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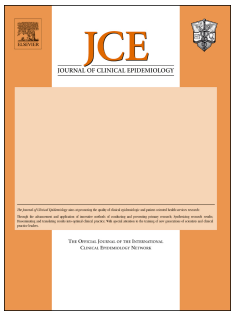

Cochrane Qualitative and Implementation Methods Group Guidance series - paper 6: Methods for question formulation, searching and protocol development for qualitative evidence synthesis

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Title:

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Cochrane Qualitative and Implementation Methods Group Guidance series - Paper 6: Methods for question formulation, searching and protocol development for qualitative evidence synthesis

Abstract

This paper updates previous Cochrane guidance on question formulation,searching and protocol development, reflecting recent developments in methods for conducting qualitative evidence syntheses to inform Cochrane intervention reviews. Examples are used to illustrate how decisions about boundaries for a review are formed via an iterative process of constructing lines of inquiry, and mapping the information available to ascertain whether evidence exists to answer questions related to effectiveness, implementation, feasibility, appropriateness, economic evidence, and equity. The process of question formulation allows reviewers to situate the topic in relation to how it informs and explains effectiveness, using the criterion of meaningfulness, appropriateness, feasibility and implementation. Questions related to complex questions and interventions can be structured by drawing on an increasingly wide range of question frameworks. Logic models and theoretical frameworks are useful tools for conceptually mapping the literature to illustrate the complexity of the phenomenon of interest. Further, protocol development may require iterative question formulation and searching. Consequently, the final protocol may function as a guide rather than a prescriptive route-map, particularly in qualitative reviews that ask more exploratory and open ended questions.

Keywords: Systematic reviews, question formulation, Cochrane Collaboration, methods, qualitative evidence synthesis.

Running title: Title. **Methods for question formulation, searching and protocol development for qualitative evidence synthesis: Cochrane Qualitative and Implementation Methods Group Guidance**

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Key findings:
Tools and methods are recommended to assist reviewers in developing protocols, which accommodate alternative approaches to question formulation and searching and protocol development for qualitative evidence synthesis.

What this adds to what was known?
Questions within qualitative and implementation systematic review protocols may be indicative, allowing more detailed questions to be formulated when more information is needed on specific aspects of the review. A broader range of question formats is presented, to reflect the need for reviews that explore and generate theory.

What is the implication and what should change now?

This guidance provides examples of protocols for qualitative evidence synthesis that are flexible, to allow the incorporation of open-ended and exploratory review questions and iterative searching methods.

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Introduction

The first paper in the Cochrane Qualitative and Implementation Methods series updates previous Group guidance on question formulation [1], literature searching [2] and protocol development [3] for qualitative evidence syntheses published in 2008 and 2011. This updated guidance is based developments in the field that are catalogued via the Cochrane Qualitative and Implementation Methods Group Register http://methods.cochrane.org/qi/methodology-register. Qualitative evidence synthesis in the context of Cochrane systematic reviews explores the meanings that people attach to phenomena, using people's experiences of conditions, of receiving interventions or delivering interventions to help explain, interpret and apply the results of an intervention review. It recognises the need for new approaches to question formulations and development of qualitative evidence synthesis review protocols that allow us to 'recontextualise' effectiveness. Recontextualising requires considering effectiveness research in relation to issues in society [4] to enable a decision-maker to make an informed decision about whether an intervention is likely to be useful and whether that intervention is applicable to their local population. Qualitative research produces contingent and experiential knowledge on *why* interventions work the way that they do (or fail to work) [5]. Further, implementation questions provide information on *how* the implementation process produces (or fails to produce) improvements in health. Patients, policy makers, providers, purchasers, payors, and the public are the end users of systematic reviews. The ultimate aim of any review team, therefore, is to produce pragmatic evidence on *what* actions need to be taken to achieve health outcomes and improve health and social systems.

Qualitative evidence synthesis present numerous challenges which include, but are not limited to, the following:

- By their very nature, qualitative reviews ask 'how and why questions', meaning that the review embodies a process of discovery and learning.

- As a process of discovery, the questions formulated for qualitative reviews are exploratory, aiming to identify what is known from multiple perspectives and reveal different factors, dimensions and explanations.
- The exploratory process means that initial qualitative review questions may be broad in order to map what is known, before formulating or refining questions.
- The sources of information may be diverse, and preferred sources may change as understanding of the topic is developed during the review.
- The resultant protocol needs to be flexible and iterative, representing the general research territory to be explored and signposting the direction of synthesis [6].
- A qualitative review that aims to support decision making in local contexts should draw on stakeholder knowledge to facilitate translation.

This paper describes how to formulate questions and construct protocols for reviews that use qualitative evidence either in combination with Cochrane intervention reviews or in Cochrane qualitative evidence syntheses to explore effectiveness and/or the implementation of interventions. The paper conceives question formulation, literature searching and protocol development as iterative processes **(Figure 1)**. The steps in this process can be completed with reference to the guidance provided in paper 2, which presents methods for assessing methodological limitations, data extraction, synthesis and confidence in synthesized qualitative findings. Examples of implementation questions can be read in conjunction with paper 2, which provides guidance on mixed-methods reviews addressing implementation. The guidance provided in paper 4 on integrating qualitative evidence synthesis with evidence of intervention effectiveness, and paper 5 guidance on selection and application of reporting guidelines will be relevant to protocol development.

