

Right Review v3.0



Explanation and Elaboration

Before using the tool, please note that you will be prompted to answer a series of questions related to your planned evidence synthesis. We recommend that you conduct a preliminary search to gain background on the relevant literature for your chosen topic in order to accurately answer each question in the tool.

Kindly note that some of the suggested combination(s) of evidence synthesis methods are theoretically possible, but not currently used in practice (i.e., we could not locate published examples in the literature). In these cases, we advise users of the tool to use their own judgement when deciding whether or not to proceed with a given method.

<u>Purpose of tool</u>: Through nine guiding questions related to the content, conduct, and reporting of a review, the tool aims to recommend the most appropriate evidence synthesis method(s).

Please contact Dr. Andrea Tricco at <u>KnowledgeSynthesis@smh.ca</u> for more information on this tool.

Question 1: What is your goal or objective or key contribution to knowledge by doing the review?

Answer Response A: Assess the effectiveness and/or safety of interventions

- The **effectiveness of interventions** refers to the effects of an intervention under real life conditions (e.g., the effects of a vaccine in older adults), as compared to efficacy, which refers to the effect of an intervention in research studies, such as randomized controlled trials (e.g., the effects of a vaccine among participants in a randomized controlled trial).
 - Example 1: Ketamine as a component of multimodal analgesia for pain management in bariatric surgery: A systematic review and meta-analysis of randomized controlled trials

"Background: Anaesthesia in morbidly obese people is challenging with a high dose of opioid consumption.

Objective: This systematic review and meta-analysis of randomised controlled trials (RCTs) summaries evidence comparing ketamine to placebo for pain management after bariatric surgery."¹



 <u>Example 2: Intraoperative and postoperative outcomes of robot-assisted</u> cholecystectomy: a systematic review

"Background: Rapid adoption of robotic-assisted general surgery procedures . . . continues while questions remain about its benefits and utility.

Objective: To compare the clinical effectiveness of robot-assisted cholecystectomy for benign gallbladder disease as compared with the laparoscopic approach."²

Example 3: Splinting for carpal tunnel syndrome

"Background: Carpal tunnel syndrome (CTS) is a compression neuropathy of the median nerve causing pain and numbness and tingling typically in the thumb, index and middle finger . . . Splinting the wrist . . . using an orthosis is usually offered to people with mild-to-moderate findings, but its effectiveness remains unclear.

Objectives: To assess the effects (benefits and harms) of splinting for people with CTS."3

- The **safety of interventions** refers to the assessment of harms associated with an intervention. For example, determining the risk of adverse events when taking a blood pressure medication.
 - o Example 1: Systematic review: Comparative effectiveness and harms of treatments for clinically localized prostate cancer

"Background: The comparative effectiveness of localized prostate cancer treatments is largely unknown.

Objectives: To compare the effectiveness and harms of treatments for localized prostate cancer."4

Example 2: Fatal and non-fatal repetition of self-harm. Systematic review

"Background: Non-fatal self-harm frequently leads to non-fatal repetition and sometimes to suicide. We need to quantify these two outcomes of self-harm to help us to develop and test effective interventions.

Objectives: To estimate rates of fatal and non-fatal repetition of self-harm."5

o <u>Example 3: Khat (Catha edulis): A systematic review of evidence and literature</u> pertaining to its harms to UK users and society

"Background: Khat (*Catha edulis*) is a woody plant cultivated predominantly in north east Africa and the Arabian Peninsula . . . The traditional use of khat may be considered largely functional – to assist with religious studies, arduous work demands, food shortages, and social cohesion, and to self medicate for a range of ailments including depression.



Objectives: To collate and evaluate systematically evidence relating to physiological harms (physical and mental) caused by, or associated with, khat use in the UK. To compare evidence of societal harms caused by/ associated with khat use between countries where khat is legal and countries where it is controlled. To distinguish between evidence of causal relationships and evidence of associative relationships pertaining to khat harms. To identify evidence gaps relating to harms caused by/associated with khat use in the UK."⁶

Answer Response B: Assess the burden of illness, monetary costs alone or the costeffectiveness of interventions

- **Cost studies** examine monetary cost, or direct financial expenditures, related to diseases or health conditions, such as the costs of care for individuals with HIV.
 - o Example 1: The Cost of Atrial Fibrillation: A Systematic Review

"Background: Atrial fibrillation (AF) is the most common cardiac arrhythmia, with an increasing incidence and prevalence because of progressively aging populations. Costs related to AF are both direct and indirect.

Objectives: This systematic review aims to identify the main cost drivers of the illness, assess the potential economic impact resulting from changes in care strategies, and propose interventions where they are most needed."⁷

<u>Example 2: Safe Healthcare Facilities: A Systematic Review on the Costs of</u>
 <u>Establishing and Maintaining Environmental Health in Facilities in Low- and Middle-Income Countries</u>

"Background: A hygienic environment is essential to provide quality patient care and prevent healthcare-acquired infections. Understanding costs is important to budget for service delivery, but costs evidence for environmental health services (EHS) in healthcare facilities (HCFs) is lacking.

Objective: To evaluate the costs of establishing, operating, and maintaining EHS in HCFs in low- and middle-income countries (LMICs)."8

- Burden of illness studies aim to quantify the impact of a particular disease or health
 condition on a population. In an economic context, this type of study assesses both the
 direct and indirect effects of the disease (i.e., the economic burden of a specific condition
 from both a societal and individual perspective).
 - <u>Example 1: Epidemiology and Economic Burden of Chikungunya: A Systematic</u>
 <u>Literature Review</u>

"Background: Chikungunya (CHIK) is a re-emerging viral infection endemic in tropical and subtropical areas. While the typical clinical presentation is an acute febrile syndrome, long-term articular complications and even death can occur.



Objective: This review characterizes the global epidemiological and economic burden of chikungunya."⁹

o <u>Example 2: Burden of Illness in People with Alzheimer's Disease: A Systematic</u> Review of Epidemiology, Comorbidities and Mortality

"Background: Alzheimer's disease (AD) is the most common neurodegenerative disease worldwide, and an updated quantification of its impact on morbidity, disability, and mortality is warranted . . .

