All years

#4. TS=(Pain* OR Symptom* OR "Medic* management") Indexes=SCI-EXPANDED, SSCI, A&HCI, BKCI-S, BKCI-SSH, ESCI Timespan=All years

#3. SO=(AMERICAN JOURNAL OF HOSPICE PALLIATIVE MEDICINE OR JOURNAL OF PALLIATIVE CARE OR JOURNAL OF PALLIATIVE MEDICINE OR PALLIATIVE MEDICINE OR PALLIATIVE SUPPORTIVE CARE OR JOURNAL OF PAIN PALLIATIVE CARE PHARMACOTHERAPY OR SUPPORTIVE CARE IN CANCER OR THE JOURNAL OF SUPPORTIVE ONCOLOGY OR DEATH EDUCATION OR DEATH STUDIES OR AMERICAN JOURNAL OF HOSPICE CARE) OR TS=(End-of-life OR End of Life OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR Life-threatening OR ((Final OR Advance* OR Incurable) NEAR/3 (ill* OR disease$ OR condition$)) OR ((Approach* OR Close* OR Near* or Imminent* or Impending) NEAR/3 (Death)) OR Deathbed* OR Death Bed OR Passing Away OR Passing On OR Expiring OR Expiration OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEAR/1 (Phase$ OR Stage$)) OR Hospice* OR Advanced Care Planning OR Life support care OR bereave*)

#2. TS=(Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*) Indexes=SCI-EXPANDED, SSCI, A&HCI, BKCI-S, BKCI-SSH, ESCI Timespan=All years

#1. TS=(Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy$ OR Girl$ OR Schoolchild* OR "School age$" OR School-age$ OR Preschool* OR Pre-school* OR Kid$ OR Kindergartan$ OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor* OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*) Indexes=SCI-EXPANDED, SSCI, A&HCI, BKCI-S, BKCI-SSH, ESCI Timespan=All years

Database: ProQuest Dissertations & Theses Database

1. mainsubject.Exact("children & youth") OR ab(Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy* OR Girl* OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid? OR Kindergartan* OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor? OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*) OR ti(Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler OR Child* OR Boy* OR Girl* OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR "Pre-school" OR Kid? OR Kindergartan* OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor? OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR OR Paediatric* OR Pediatric*)

2. mainsubject.Exact("caregivers") OR ab(Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*) OR ti(Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*)

3. mainsubject.Exact("palliative care") OR ti(End-of-life OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR ((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* OR Imminent* OR Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice OR "Advanced Care Planning" OR "Bereav* OR " Life Support Care") OR ab(End-of-life OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR ((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* OR Imminent* OR Impending) N3 (Death)) OR Deathbed* OR "Death Bed" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEXT (Phase# OR Stage#)) OR Hospice OR "Advanced

Care Planning" OR "Bereav* OR " Life Support Care")

4. mainsubject.Exact("pain") OR ab(pain* OR symptom* OR "Medic* management) OR ti(pain* OR symptom* OR "Medic* management)

5. #1 OR #2 OR #3 OR #4 Limit to English language

Database: OpenGrey

#1 lang:"en" (Infant* OR Neonat* OR Newborn OR New-born OR Perinatal OR Babies OR Baby OR Toddler* OR Child* OR Boy* OR Girl* OR Schoolchild* OR "School age*" OR School-age* OR Preschool* OR Pre-school* OR Kid? OR Kindergartan* OR Highschool* OR Youth* OR "Young adult*" OR "Young person" OR "Young people" OR Preteen* OR Teen* OR Adolescen* OR Juvenile* OR Minor? OR Puberty OR Prepuberty OR Pubescen* OR Prepubescen* OR Paediatric* OR Pediatric*) **AND** (Carer* OR Caregiver* OR Parent* OR Mother* OR Father* OR Famil* OR Guardian* OR "Healthcare Professional*" OR "Health care professional*" OR "Health care support worker*" OR "Healthcare Support Worker*" OR Doctor* OR Nurse* OR Consultant* OR GP OR "General Practitioner*" OR Patient* OR Pharmacist* OR "Hospice Staff" OR Practitioner* OR Psychologist*) **AND** (End-of-life OR "End of Life" OR EOL OR Palliat* OR Dying OR Life-limit* OR Termina* OR "Life-threatening" OR ((Final OR Advance* OR Incurable) N3 (ill* OR disease# OR condition#)) OR ((Approach* OR Close OR Near* OR Imminent* OR Impending) N3 (Death)) OR Deathbed* OR "Death Bed*" OR "Passing Away" OR "Passing On" OR "Expiring" OR Expiration OR ((Advanced OR Late OR Last OR End OR Final OR Terminal) NEAR/1 (Phase# OR Stage#)) OR Hospice OR "Advanced Care Planning" OR "Bereav* OR "Life Support Care") **AND** (Pain* OR Symptom* OR "Medic* management")

Database: Evidence Search Health and Social Care (NICE)

S1 Infant* Caregiver* "End of Life" Pain*

S2 Infant* "End of Life" Pain*

S3 "End of Life" Pain*

S4 "End of Life" Symptom*

Key:
Ab = abstract
DE = subjects [exact]
Diskw = Index term (key term)
Mainsubject Exact = Subject Heading
MH = Subject Heading
MeSH = Medical Subject Heading
MA = Medical Subject Heading
SO = Journal title
TS; TI = Title