We describe question formulation and protocol development as a process of problem framing, constructing a preliminary framework or logic model to illustrate relationships, and developing an understanding of context. These activities lead to identifying potential lines of enquiry and searching to identify available evidence. Questions are then formulated and focused, followed by protocol development.

Guidance for each stage is presented with illustrative examples.

<<INSERT FIGURE 1 HERE>>

1. Problem framing

Problem framing, which is the first step in formulating a review question and designing a protocol, is the process of organizing information by using an interpretive framework to make sense of a problem [7]. Because qualitative evidence synthesis is used to increase understanding, problems will be directly linked to the need for evidence that describes or explains the phenomenon in a Cochrane quantitative systematic review. Problems can be framed in multiple ways, producing very different causal arguments and solutions depending on the policy context [8]. When evidence is needed to position a problem on a policy agenda, however, the initial framing may only represent the dominant view, producing bias in both the evidence collected and the synthesis [9]. A transparent process for framing problems and making decisions about the scope of the review is recommended because the problem frame, as exemplified by the review question, may be revised on the basis of preliminary review findings. Further, it may not be clear at the beginning of the process whether aspects of the review question can be answered using existing theory or whether theory needs to be generated [10]. Reviews of theory provide a useful starting point for problem framing, as they can be used to map the various explanations of relationships between individual circumstances, wellbeing and health [11]. Logic models can be used to articulate relationships between cause and effect using root cause analysis [12-16].

<<INSERT BOX 1 HERE>>

These recently developed review methods reveal the different dimensions of problems with the potential to provide policymakers with information that goes beyond 'what works' to explaining 'what happens' when an intervention is implemented [17]. Although different perspectives of the problem are rarely described [18] a review team needs to acknowledge their importance as the first step in the review process because perspectives influence question formulation and ultimately the direction for the review.

Involving patients, providers, policymakers and the public in co-production of evidence is now proposed as a way to address the disconnect between the academic process of evidence synthesis and the 'messy nature of practice' [19]. Problem framing begins with stakeholder consultation to explore 'What is the (health) problem?' For whom is it a problem? Why is it a problem?' A review team needs to decide which types of stakeholders to involve, the level of involvement needed, and their working relationship with the review team. The importance of issues such as acceptability and implementation difficulty will become apparent through the consultation process. According to the centrality of these issues to their specified review question a review team may decide to briefly describe them within the Background of the protocol, perhaps in the Section on "How the Intervention Might Work", substantiated by relevant individual qualitative studies. Alternatively, they may decide to support information on the effectiveness of the intervention with a full qualitative evidence synthesis designed for integration with the intervention review. These decisions will be enacted within the review protocol, either in registering an intervention review or in using a flexible review template to accommodate and register a mixed method research synthesis [20].

Approaches to involving stakeholders in the review process may be broadly characterised as before-after involvement, iterative involvement and synchronous involvement [21-23] as described in Box 2.

<<INSERT BOX 2 HERE>>

2. Constructing a preliminary framework or logic model

Many quantitative and qualitative reviews now use theoretical frameworks or logic models to present relationships between problem, explanatory evidence, implementation and outcomes [24, 46]. Theoretical frameworks explain the possible relationships between concepts in general terms; logic models are usually more pragmatic illustrations of how the components of a specific programme or intervention work together to produce the desired outcomes for a particular population in a given context [25-27]. The protocol can present

an initial logic model or theoretical framework representing what is found in the empirical research.

The protocol for a mixed method review on WASH Promotion Programmes [28] presents a logic model based on the RANAS theoretical model [29], the PROGRESS framework [30] and the Checklist for Implementation (Chimp) [31]. It was refined by inviting key-stakeholders to comment on the different components and the overall structure of the logic framework. A simplified, more generic version of this logic model is shown below for illustrative purposes **(Figure 2)**.

<<INSERT FIGURE 2 HERE>>

For some types of review, stakeholders may be involved in construction of the programme theory for the preliminary model [32]. In qualitative and implementation protocols, preliminary models are considered a starting point, acknowledging that what emerges during the review process may alter or refine the original model. Although qualitative and implementation protocols may be exploratory and allow for iterative searching and subsequent question reformulation and refocusing, the protocol should aim for transparency, by including a statement that deviations from the expected process will be documented and justified [33].

3. Developing an understanding of context

The context in which healthcare is delivered extends to "a variety of settings, communities, and cultures that are all influenced by economic, social, political, fiscal, historical, and psychosocial factors" [34, 79]. A recent concept analysis has sought to untangle the complexity that surrounds the term [35]. The selection of a contextual frame is not arbitrary but should be sensitive to the level and nature of the review question. Numerous frameworks exist from which the most appropriate should be selected **(Box 3)**.

<<INSERT BOX 3 HERE>>

Consultation with stakeholders, together with preliminary scoping of the literature, will help to establish 'What situational circumstances surround the problem?" Many relevant

contextual factors are identifiable at an early stage of protocol development and will inform such decisions as the ultimate scope of the search, the inclusion and exclusion criteria and later considerations of transferability. A decision needs to be made at the outset as to whether the review will address a single context or multiple contexts [38].

4. Identifying potential lines of inquiry for the qualitative review question

A qualitative review selects one or more lines of inquiry for the question, that serve as a lens for identifying, selecting and interpreting data from different perspectives. Lines of inquiry include questions about meaningfulness, appropriateness, feasibility, equity, affordability, and implementation [31, 39-40]. Questions may include one or more lines of enquiry as illustrated by the sample questions from Cochrane qualitative and mixed method reviews and protocols in Box 4.