Objective: We conducted a systematic literature review, focusing on the past decade, to characterize AD and assess its impact on affected individuals . . ."¹⁰

- Cost-effectiveness studies assess the trade-offs of effectiveness and costs of interventions (i.e. examining the amount of money spent to gain a certain amount of effectiveness or benefits). Systematic reviews of cost-effectiveness studies are often used to support decision-making. For example, a Public Health agency may want to compare the effectiveness and costs of different vaccine strategies, such as a universal program to reduce the burden of the common flu. As an alternative strategy, the program may target the elderly and high-risk groups who are immunologically compromised to decide which program offers the best value for money.
 - o Example 1: A systematic review and meta-analysis of the direct epidemiological and economic effects of seasonal influenza vaccination on healthcare workers

"Background: Given the uncertainty in attributions of patient benefits to healthcare workers (HCW) vaccination, having strong evidence of the direct effectiveness of vaccination on healthcare workers and the cost-effectiveness of these campaigns in reducing the incidence of illness and absenteeism among HCW is important . . .

Objective: The specific objective in this review was to synthesize evidence to whether influenza vaccines reduced influenza related morbidity among HCWs, which includes incidence rate and absenteeism, and the associated costs of these programs."¹¹

o <u>Example 2: Cost-effectiveness analyses of colorectal cancer screening: a systematic</u> review for the U.S. Preventive Services Task Force

"Objective: To perform a systematic review of the cost-effectiveness of colorectal cancer screening for the U.S. Preventive Services Task Force." 12

o <u>Example 3: Cost-effectiveness of metabolic surgery for the treatment of type 2</u> diabetes and obesity: a systematic review of economic evaluations

"Objective: To systematically identify and appraise the international literature on the cost-effectiveness of metabolic surgery for the treatment of comorbid type 2 diabetes (T2D) and obesity." 13



Answer Response C: Assess the epidemiology of a disease or health condition

- **Epidemiological studies** often measure the prevalence and incidence of a disease or health condition on the population level, as well as variation in epidemiological findings.
 - <u>Example 1: The worldwide incidence of preterm birth: A systematic review of</u> maternal mortality and morbidity

"Objective: To analyse preterm birth rates worldwide to assess the incidence of this public health problem, map the regional distribution of preterm births and gain insight into existing assessment strategies." ¹⁴

o <u>Example 2: Global Prevalence of Severe Neonatal Jaundice among Hospital</u> Admissions: A Systematic Review and Meta-Analysis

"Background: Evidence regarding the adverse burden of severe neonatal jaundice (SNJ) in hospitalized neonates in resource-constrained settings is sparse.

Objective: We attempted to determine the prevalence of SNJ, described using clinical outcome markers, in all World Health Organization (WHO) regions in the world."15

 <u>Example 3: Prevalence of human papillomavirus (HPV) in Brazil: A systematic review</u> and meta-analysis

"Objective: This study aimed to estimate the prevalence of genital, anal and oral HPV infection in Brazil through systematic review and meta-analysis." 16

- Other types of **epidemiological studies**, for example cohort studies, evaluate the association between exposures and outcomes (e.g. association of body weight with total mortality and with cardiovascular events in coronary artery disease)."
 - Example 1: Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies

"Background: Studies of the association between obesity, and total mortality and cardiovascular events in patients with coronary artery disease (CAD) have shown contradictory results.

Objective: Our aim was to undertake a systematic review of cohort studies and perform a meta-analysis to better estimate the effect of bodyweight and other measures of obesity on total mortality, cardiovascular mortality, re-infarction, and revascularization in patients with established CAD."¹⁷

 Example 2: Risks of stillbirth and neonatal death with advancing gestation at term: A systematic review and meta-analysis of cohort studies of 15 million pregnancies

"Background: Prolonged pregnancy is a known risk factor for stillbirth. To avoid this adverse outcome, women are routinely offered induction of labour after 41 weeks gestation . . . However, 1 in 3 stillbirths occur prior to 41 weeks gestation. The



stillbirth risks before 41 weeks are not routinely discussed with women who have no clinical indication for delivery . . .

Objective: We undertook a systematic review to evaluate the additional weekly risks of stillbirth in term pregnancies that continue versus deliver at various gestational ages. We also assessed the week-specific risks of neonatal death by gestational age at birth."¹⁸

Answer Response D: Assess the prognosis of a disease or health condition

- Prognostic studies examine the likely course or development of a disease or health condition.
 - o <u>Example 1: Cardiovascular risk prediction models for women in the general</u> population: A systematic review

"Objective: To provide a comprehensive overview of cardiovascular disease (CVD) risk prediction models for women and models that include female-specific predictors." ¹⁹

 Example 2: Risk factors for necrotizing enterocolitis in neonates: a systematic review of prognostic studies

"Background: Many observational studies have reported clinical and non-clinical risk factors associated with necrotizing enterocolitis (NEC), but the prognostic value usually is unclear . . . To identify independent risk factors for a complex disease as NEC, a (preferably prospective) prognostic cohort design with multivariable analysis including multiple co-variates is considered most appropriate.

Objective: The aim of this study was to provide a systematic review of the literature on prognostic studies reporting on independent risk factors for NEC in neonates."²⁰

 Example 3: Anticholinergic burden (prognostic factor) for prediction of dementia or cognitive decline in older adults with no known cognitive syndrome

"Background: Medications with anticholinergic properties are commonly prescribed to older adults. The cumulative anticholinergic effect of all the medications a person takes is referred to as the 'anticholinergic burden' because of its potential to cause adverse effects. It is possible that high anticholinergic burden may be a risk factor for development of cognitive decline or dementia.

Objective: To assess whether anticholinergic burden is a prognostic factor for future cognitive decline or dementia in cognitively unimpaired older adults."²¹

Answer Response E: Assess a diagnostic test for precision and accuracy

A diagnostic test or procedure is an examination to identify an individual's specific areas
of weakness and strength to determine a condition, disease or illness. It is used to gather
clinical information on an individual in order to make a diagnosis (e.g., x-rays, CT scan etc.).



 Example 1: Diagnostic Accuracy of (Computed Tomography) CT for Local Staging of Colon Cancer: A Systematic Review and Meta-Analysis

"Background: CT is being used as a staging tool in the FOxTROT trial, but it remains unclear what the accuracy of CT is for selection of these high-risk colon cancer tumors . . .