<<INSERT BOX 4 HERE>>

These lines of inquiry are combined in different ways to explain variations in effectiveness (see Table 1). Researchers, commissioners, decision-makers and engaged stakeholders may prioritise these questions differently. Ultimately, question selection depends on the amount of research evidence and the relevance of evidence in relation to the target contexts (Box 5).

<INSERT TABLE 1 HERE>>

<<INSERT BOX 5 HERE>>

5. Searching to explore the evidence base

For any line of inquiry, the boundaries of a review need to be pragmatically limited to what is already known. In the first instance a scoping process seeks to quantify the availability of relevant research and make a preliminary assessment of its quality, as characterised at a study type level in order to inform subsequent review [42]. A useful tool is the PubMed Health Services Research Queries interface

(https://www.nlm.nih.gov/nichsr/hedges/search.html) which allows you to conduct preliminary searches relating to Appropriateness, Process Assessment, Qualitative Research or Quality Improvement using either Broad filters (for a sensitive search) or Narrow filters (for a specific search).

In the context of Cochrane reviews, review authors can opt to include qualitative 'trial sibling' studies conducted alongside the trial as well as 'unrelated' qualitative studies that report on similar interventions or health conditions and topics in broadly similar contexts [43, 44]. Published guidance exists to help review authors to select different qualitative study types for inclusion in a qualitative evidence synthesis [45]. Qualitative studies from contexts other than those of included trials can extend the pool of available evidence and make a useful theoretical and explanatory contribution to the synthesis [46, 47]. "Unrelated" studies may also be used provided sufficient checks are in place to establish that the interventions were broadly similar and the contexts map onto the review question. However, as mentioned above, definitions of what constitutes "relevant context" are both contested and review-specific and should be informed by the subsequent claims to be made by any individual review [35, 38, 79].

Unpublished studies and grey literature reports may also provide an additional pool of evidence, especially in critically under researched areas. Scoping searches and review team knowledge of the breadth, number and type of available of contemporary qualitative studies will be helpful in informing decision-making about qualitative study type.

As with other types of research, qualitative research may be located in sources other than the peer-reviewed journal literature [48]. Search strategies may need to include supplementary techniques such as citation searching and reference chasing [49]. Unpublished studies, and grey literature reports, websites for interventions and programs may yield an additional pool of evidence, especially in critically under-researched areas. Exploration is currently underway to determine how publication bias may operate within qualitative research but it is likely, at least, that unpublished studies and reports may offer a more-extensive, but less-filtered, representation of the phenomenon of interest.

An agreement between funders/policymakers and the review team is reached with the aim of compiling evidence to improve understanding and with practical application [50]. No

precise formula exists for deciding whether there is 'enough' research on a topic to answer a review question, it depends rather on the combination of how much relevant information exists alongside its richness (and "thickness") of detail [51].

After the initial scoping, searches are used to develop each section of the protocol, which includes mapping types of studies, participants, phenomenon related to the intervention and information related to outcomes. Searches can also be used to identify theories explaining the relationships between phenomenon, interventions and outcomes [52-54]. This is important because the protocol needs to be situated not only in relation to the type of research that exists, but also in relation to explanations advanced within the included studies or within a wider body of literature [45]. Finfgeld-Connett & Johnson position syntheses between summative/aggregative syntheses on the one hand and "knowledge building" and "theory generating" syntheses on the other [55]. Summative/aggregative syntheses require identification of as comprehensive a sample of studies as possible with a prevailing acknowledgement that "every study counts" in contributing to understanding of a phenomenon. In contrast, knowledge building and theory generating reviews are predicated on a view that "every meaning matters", arguing that there may be minimal added value in identifying multiple studies that simply confirm the existence of the same concept. Further discussion can be found in paper 2 in the series.

Expanded guidance on searching for qualitative research is available elsewhere [57] but the basic "7S" principles can be summarised as follows:

- **Sampling** – If comprehensive sampling is not used reviewers must **justify** their sampling strategy, **match** it to their synthesis method and **describe it in full**.
- Preferred **Sources** for health topics require MEDLINE and CINAHL as a minimum, augmented by topic-specific and setting-specific sources. Reviewers should devise specific strategies for **specific types** of grey literature, if included.
- **Structured Questions** should use a format appropriate to the purpose and focus of the review. The review question for the qualitative evidence synthesis **may or may not match that for an accompanying review of effectiveness;** it may be broader, for example in examining patients' experience of a condition, or may be narrower, for example in focusing on a specific stage of an implementation pathway [58].

- **Search Procedures** should generally **privilege specificity** (retrieval of only relevant items) over sensitivity (retrieval of all potential items) in recognition that qualitative research is far less prevalent than quantitative research and so subject searches run without methodological filters will contain a higher proportion of irrelevant hits. Retrieved relevant items act as a starting point for supplementary search techniques. This should not, however, be used as a rationale for a less intensive search effort as reviewers should compensate for reported deficiencies in indexing with a broad **range of supplementary strategies.**
- **Search Strategies and Filters** should be **commensurate with the intended purpose of the review**. When extensive supplementary non-database strategies are employed to offer improved sensitivity a simple one-line filter has been shown to suffice, albeit only in a limited number of case studies [58] [63].
- **Supplementary Strategies** require reference checking to be a default for every review. For diffuse topics, or those with significant variation in terminology, **handsearching, citation searching or contact with authors/experts** may be productive. Where context or theory is important **the CLUSTER method** [51] may be appropriate. **Trial identifiers** (ISRCTN or trial name) may be useful for sibling or kinship studies for trials [59].
- In the absence of consensual **Standards** for reporting **ENTREQ** [60], **supplemented by PRISMA** [61] **and STARLITE** [62] **should be used when reporting a search** (see Flemming et al. Article in this Series Under review)

6. Formulating and focusing questions

Decisions about boundaries for a review are formed via an iterative process of constructing lines of inquiry, mapping the information available, and reframing the topic of interest. In this way a review team arrives at a set of questions that generate meaningful information to inform decisions (Figure 3).