Objective: The purpose of this article is to determine the accuracy of CT in the detection of tumor invasion beyond the bowel wall and nodal involvement of colon carcinomas."²²

o <u>Example 2: Algorithm based smartphone apps to assess risk of skin cancer in adults:</u> systematic review of diagnostic accuracy studies

"Objective: To examine the validity and findings of studies that examine the accuracy of algorithm based smartphone applications to assess risk of skin cancer in suspicious skin lesions." ²³

Example 3: Magnetic resonance imaging (MRI) for diagnosis of acute appendicitis

"Background: Appendicitis remains a difficult disease to diagnose, and imaging adjuncts are commonly employed. Magnetic resonance imaging (MRI) is an imaging test that can be used to diagnose appendicitis . . . As it does not expose patients to radiation, it is an attractive imaging modality, particularly in women and children.

Objective: The primary objective was to determine the diagnostic accuracy of MRI for detecting appendicitis in all patients . . . "24"

- Screening tools (e.g., self-assessment questionnaires) and clinical assessments (e.g., psychometric testing) can be used to assist with determining a specific diagnosis.
 - o Example 1: Screening for alcohol problems in primary care: A systematic review

"Background: Primary care physicians can play a unique role in recognizing and treating patients with alcohol problems.

Objective: To evaluate the accuracy of screening methods for alcohol problems in primary care."²⁵

 Example 2: Clinical neurophysiological assessment of sepsis-associated brain dysfunction: A systematic review

"Background: Several studies have reported the presence of electroencephalography (EEG) abnormalities or altered evoked potentials (EPs) during sepsis. However, the role of these tests in the diagnosis and prognostic assessment of sepsis-associated encephalopathy remains unclear.

Objective: The aim of our study was to answer the following questions:

1. What is the incidence of EEG/EP alterations in patients with severe infections or sepsis?



- 2. What is the accuracy of EEG/EP abnormalities in the diagnosis of SAE/SABD?
- 3. What is the prognostic value of such abnormalities in this setting?"26

Answer Response F: Identify/clarify concepts, definitions, available research; identify research gaps; and propose research agenda

- This response pertains to the need to clarify concepts, working definitions and/or the conceptual boundaries of a research topic as well as research gaps (e.g., research questions or problems which have not been answered appropriately or at all in a given topic). These types of reviews can also seek to identify, describe, and catalogue the available evidence relating to the question of interest and evidence gaps in a broader topic area.²⁷
 - Example 1: Utility of social media and crowd-intelligence data for pharmacovigilance: a scoping review

"Background: In order to advance pharmacovigilance . . . is being researched as a potential to supplement traditional drug safety surveillance systems. Three reviews have been recently published to explore the breadth of evidence on the methods and use of social media data for pharmacovigilance; however, none of the reviews found rigorous evaluations of the reliability and validity of the data.

Objective: To assess the utility of social media data for detecting adverse events related to health products, including pharmaceuticals, medical devices, and natural health products.

The specific research questions were:

- (1) Which social media listening platforms exist to detect adverse events related to health products, and what are their capabilities and characteristics?
- (2) What is the validity and reliability of data from social media for detecting these adverse events?"²⁸
- <u>Example 2: What do clinical practice guidelines say about de-prescribing? A scoping review</u>

"Background: Deprescribing (medication dose reduction or cessation) is an integral component of appropriate prescribing. The extent to which de-prescribing recommendations are included in clinical practice guidelines is unclear.

Objectives: To identify guidelines that contain de-prescribing recommendations, qualitatively explore the content and format of de-prescribing recommendations and estimate the proportion of guidelines that contain de-prescribing recommendations."²⁹

 Example 3: Non-familial intergenerational interventions and their impact on social and mental wellbeing of both younger and older people-A mapping review and evidence and gap map

"Background: Opportunities for social connection between generations in the UK have diminished over the last few decades because of changes in the way that we live and work . . . Evidence suggests that intergenerational activity can have a



positive impact on participants, for example, in reducing loneliness and exclusion for both older people and children and young people, improving mental health, increasing mutual understanding and addressing important issues such as ageism, housing and care. There are currently no other EGMs that exist that address this type of intervention; however, it would complement existing EGMs addressing child welfare.

Objectives: To identify, appraise and bring together the evidence on the use of intergenerational practice, to answer the following specific research questions:

- What is the volume, nature and diversity of research on, and evaluation of, intergenerational practice and learning?
- What approaches have been used to deliver intergenerational activities and programmes that may be relevant to providing such services during and in the subsequent recovery from the COVID-19 pandemic?
- What promising intergenerational activities and programmes have been developed and are being used but have not yet been subject to formal evaluation?"³⁰
- o <u>Example 4: Interventions to manage use of the emergency and urgent care system</u> by people from vulnerable groups: a mapping review

"Background: The NHS currently faces increasing demands on accident and emergency departments. Concern has been expressed regarding whether the needs of vulnerable groups are being handled appropriately or whether alternative methods of service delivery may provide more appropriate emergency and urgent care services for particular groups.

Objective: Our objective was to identify what interventions exist to manage use of the emergency and urgent care system by people from a prespecified list of vulnerable groups. We aimed to describe the characteristics of these interventions and examine service delivery outcomes (for patients and the health service) resulting from these interventions."³¹

Answer Response G: Synthesis of qualitative data

- A synthesis of qualitative data identifies all relevant studies and summarizes rich, in-depth texts from multiple sources to attain a comprehensive and nuanced understanding of complex phenomena in healthcare and other fields.^{32, 33}
 - Example 1: Experiences and involvement of family members in transfer decisions from nursing home to hospital: a systematic review of qualitative research

"Background: Nursing home residents (NHR) are characterized by increasing frailty, multimorbidity and care dependency. These conditions result in frequent hospital transfers which can lead to negative effects on residents' health status and are often avoidable. Reasons for emergency department (ED) visits or hospital admissions are complex. Prior research indicated factors influencing transfer decisions in view of nursing staff and general practitioners.



Objective: The aim of this systematic review is to explore how family members experience and influence transfers from nursing home (NH) to hospital and how they are involved in the transfer decision."³⁴

o <u>Example 2: Factors influencing obesogenic behaviours of adolescent girls and</u> women in low- and middle-income countries: A qualitative evidence synthesis

"Objective: This systematic review synthesized the qualitative evidence on factors influencing obesogenic behaviours in adolescent girls and women of reproductive age in low- and middle-income countries (LMICs)." 35

o <u>Example 3: Experiences and challenges of acute coronary syndrome patients in care provision: a qualitative systematic review</u>

"Background: Coronary artery disease including acute coronary syndrome (ACS) constitutes the most common cause of death in people with cardiovascular disease. Prompt diagnosis and early initiation of treatment significantly impact on patient outcomes. Positive patient experience with their initial care is linked to positive clinical outcomes.

Objective: This qualitative review aimed to investigate patients' experience of care provision and the challenges faced by them during their different stages of care following an ACS."³⁶

Answer Response H: Adoption of a new perspective

- While you want to stay true to the data in the primary studies, you can adopt new
 perspectives that emerge by looking across the body of evidence. This synthesis can
 provide added value beyond what's available in the individual studies alone.³⁷
 - Example 1: A qualitative synthesis of research into social motivational influences across the athletic career span

"Background: The review used an iterative approach to the review process by treating the literature as unsettled and uncertain, applying new perspectives to iteratively make sense of findings from included studies in order to reach the points of saturation, and developing a model of the overall 'motivational atmosphere' in sport.

Objective: Although knowledge on athlete motivation had already been developed before the review, the authors explicitly frame it in a holistic context."38

 Example 2: Women's experiences with yoga after a cancer diagnosis: a qualitative meta-synthesis-part I

"Background: Qualitative research on women's experiences participating in yoga after a cancer diagnosis is growing; systematic synthesis and integration of results are necessary to facilitate the transfer and implementation of knowledge among researchers and end-users.

Objectives: This review integrates findings from qualitative studies, compares and contrasts findings to elucidate patterns or contradictions in conclusions, and



develops an overarching interpretation of women's experiences participating in yoga after a cancer diagnosis."39

Answer Response I: Theory building

- Evidence syntheses that contribute to theory building, summarize findings in ways that can generate new theoretical insights beyond what is available in individual studies. The interpretive nature of this work allows for creative conceptual leaps that can advance theoretical understanding in ways not possible through other research methods.³⁷
 - <u>Example 1: A meta-study of qualitative research examining determinants of</u> children's independent active free play

"Background: The authors identified determinants of independent active free play related to child characteristics, parental restrictions, neighborhood and physical environment, societal changes, and policy issues. They created an ecological model depicting these factors, and the relationships therein. This model may be viewed as a contribution to theory building.

Objective: To produce a meta-study by completing a systematic review of qualitative research examining determinants of independent active free play in children."⁴⁰

Example 2: Legacy in End-of-Life Care: A Concept Analysis

"Background: Comprehending the significance of legacy in end-of-life (EoL) situations helps palliative care professionals enhance person-centered outcomes for those with a life-threatening illness and their families.

Objective: Our purpose was to conduct a concept analysis of legacy in EoL care. By employing Walker and Avant's approach, we identified the concept's defining characteristics. Subsequently, we established the antecedents, consequences, and empirical referents."41

Answer Response J: Theory testing

- By uncovering insights from the included studies, you can advance your understanding of complex phenomena and use the study findings and insights to test theories that generalize the study results.⁴²
 - <u>Example 1: Uncovering treatment burden as a key concept for stroke care: a</u> <u>systematic review of qualitative research</u>

"Background: Patients with chronic disease may experience complicated management plans requiring significant personal investment. This has been termed 'treatment burden' and has been associated with unfavourable outcomes.

Objective: The aim of this systematic review is to examine the qualitative literature on treatment burden in stroke from the patient perspective."⁴³

 Example 2: Factors influencing obesogenic behaviours of adolescent girls and women in low- and middle-income countries: A qualitative evidence synthesis



"Background: Adolescent girls and women of reproductive age are particularly vulnerable to malnutrition . . . due to poor dietary intakes, inequitable distribution of food within households, dietary taboos and gender inequality.

Objective: This review synthesized the qualitative evidence on factors influencing obesogenic behaviours in adolescent girls and women of reproductive age in low-and middle-income countries (LMICs). It followed the framework synthesis approach to extract, analyse and synthesize data."³⁵

Answer Response K: Explore how and why interventions/programs work (or do not work) in particular contexts or settings

- Evidence syntheses can be used to develop rich and contextual understandings of how interventions operate in real-world settings, going beyond simply asking "what works" to explore the crucial questions of how, why, for whom, and in what circumstances interventions are effective.⁴⁴
 - o <u>Example 1: A realist systematic review of evidence from low- and middle-income</u> countries of interventions to improve immunization data use

"Background: Although the barriers to using health data have been relatively well studied and point to insufficient skills in data use core competencies among health workers, lack of trust in data due to poor quality, and inadequate availability because of fragmented data across multiple sources, among others, to date there is no formal review of evidence from existing efforts to strengthen immunization data use.

Objectives: To address this gap, we conducted a realist systematic review of existing research evidence on immunization data use interventions in low- and middle-income countries (LMICs). Our review was designed to answer two specific research questions: 1. What are the most effective interventions to improve the use of data for immunization program and policy decision-making? 2. Why do these interventions produce the outcomes that they do?"⁴⁵

Example 2: Large-System Transformation in Health Care: A Realist Review

"Background: An evidence base that addresses issues of complexity and context is urgently needed for large-system transformation and health care reform. Fundamental conceptual and methodological challenges also must be addressed.