<<INSERT FIGURE 3 HERE>>

Once the scope of the review is established, the questions can be formulated using qualitative or mixed questions frameworks such as PICOC, SPICE and SPIDER (Table 2).

<<INSERT TABLE 2 HERE>> [53, 64-70]

PICO or SPICE question formulations represent the simplest form of framework or model, and are also used in quantitative reviews, but may prove insufficient when representing complex interventions [45]. Nevertheless, simple question frameworks continue to prove useful in specifying concepts when constructing the search strategy. However, we recommend that users privilege a formulation that includes the important aspect of context (i.e. Setting, Context or Environment) **(Box 6)** in recognition of the context-sensitivity of many qualitative questions. A comprehensive list of question formulation structures has been published elsewhere [57]

<<INSERT BOX 6 HERE>>

If preliminary searches indicate that individual study reports may lack details of context, review authors may seek to identify "clusters" of related study reports in order to reconstruct the study context. Search procedures, characterized by the CLUSTER mnemonic **(Box 7)**, have been developed to identify such clusters [51]. Specification of a particular context in the review question e.g. geographical limits will typically exert an important influence on the selection of appropriate sources [38, 71].

<<INSERT BOX 7 HERE>>

7. Developing the protocol

Protocols present a grounded argument for the importance of a topic, explaining why a qualitative or implementation review or specific review on implementation evidence is appropriate, and illustrating the relationship between the review design and review methods [72]. The coherence of the protocol framework **(Box 8)** gives the review credibility.

<<INSERT BOX 8 HERE>>

We have monitored how approaches to protocol development have continued to evolve since 2011 The latest version of REVMan allows for a 'flexible review' format whereby additional material relevant to qualitative evidence synthesis is placed under the top-level headings for the main sections of the review **(Box 9)**.

<<INSERT BOX 8 HERE>>

Examples below illustrate types of material now being included as top level headings relevant to qualitative reviews:

The *Background section* explains why qualitative evidence is needed, with a specific link to the relevant Cochrane quantitative review question. It states whether the aim of the review is to generate knowledge and theory within a mixed methods Cochrane review, or alternatively describes how the qualitative review will increase understanding of an intervention. Objectives will be aligned with the problem framing, the review questions and strategies for searching and identifying studies.

Methods

Criteria for selecting studies covers will depend on the question that is asked and how the review question relates to the parallel intervention review. Types of studies, for example, may include those that specifically discuss theory, studies that inform the intervention design, process studies conducted alongside effectiveness studies and those that were conducted after the effectiveness study on the same groups. When interventions have little qualitative inquiry, the team may need to consider how patients experience the condition or which outcomes are valued by people with the condition and other stakeholders, comparing these with outcomes considered important by providers [41]. (See protocol example Box 5). Selection of studies may be based on relevance alongside consideration of quality [79]. Relevance refers to the potential of qualitative studies to inform a Cochrane intervention review.

Search methods can focus not only on the phenomenon of interest but also on identification of existing theory and concepts that enable theory development. Searches may be iterative, consisting of a series of searches where each successive strategy is informed by what was previously learnt.

Studies may focus on the same intervention and population and review all relevant studies (Box 10); or the protocol may explicitly state that a sample will be selected (Box 11).

<<INSERT BOX 10 >>

Where approaches to study selection are dependent upon the number of relevant studies found, the protocol should state what sort of rationale or sampling method will be used for selection, as illustrated in Box 11.

<<INSERT BOX 11>>

Proximity to the intervention is considered in both of the above examples – where Hurley et al [73] limit selection to qualitative studies on the same intervention, Bohren et al [74] state that in sampling they will privilege qualitative studies that were linked to a specific quantitative intervention but not be directly linked with the quantitative studies in the intervention review

Sampling and screening procedures are described in section 5 and in paper 2 in the series. Further guidance to consider when developing the study selection section of a protocol can be found in paper 2 of this series.

Assessment of study quality can be reviewed at different points in the selection process. The protocol should state whether appraisal will be conducted after the initial search to establish a quality threshold, or after identification of relevant data when making judgements on the relative strength of messages in the included research.
There is an extensive literature and much debate on different approaches to critical appraisal of study quality in qualitative evidence synthesis, which is discussed in greater detail in paper 2 in the series.

Data extraction and synthesis approaches will be described, referencing tools that have been developed for different types of qualitative and mixed methods reviews such as logic

models and frameworks [26, 45, 78] which are discussed in paper 2 of the series; and checklists to assess implementation [31] which are described in paper 3. Qualitative reviews that are commissioned to enable policy making could use the SURE framework for implementing policy, which enables teams to identify where further information is needed before deciding to pursue a particular policy option [78]. A range of approaches can be used which are detailed in paper 2 of this series.

Assessment of confidence in the Evidence from Reviews of Qualitative Research will be outlined to identify methodological limitations, relevance, coherence, and adequacy of the qualitative data. The Confidence in the Evidence from Reviews of Qualitative research approach (CERQual) [79], which seeks to offer a transparent assessment process analogous to the use of GRADE [80] for effectiveness reviews, is now being used in Cochrane qualitative protocols to appraise review findings [41] [77].

Conclusions

This paper documents the evolution of question formulation and protocol development since the Cochrane Handbook Supplemental Guidance was published in 2011. Key considerations include selecting lines of enquiry that are most relevant to the target context, setting review boundaries in accordance with available evidence, and iterative question formulation and repeated searching. The final review questions should have the ultimate aim of usefully informing effectiveness reviews. Protocols should describe how the qualitative evidence synthesis is integrated with the effect review, how it can inform the ongoing design and conduct of the effect review, or how it will increase understanding of the findings from an effect review. The protocol should state whether included studies aim to directly inform effectiveness and/or increase understanding of the phenomenon in general. Logic models and theoretical frameworks may be required to propose how qualitative evidence contributes to understanding of how an intervention ought to work, and they can also be used to describe how data will be extracted to map the full complexity of the phenomenon of interest. Consequently, the final protocol may function as a guide

rather than a prescriptive route-map, particularly in qualitative reviews that ask more exploratory and open ended questions.

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Box 1 – Examples of root cause analysis, services and systems modelling

Root cause analysis is a set of tools and methods for establishing relationships between an initiating event or situation, and the chain of effects leading to observed problems. Originating in industry, the approach can be used to:

- Retroactively or proactively assess risk, identifying factors that compromise patient safety [14]
- Map flows and blockages in services at a systems level [15]
- Help policymakers do actionable cause analysis, in order to prioritise the problems that are most feasible to address [16]

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Box 2 - Approaches to involving stakeholders in reviews

1) Before-After involvement: Stakeholders are included during the problem framing stage, and then comment on the results of the review towards the end of the process. [19]

2) Iterative involvement: Stakeholders are consulted at agreed milestones during the review which may entail a number of milestones with the aim of promoting higher levels of engagement, ownership and active dissemination of findings [20]

3) Synchronous involvement: is 'real time' two-way involvement representing an active exchange and comparison of review findings with practitioner and service user experience.,where involvement is used to collectively interpret and co-produce the review. [21].

Before-after involvement requires skills in promoting dialogue about the meaning of evidence and reflexivity, and in eliciting multiple views. When dealing with complexity, and when aiming to ensure that review findings are mobilized, iterative and synchronous involvement can help to create shared ownership of the review process.

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Box 3 - Illustrative Frameworks for Context

The PARiHS Framework [34] reserves "context" to refer to "the environment or setting in which people receive healthcare services, or in the context of getting research evidence into practice, the environment or setting in which the proposed change is to be implemented".

The PROGRESS-Plus Framework [30] seeks to apply an equity lens to the context which surrounds specific interventions. Originally known simply as PROGRESS it emphasizes that multiple contextual factors affect health inequity. The original acronym stands for **P**lace of residence; **R**ace/ethnicity/ culture/ language; **O**ccupation; **G**ender/sex; **R**eligion; **E**ducation; **S**ocioeconomic status; and **S**ocial capital. To acknowledge that, in some contexts, additional factors may affect the impact of an intervention on equity PROGRESS was expanded into PROGRESS-Plus [36] to include other context-specific factors that facilitate disadvantage. These factors include: personal characteristics associated with discrimination (e.g., age, disability), features of a relationship (e.g., smoking parents, excluded from school), time-dependent relationships and other circumstances that may indicate disadvantage.

The CICI Framework [36] is an overarching framework of interacting dimensions of context (including setting) and implementation. This framework comprises eight domains of context (i.e. setting, geographical, epidemiological, socio-cultural, socio-economic, ethical, legal and political) and four domains of implementation (i.e. provider, organisation and structure, funding and policy)

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Feasibility: the extent to which an activity or intervention is physically, culturally or financially practical or possible within a given context.

Sample review question: What are the factors influencing how healthcare professionals use protocols to wean adults and children from mechanical ventiliation? Findings revealed issues with feasibility e.g. resources for implementation, as well as appropriateness – the social and cultural environment where the protocol was implemented. [41]

Appropriateness: the extent to which an intervention or activity – or strategies for implementation - fits with the situation of the patient and/or the context in which care is given.

Meaningfulness: the extent to which an intervention or activity relates to the personal experience, opinions, values, thoughts, beliefs and interpretations of patients or clients.

Sample review question: How do people feel they may benefit from participation in environmental enhancement and conservation activities? [42]

Sample review question: What are the factors influencing the uptake of routine antenatal care from the perspective of pregnant and postnatal women? This protocol posits that prior attitudes and beliefs about the value of care, local social norms and control and autonomy about attendance, and finances may all influence uptake. Findings from the completed review may include aspects of feasibility, appropriateness, and meaningfulness. [43]

Effectiveness: the extent to which an intervention, when used appropriately, achieves the intended effect.

Affordability: the extent to which an optimal allocation of limited resources for the production of benefit to society is achieved.

Equity: the extent to which an intervention reduces unfair and avoidable or remediable differences in health among social groups

Adapted from [39, 40]

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Box 5 - Using type of available evidence and relevance to shape the question

Rashidian et al. [41] structured their protocol for doctor-nurse substitution strategies by noting that one common strategy is to delegate tasks to less highly skilled health workers. Because the setting of interest was low income countries, they narrowed the focus from health workers to doctor-nurse substitution, a common strategy in LMIC settings that was found to be effective in higher income countries. They note, however, that the relative effectiveness of nurses may depend on a combination of contextual elements that play out differently across different settings. This consideration of context is a key step in refining the scope of a review. Various explanations for using substitution were put forward, including propositions that: nurses may be more affordable; may improve access and quality; and may promote retention of nurses. Ability to establish these relationships, however, is dependent upon the amount of evidence available that explains how and why the intervention works.