Objective: This review analyzes examples of successful and less successful transformation initiatives, synthesizes knowledge of the underlying mechanisms, clarifies the role of government, and outlines options for evaluation."⁴⁶

Answer Response L: Evaluate the quality of outcome measurement instruments based on available evidence

 You can conduct evidence synthesis to evaluate the quality of outcome measurement instruments based on available evidence, especially considering the intended use of the instrument (e.g., evaluative, predictive) and link its use to specific measurement properties.⁴⁷



 Example 1: Health-related quality of life in women with breast cancer: a review of measures

"Objective: To identify and describe the breast cancer-specific health-related quality of life (HRQoL) instruments with evidence of validation in the breast cancer population for potential use in patients treated for breast cancer (excluding surgery)."

o <u>Example 2: Patient-reported outcome measures in dysphagia: a systematic review of instrument development and validation</u>

"Background: Patient-reported outcome (PRO) measures are commonly used to capture patient experience with dysphagia and to evaluate treatment effectiveness. Inappropriate application can lead to distorted results in clinical studies.

Objectives: A systematic review of the literature on dysphagia-related PRO measures was performed to (1) identify all currently available measures and (2) to evaluate each for the presence of important measurement properties that would affect their applicability."⁴⁹

 Example 3: Parent Responses to Their Child's Pain: Systematic Review and Meta-Analysis of Measures

"Background: Parent responses can have a major impact on their child's pain.

Objectives: The purpose of this systematic review is to (a) identify and describe measures assessing pain-related cognitive, affective, and behavioral responses in parents of children with chronic pain and (b) meta-analyze reported correlations between parent constructs and child outcomes (i.e., pain intensity, functional disability, and school functioning)."50

Answer Response M: Both quantitative and qualitative goals

- Evidence syntheses can be used to collect and analyze both quantitative and qualitative data and to integrate both data during collection, analysis, interpretation. You can frame the synthesis within relevant philosophical/theoretical models in order to attain the goals of your review,⁵¹ which are supported by both qualitative and quantitative findings from the included studies.
 - o <u>Example 1: A mixed-methods systematic review of nurse-led interventions for people with multimorbidity</u>

"Objective: To identify types of nurse-led interventions for multimorbidity and which outcomes are positively affected by them." 52



<u>Example 2: Knowledge, attitudes and practices concerning catheter-associated urinary tract infection amongst healthcare workers: a mixed methods systematic review</u>

"Objective: To evaluate healthcare workers' knowledge, attitudes and practices level of prevention and management of catheter-associated urinary tract infection." ⁵³

Question 2: Is your review aim to compare between pairs of interventions/diagnostic tests (i.e. an experimental intervention and a comparator intervention) or compare between multiple competing interventions/diagnostic tests?

• This question is referring to the number of interventions or diagnostic tests that will be assessed in your review. It is only relevant if your goals and objectives involved interventions (i.e., your answer to question 1 is "Assess the effectiveness and/or safety of interventions", "Assess the burden of illness, monetary costs alone or the cost-effectiveness of interventions", or diagnostic tests (i.e., your answer to question 1 is "Assess a diagnostic test for precision and accuracy"). This question is not about the number of comparisons, subgroups or outcomes you will be evaluating.

Answer Response A: Pairwise comparison (i.e., an experimental intervention and a comparator intervention or a diagnostic test and a reference standard)

- [2 interventions]
 - <u>Example 1: Comparison of early intervention services vs treatment as usual for early-</u> phase psychosis: A systematic review, meta-analysis, and meta-regression
 - This systematic review compares early intervention versus treatment as usual for early-phase psychosis services.⁵⁴
 - Example 2: Ketamine as a component of multimodal analgesia for pain management in bariatric surgery: A systematic review and meta-analysis of randomized controlled trials
 - "This systematic review and meta-analysis of randomised controlled trials (RCTs) summaries evidence comparing ketamine to placebo for pain management after bariatric surgery."1
- [2 diagnostic tests]
 - <u>Example 1: Diagnostic accuracy of point-of-care natriuretic peptide testing for chronic</u>
 heart failure in ambulatory care: Systematic review and meta-analysis
 - This systematic review evaluated the diagnostic accuracy of two point-of-care tests, natriuretic peptide testing (B-type natriuretic peptide (BNP) or N terminal fragment pro B-type natriuretic peptide (NTproBNP)), against any



relevant reference standard, including echocardiography, clinical examination, or combinations of these, in humans.⁵⁵

Answer Response B: Multiple competing interventions/diagnostic tests

- [>2 interventions]
 - Example 1: Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis
 - In this systematic review, 21 antidepressant drugs were assessed.⁵⁶
 - <u>Example 2: Comparative Efficacy of First-Line Immune-Based Combination</u>
 <u>Therapies in Metastatic Renal Cell Carcinoma: A Systematic Review and Network</u>

 Meta-Analysis
 - This systematic review aimed to compare ipilimumab-nivolumab, pembrolizumab-axitinib, and avelumab-axitinib as treatments for metastatic renal cell carcinoma.⁵⁷
- [>2 diagnostic tests]
 - Example 1: Diagnostic performance of imaging modalities in chronic pancreatitis: a systematic review and meta-analysis
 - In this systematic review, three diagnostic tests were assessed: endoscopic ultrasonography, magnetic resonance imaging, and computed tomography molecular rapid diagnostic testing.⁵⁸
 - o Example 2: Universal screening for SARS-CoV-2 infection: a rapid review
 - This rapid review assesses the effectiveness of universal screening for SARS-CoV-2 infection compared with no screening, and the accuracy of universal screening in people who have not presented to clinical care for symptoms of COVID-19.⁵⁹
 - As part of this rapid review, the accuracy of various screening modalities were assessed relative to a reference reverse transcriptase polymerase chain reaction (RT-PCR) test, including single point-in-time screening; screening using direct temperature measurement, international travel history, exposure to known infected people, or suspected infected people, and a combination of these screening modalities.⁵⁹



Answer Response C: Not applicable

 Select this answer response if your answer response to question 1 does not involve interventions or diagnostic tests.

Question 3: What type of evidence will you be using?

Answer Response A: Systematic reviews only of any type

- A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility
 criteria in order to answer a specific research question. Specifically, the unit of synthesis in a
 systematic review is a primary study (as defined below).
 - <u>Example 1: Interventions for adolescent mental health: an overview of systematic</u> reviews
 - This review provides a summary of findings from systematic reviews of interventions for adolescent mental health.⁶⁰
 - <u>Example 2: Effectiveness and safety of interventions to manage childhood</u>
 overweight and obesity: An Overview of Cochrane systematic reviews
 - This is an overview of Cochrane systematic reviews on the effectiveness and risks of interventions to treat overweight and obesity in children and adolescents.⁶¹

Answer Response B: Primary studies only

- Primary studies refer to research studies in which data were often collected from individuals, such as patients. Specifically, the unit of analysis in a primary study is an individual. In the context of evidence synthesis, you would only consider primary studies as eligible sources to be included in your review.
 - <u>Example 1: Alterations in fecal microbiota composition by probiotic supplementation</u> <u>in healthy adults: A systematic review of randomized controlled trials</u>
 - This systematic review includes randomized controlled trials only.⁶²
 - Example 2: Splinting for carpal tunnel syndrome
 - This systematic review includes randomized controlled trials only.³

Answer Response C: Both systematic reviews and primary studies

 Select this answer response if you plan to use both systematic reviews and primary studies in your review.



- o <u>Example 1: Scoping review of patients' attitudes about their role and behaviours to</u> ensure safe care at the direct care level
 - This review included systematic reviews, quantitative studies, qualitative studies, mixed-methods studies, scoping reviews, literature reviews, quality improvement projects, as well as opinion and discussion papers.⁶³
- Example 2: Strategies for addressing the needs of children with or at risk of developmental disabilities in early childhood by 2030: a systematic umbrella review
 - "We conducted a global systematic umbrella review to assess the evidence on prevention, early detection and rehabilitation interventions for child functioning outcomes related to developmental disabilities in children under 5 years. We focused on prevalent disabilities worldwide and identified evidence-based interventions."⁶⁴

Question 4: What type of analysis will you conduct?

Answer Response A: Descriptive analysis only

- Descriptive analysis refers to tabulating and summarizing characteristics of included studies and narratively summarizing the results and findings of the included studies. No statistical analysis is planned or feasible because you anticipate large variation among the study findings (i.e., heterogeneity) or you intend to broadly summarize the included research.
 - Example 1: Effectiveness of diet, psychological, and exercise therapies for the management of bile acid diarrhoea in adults: A systematic review
 - "We anticipated that performing any meta-analyses would not be possible as a result of few studies reporting specific dietary interventions with available data. A narrative synthesis of the results was conducted by one investigator using the Synthesis Without Meta-analysis guideline to guide on reporting and presentation . . ."⁶⁵
 - Example 2: Global evidence on falls and subsequent social isolation in older adults:
 a scoping review
 - "A charting form was developed to capture data on study characteristics, population characteristics and outcomes of interest . . . The review findings were summarized descriptively using summary tables."66
 - <u>Example 3: Gestational diabetes mellitus in relation to serum per- and polyfluoroalkyl</u> <u>substances: A scoping review to evaluate the need for a new systematic review</u>



"We summarized the findings narratively or in tables. Because this was a scoping review, we did not run any data analysis or risk of bias appraisal for the included studies."⁶⁷

Answer Response B: Quantitative synthesis only

- Quantitative synthesis:
 - A meta-analysis synthesizes quantitative results comparing pairs of interventions of the included studies.
 - Example 1: Aspirin for the prevention of preterm and term preeclampsia: systematic review and metaanalysis
 - "We performed a systematic review and meta-analysis that evaluated the prophylactic effect of aspirin during pregnancy... Relative risks of the prophylactic effects were calculated with their 95% confidence intervals."⁶⁸
 - Example 2: Ketamine as a component of multimodal analgesia for pain management in bariatric surgery: A systematic review and meta-analysis of randomized controlled trials
 - "One of the outcomes used to assess the effectiveness of ketamine was opioid consumption during the first 24 h after surgery . . . Metaanalysis was used to estimate mean differences in opioid consumption between treatment groups."
 - "We used the RevMan 5.3.5 statistical package from the Cochrane collaboration for meta-analyses. We selected the mean difference (MD) as an effective measure for continuous data. For dichotomous variables, odds ratios (OR) with 95% confidence intervals (95% CI) were calculated. Random effects model was used. The threshold of statistical significance was set to 0.05."1
 - A network meta-analysis synthesizes quantitative results comparing three or more interventions of the included studies, allowing for indirect comparisons of interventions that have not been directly compared in these studies (see below).

Known comparisons: A vs. B and B vs. C Unknown comparison: A vs. C Method: A vs. C = (A vs. B) – (B vs. C)

 Example 1: Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis



- "We included placebo-controlled and head-to-head trials of 21 antidepressants used for the acute treatment of adults (≥18 years old and of both sexes) with major depressive disorder . . . We estimated summary odds ratios (ORs) using pairwise and network meta-analysis with random effects."⁵⁶
- Example 2: Comparative Efficacy of First-Line Immune-Based Combination
 Therapies in Metastatic Renal Cell Carcinoma: A Systematic Review and
 Network Meta-Analysis
 - "Three drug combinations, ipilimumab-nivolumab (Ipi-Nivo), pembrolizumab-axitinib (Pembro-Axi), and avelumab-axitinib (Ave-Axi), have received regulatory approval in the USA and Europe for the treatment of metastatic renal cell carcinoma with clear cell component (mRCC)."57
 - "However, since no clinical trial has provided any head-to-head comparison data of these combinations, we conducted a network meta-analysis (NMA) to indirectly compare their efficacies in terms of progression-free survival (PFS), overall survival (OS), and objective response rate (ORR) in the first-line setting for patients with mRCC."57

Answer Response C: Qualitative synthesis only

Qualitative evidence synthesis is a systematic approach to reviewing and combining findings from multiple qualitative research studies on a specific topic.⁶⁹

- Example 1. Experiences and challenges of acute coronary syndrome patients in care provision: a qualitative systematic review
 - "Data were extracted using the standardized data extraction tool from JBI. Data synthesis following the JBI approach was performed."³⁶
- Example 2. A qualitative evidence synthesis of employees' views of workplace smoking reduction or cessation interventions
 - "For all papers, two reviewers each independently extracted data and coded Results data against the a priori framework. This coding was then supplemented by secondary thematic analysis of any data not captured by the framework."