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Box 6 - Worked Example of a SPICE Question

For example, a systematic review of qualitative research conducted for the National Institute for Clinical Excellence identified the following research question:

Among people from high-risk groups identified to be at a high risk of hepatitis B and C infection, their close contacts, and practitioners, what are their knowledge, beliefs and practices in relation to hepatitis B and C?

This translates into the SPICE framework as follows:

Setting	**Perspective(s)**	**Interest, Phenomenon of**	**Comparison**	**Evaluation**
In the Community	People at high risk; close contacts; practitioners	Hepatitis B and C	*By implication only,* compared with those at low risk	Knowledge, beliefs and practices

Example adapted from [75]

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Box 7 – Components of the CLUSTER Method [51]

CLUSTER Method – A systematic attempt, using a variety of search techniques, to identify papers or other research outputs that relate to a single study. This relation may be direct (i.e. "sibling" papers produced from the same study) or indirect ("kinship" studies that inform theoretical or contextual elements of the study of interest) [51].

Citations	Identify at least one key "pearl" citation, agreed through consensus by the review team
Lead Authors	Check Reference list for additional relevant citations by the Authors and re-check review Reference Management database for additional references by same authors possibly overlooked by the sift process.
Unpublished materials	Search Google for lead author (and other authors as appropriate). Seek to identify Contact email, Publications list, Institutional repository
Scholar searches	Conduct citation searches on Google Scholar for key pearl citation (and other publications as appropriate), extending to Web of Science or Scopus is available.
Theories	Follow up key pearl citation and other cluster documents for citation of theory
Early Examples	Follow up key pearl citation and other cluster documents for citations to project antecedents and related projects
Related Projects	Conduct named project and citation searches for relevant projects identified from cluster documents

Box 8 – Features and Functions of The Review Protocol

The final protocol should

- Frame the problem according to the interests of stakeholders
- Present an argument for the importance of the review, its relevance to the problems described and its potential utility to policymakers
- Describe the amount and type of relevant research potentially available
- Present review question(s) that are an outgrowth of the argument presented
- Describe how and why the intervention works, providing a preliminary theoretical framework or logic model where appropriate
- Describe the methods for identifying relevant studies for knowledge building or theory generating reviews, as appropriate
- Describe methods for data extraction that allow exploration of the review question(s)
- Include an approach to synthesis that potentially enables reviewers to answer the questions

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Box 9 - Sections of a protocol for a Qualitative Evidence Synthesis

Title
Protocol information:
- Authors*
- Contact person*
- Dates
- What's new
- History

The protocol:
- Background
- Objectives
- Methods:
  - Criteria for selecting studies for this review:
    - Types of studies
    - Types of participants
    - Topic of interest
  - Search methods for identification of studies
    - Data collection
    - Sample and Screening procedure
  - Assessment of study quality
  - Assessment of confidence in the Evidence from Reviews of Qualitative Research
  - Data-extraction and synthesis approach
- Acknowledgements
- References:
  - Other references:
    - Additional references
    - Other published versions of this review
- Tables and figures:
  - Additional tables
  - Figures

Supplementary information:
- Appendices
- Feedback:
  - Title
  - Summary
  - Reply
  - Contributors

About the article:
- Contributions of authors
- Declarations of interest
- Sources of support:
  - Internal sources
  - External sources
- Published notes

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Table 1: Typology of questions for review using qualitative research

Effectiveness Inquiry (Quantitative) : Does it work ?	**Meaningfulness Inquiry: What are the experiences, perceptions, opinions of the target group?**	**Appropriateness Inquiry: To what extent will it fit (or is it likely to fit) with the cultural, ethical or equity context from the perspectives of providers and beneficiaries?**
• What is the effectiveness of (intervention) (compared to…) for the population? • Do the effects vary in relation to subgroups within the population? • How well does (intervention) solve (problem)? • Which variables moderate the impact on the (intervention) on the outcome?	• What does it mean to have (condition) • What does it mean to be (characteristic of individual or target group) • What is the problem experienced by (target group)? • How does the (target group) feel about (participating in) (intervention)? • What was gained from participating in the intervention? • In what way, if any, has the intervention influenced the target group's practice?	• How do people perceive the effectiveness of (intervention) (compared to…)? • Is the intervention appropriate, acceptable and accessible to people within their local context? • How does the intervention (potentially) impact on equity from both a positive and negative perspective for different population groups? • Are the desired outcomes the outcomes that are valued by the population? • Are the desired outcomes consistent with people's priorities and/or beliefs? • What is the population's perception/experience of negative consequences of the intervention? • What particular events, beliefs, attitudes or policies may impact on the outcomes?