Answer Response D: Quantitative and qualitative synthesis

Evidence synthesis that involves both quantitative and qualitative data is a systematic approach to combining and analyzing different types of research evidence on a specific topic.⁵¹



- <u>Example 1. The Work Environment during Coronavirus Epidemics and Pandemics: A</u>
 <u>Systematic Review of Studies Using Quantitative, Qualitative, and Mixed-Methods</u>
 <u>Designs</u>
 - The authors included 73 studies that used quantitative methods, and 22 studies used qualitative or mixed methods; the majority were based on cross-sectional data.⁷¹
- Example 2. Exercise interventions and patient beliefs for people with hip, knee or hip and knee osteoarthritis: a mixed methods review
 - The authors included 21 trials, and 12 studies used qualitative methods.⁷²

Question 5: Is your primary review question fixed (that is, following a framework with predefined parameters such as PICO) or emergent (that is, more akin to an overall objective but does not have a set of pre-defined parameters)?

- The review question should be clear and focused.
- The review question helps guide the review process and determines what kind of data you are collecting and how you will collect it.

Answer Response A: Fixed

- A fixed question can have elements of the PICO (Population, Intervention, Comparison, and Outcome) approach that is used in a quantitative evidence synthesis of interventions (e.g., systematic review and meta-analysis).⁴²
- Frameworks for articulating a question to be answered by qualitative research include:
 - o **PICo**: Population-phenomenon of Interest-Context,
 - o **SPICE**: Setting-Perspective-phenomenon of Interest-Comparison-Evaluation,
 - o SPIDER: Sample-Phenomenon of Interest-Design-Evaluation-Research type, and
 - PICOC: Population-Intervention-Comparison-Outcome-Context
- A fixed question is defined by the elements that serve to "anchor" a synthesis. For example, you could use these elements as concepts to generate lists of keywords for each concept to identify relevant studies and aggregate the findings.⁴²
 - <u>Example 1: Enablers and barriers to the implementation of primary health care</u> interventions for Indigenous people with chronic diseases: A systematic review
 - Research Question: "What are the factors that support (enablers) and inhibit (barriers) the implementation of interventions aimed at improving chronic disease care for Indigenous people within a primary health care setting?"⁷³
 - > Population: Indigenous people with chronic disease
 - > Intervention: Interventions aimed at improving chronic disease care
 - Outcome: Enablers and barriers to implementation



- <u>Example 2: An exploration into physician and surgeon data sensemaking: a</u> <u>qualitative systematic review using thematic synthesis</u>
 - Research Objective: "Thus, the primary objective of this research was to explore physician and surgeon sensemaking when presented with electronic health data associated with their clinical performance."
 - Sample: Physicians and surgeons who practice in roles recognised by the Medical Board of Australia
 - > Phenomenon of Interest: Clinical performance data or feedback
 - > Design: All qualitative research designs
 - > Evaluation: The sensemaking process was evaluated.
 - > Research Type: Both qualitative and mixed-methods research were included, however only the qualitative aspects were analysed.
- <u>Example 3: Intraoperative and postoperative outcomes of robot-assisted</u> cholecystectomy: a systematic review
 - Research Objective: "... to compare the clinical effectiveness of robotassisted cholecystectomy for benign gallbladder disease as compared with the laparoscopic approach."²
 - Population: Patients with benign gallbladder disease
 - Intervention: Robot-assisted cholecystectomy and laparoscopic approach
 - Outcomes: Intraoperative outcomes (e.g. OR time, intraoperative complications, and conversion rates), short-term outcomes (e.g. length of stay, surgical site infection, readmissions, and pain) and the long-term outcome of incisional hernia.

Answer Response B: Emergent

- An emergent question generally does not have a set of pre-defined parameters. We can restate an emergent review question as a review objective, which serves as a "compass" that offers a general direction for the conduct of the qualitative evidence synthesis.⁴²
 - <u>Example 1: Patient adherence to tuberculosis treatment: A systematic review of</u> qualitative research
 - Research Objective: "To understand factors considered important by patients, caregivers and health care providers in contributing to tuberculosis medication adherence."



- o <u>Example 2: Systematic review to understand and improve care after stillbirth: A</u> review of parents' and healthcare professionals' experiences
 - Research Objective: "To assess the current available evidence, extract findings and highlight key themes that may help to guide midwifery and medical management, training of key healthcare workers and development of support services dealing with bereaved parents going through a stillbirth."
- <u>Example 3: A meta-ethnography of the factors that shape link workers' experiences</u>
 <u>of social prescribing</u>
 - Research Problem: "Social prescribing is an approach which seeks to address non-medical and health-related social needs through taking a holistic person-centred and community-based approach. This involves connecting people with and supporting them to access groups and organisations within their local communities . . . Despite growing literature on the implementation of social prescribing, to date there has been no synthesis that develops a theoretical understanding of the factors that shape link workers' experiences of their role."

Question 6: Within a planned qualitative evidence synthesis, reviewers can ignore, acknowledge, generate, explore, or test theory. Based on preliminary searches of the literature, is theory likely to have a role in structuring the review, in analysis or in interpreting review findings?

- In the context of this question, theory is defined as developing a conceptual understanding and can take the form of a model or framework.⁴²
- Theory can be integrated into a evidence synthesis of qualitative studies at multiple levels.⁴²
 Reviewers should be mindful of the philosophical foundations or the integrity of qualitative primary studies (i.e., ontology, epistemology, axiology, methodology).⁴²
- In planning a review, a researcher may approach the evidence synthesis of qualitative studies from differing epistemological stances.⁴² For example:
 - "A researcher synthesizing qualitative studies to inductively understand a social phenomenon may adopt a different method from the one synthesizing qualitative studies with the purpose of better understanding the effects of an empirically tested clinical intervention."⁴²
 - "Alternatively, a researcher planning to synthesize qualitative research primarily as a means of generating theory may use a different approach from the one who intends to apply the results to answering a specific clinical question."⁴²
- Within a planned review, reviewers acknowledge, generate, explore, or test theory.⁴²
 Alternatively, they might make a conscious decision not to be influenced by prevalent theories.
- Reviewers should undertake preliminary searches to assess the extent of the available qualitative evidence, including carefully reading some full-text reports of potentially relevant studies. This will guide decisions regarding how they will conduct the review.⁷⁸



• Studies with rich data on concepts and theories are likely to sustain the generation and testing of theories, whereas studies reporting only the presence/absence of some concepts or phenomena of interest are not.⁷⁹

Answer Response A: Yes

• If you expect the included studies will be rich in concepts and theories, respond "Yes" to this question.