Adapted from: [16] [18] [31] [39]

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Table 1 continued

NB: Shaded areas contain elements that cannot be addressed by QES

Feasibility Inquiry: Is it politically, economically, technologically, and legally, practical or possible within a given context	**Implementation Inquiry: What is the process for delivering the intervention/programme?**	**Economic Affordability Inquiry: How cost-effective are the programs compared in the review?**

• What are the strengths/weaknesses of the intervention in this context?
• What are the opportunities/ threats related to the intervention in this context?
• What are barriers/ facilitators to implementing the intervention in relation to:
  o Physical facilities?
  o Built environment?
  o Geographical area?
  o Local institutional arrangements or infrastructure?
  o Community and/or cultural norms and practices?
  o Cost of implementation?
	• What were the components of the intervention?
	• How was the target group recruited? Were there barriers to recruitment? (Recruitment)
	• Who participated? How many over time? Did the programme attract the target audience? (Reach)
	• What was the 'dose delivered'? (e.g. frequency, duration, intensity)
	• Did participants actually engage with the intervention
	  o Was utilization and interaction with programme strategies, materials, resources measured? (Dose received)
	  o How did participants experience the intervention and did their experiences affect engagement? (Participant engagement)
	• What were provider experiences of delivering the intervention? (Provider engagement)
	• Was the intervention implemented as planned? Why or why not? (Fidelity)
		• Cost minimization: what is the least costly program where multiple programs have demonstrated similar benefits?
		• Cost effectiveness: what are the unknown or potentially different resource implications for programs that achieve similar outcomes?
		• Cost utility: what is the benefit of a particular program in terms of quantity and quality of life?
		• Cost benefits: what do we gain or lose from applying a particular program in terms of monetary ratio?

Table 2 - Notations for Qualitative Question Formulation

Notation	Components
3WH	What (topical), Who (population), When(temporal), How (methodological) [64]
BeHEMoTh	**B**ehaviour**, H**ealth context**, E**xclusions**, M**odels **o**r **T**heories [53]
CHIP	**C**ontext of the particular study, **H**ow the study was conducted, the **I**ssues examined, and the **P**eople involved in the study [65]
CIMO	**C**ontext. **I**ntervention. **M**echanisms, **O**utcomes [66]
ECLIPSe	**E**xpectations (improvement, innovation or information), **C**lient group (recipients of service), **L**ocation (where service is housed), **I**mpact (what change in service and how measured), **P**rofessionals involved, **Se**rvice [67]
PEICO(S)	**P**erson, **E**nvironment, **I**ntervention, **C**omparison, **O**utcomes, (**S**takeholders) [68]
PICO	**P**atient/**P**opulation, **I**ntervention, **C**omparison, **O**utcomes [69]
PICo	**P**opulation, phenomenon of **I**nterest, **Co**ntext [70]
PICOC	**P**atient/**P**opulation, **I**ntervention, **C**omparison, **O**utcomes, **C**ontext [71]
PICOS	**P**atient/**P**opulation, **I**ntervention, **C**omparison, **O**utcomes, **S**tudy Type [72]
SPICE	**S**etting, **P**erspective, **I**ntervention/ phenomenon of **I**nterest, **C**omparison, **E**valuation [73]
SPIDER	**S**ample, **P**henomenon of **I**nterest, **D**esign, **E**valuation, **R**esearch type [74]

Figure 1 Flow chart for question formulation and protocol development

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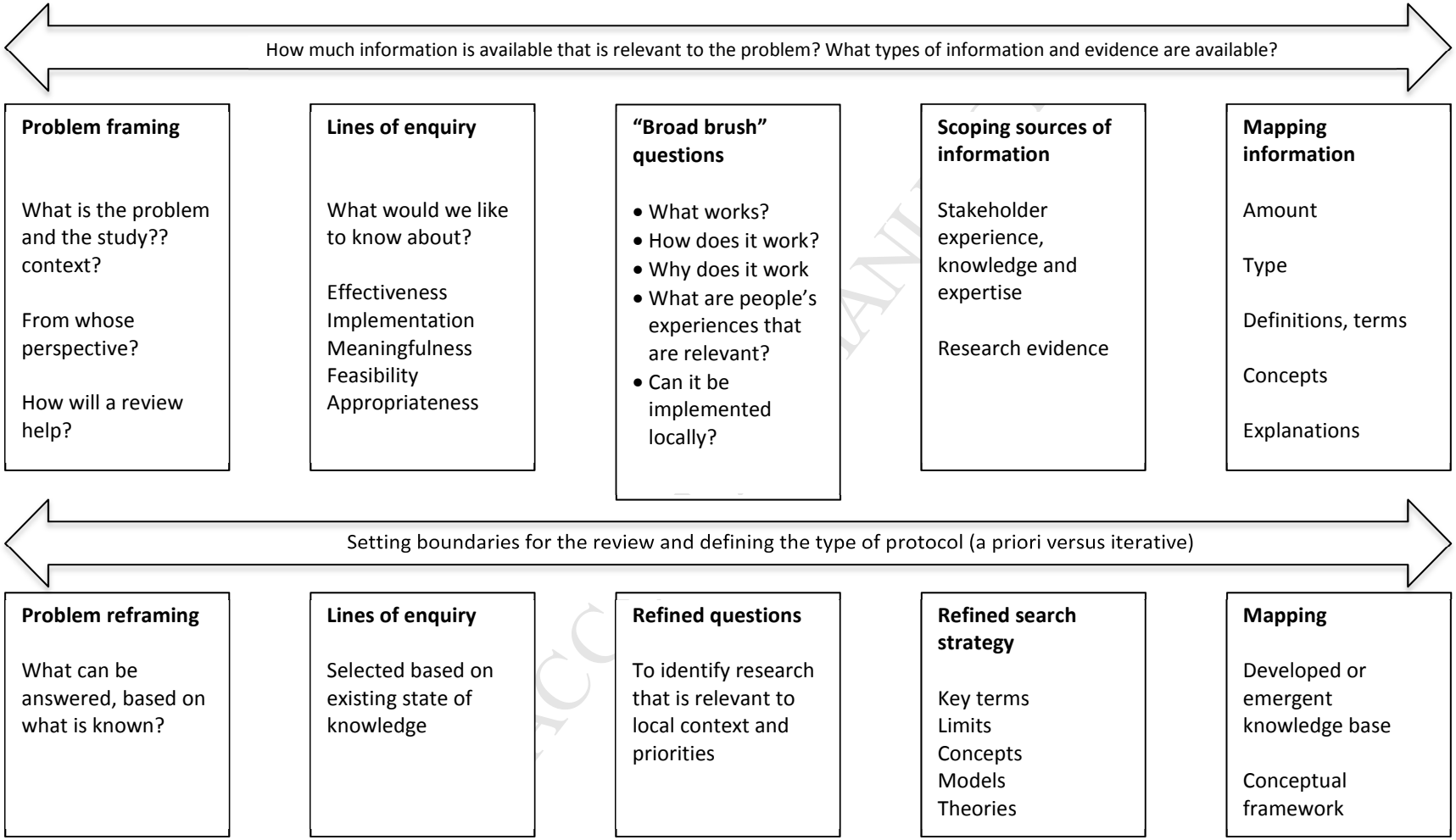
Figure 1 Iterative process for protocol development