Answer Response B: No

• If you expect the included studies will report little data on concepts and theories, respond "No" to this question.

Question 7: Will your review team include members with expertise in qualitative research?

- Qualitative research is non-numerical data analysis for understanding social reality. It is a
 method of inquiry that focuses on understanding and exploring human experiences,
 behaviors, and perspectives in depth. It generally involves collecting and/or working with
 text, images, and/or sounds, and using different kinds of data collection and analysis
 techniques (e.g., concept analysis, thematic analysis).
- Methods derived from qualitative research are often also used in evidence synthesis of
 qualitative studies (e.g., grounded theory, narrative analysis, thematic analysis). As such, for
 evidence synthesis of qualitative studies, expertise in qualitative research is highly
 desirable.

Answer Response A: Yes

• Select this response if your review team consists of members who have expertise in qualitative research.

Answer Response B: No

• Select this response if your review team does not have expertise in qualitative research.

Question 8: Do you have time, resource and/or cost constraints to complete your review?

- Well-conducted knowledge syntheses such as systematic reviews provide valid evidence to inform decision making.⁸⁰ However, systematic reviews of healthcare interventions can be time-consuming (e.g., one year to complete),⁸¹ labor-intensive (e.g., requires 1,139 personhours and five reviewers),⁸² and expensive (e.g., costs >\$100,000).⁸³
- Various methods exist to expedite the conduct of reviews to inform health policy and systems decisions. The main challenge lies in accelerating review methods while maintaining robustness and transparency. Reviewers can enhance the timeliness of reviews by taking evidence synthesis shortcuts (e.g., using one reviewer instead of two for study selection, critical appraisal, and data abstraction), using computer automation, and intensifying review steps (e.g., including many reviewers on the team).⁸⁴



- Time constraints refer to restrictions on the amount of time a review team has to complete
 the review. Note that a review team may not have control over timelines. For example,
 knowledge users (e.g., policy makers) may determine the timelines if they commissioned the
 review.
- Resource constraints refer to restrictions on human resources (e.g., limited number of reviewers, limited skills/expertise), funding (e.g., small budget, limited software licenses, and delays in interlibrary loans), the available evidence (e.g., limited number of team members to screen a large number of included studies), and what the outcome is going to be used for (e.g., one may not be willing to expend unlimited resources to complete a evidence synthesis supporting a policy decision at the hospital level versus at the national level).
- The time it takes to complete a review is likely to depend on the review question and the size of the relevant body of literature. For the purposes of this tool, we use a cut-off of six months, but this should be considered as a general rule of thumb rather than an absolute value.⁸⁵
- These constraints may be considered from the perspective of the knowledge users (i.e., the
 people requesting the review or information). Engaging with knowledge users throughout the
 review process is highly encouraged to ensure that the resulting evidence meets their
 needs.⁸⁶
- It is important to note that approaches related to the shortened timelines of reviews should not be used as a preferential choice, and if they are used, they should be transparently reported. The emergence of these mechanisms was a result of knowledge users requiring evidence within a condensed timeframe in order to make informed decisions. These approaches include using review shortcuts, narrowing the scope of the review, intensifying the work on review processes, and automating review steps.⁸⁶

Example 1: Patient safety initiatives in obstetrics: a rapid review

"... In order to provide decision-makers with timely results, a rapid review approach was collectively agreed on with a 6-week timeline for completion. Rapid reviews tailor the systematic review process to produce information that is relevant to decision-maker needs in an abbreviated period of time. The streamlined steps followed in this review included limiting: the study design to randomised clinical trials (RCTs), search dates to a period of 10 years and language of publication to English."

Answer Response A: Yes

- Generally, rapid reviews are conducted over 6 months or less, a much shorter timeline than most systematic reviews. While other reviews may be conducted in short periods (e.g., by assigning additional resources or if the review has zero or few included studies), on average, systematic reviews take six months to a year to complete.⁸⁸ If the timeframe to complete the review is <6 months, select "Yes" as your answer response.⁸⁵
- If there are resource constraints in addition to your time constraints, select "Yes".
- Cost restraints:⁸² On average, conducting a systematic review requires \$50,000-\$100,000
 CAD. If you have limited or no funding, and time constraints, select "yes". The number of appropriate evidence synthesis methods is reduced when both time and cost constraints are involved.



Answer Response B: No

• If neither of the above apply to your review, select "No" as your answer response.

Question 9: Do you aim to continually update your review, incorporating relevant new evidence as it becomes available?

This question refers to living systematic reviews, which involves: (i) continual, active monitoring of the evidence (i.e. monthly searches); (ii) immediately including any new important evidence (meaning data, studies or information); and, (iii) are supported by up-to-date communication about the status of the review, and any new evidence being incorporated.⁸⁹

Answer Response A: Yes

- If you anticipate that an update to review will be required, select "Yes" as your answer response.
 - <u>Example 1. Effectiveness and Safety of Treatments to Prevent Fractures in People</u>
 <u>With Low Bone Mass or Primary Osteoporosis: A Living Systematic Review and</u>
 Network Meta-analysis for the American College of Physicians
 - "This systematic review will be maintained as a living review with periodic literature searches and updates as new studies emerge. The reviewers will consider quantitative and qualitative factors, such as CoE [certainty of evidence], balance between benefits and harms, and contextual considerations in assessing whether the new evidence may lead to meaningful changes to the recommendations and an update is warranted."90

Answer Response B: No

- If you do not anticipate updating the review, select "No" as your answer response.
 - <u>Example 1. A systematic review of the prophylactic role of chloroquine and hydroxychloroquine in coronavirus disease-19 (COVID-19)</u>
 - "Although pre-clinical results are promising, to date there is a dearth of evidence to support the efficacy of chloroquine and hydroxychloroquine (CQ) in preventing COVID-19. Considering potential safety issues and the likelihood of imparting a false sense of security, prophylaxis with CQ against COVID-19 needs to be thoroughly evaluated in observational studies or high-quality randomized controlled studies."91



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