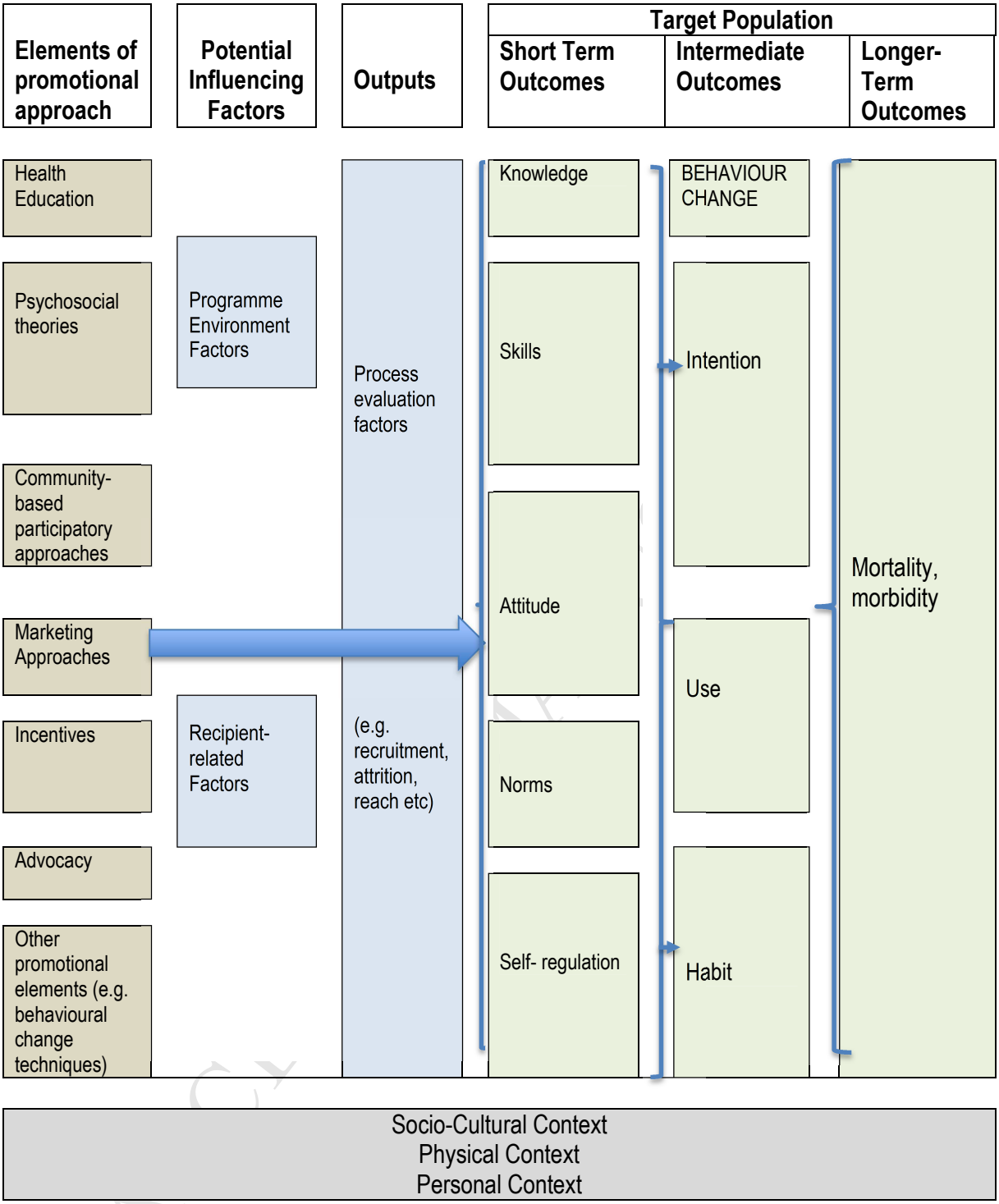


Figure 2 – Simplified Logic Model (Redrawn from [28])

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Figure 3: Relationships between lines of enquiry and logic model