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# AHRQ series on complex intervention systematic reviews—paper 2: defining complexity, formulating scope, and questions

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## Abstract

**Background:** The early stages of a systematic review set the scope and expectations. This can be particularly challenging for complex interventions given their multidimensional and dynamic nature.

**Rationale:** This paper builds on concepts introduced in paper 1 of this series. It describes the methodological, practical, and philosophical challenges and potential approaches for formulating the questions and scope of systematic reviews of complex interventions. Furthermore, it discusses the use of theory to help organize reviews of complex interventions.

**Discussion:** Many interventions in medicine, public health, education, social services, behavioral health, and community programs are complex, and they may not fit neatly within the established paradigm for reviews of straightforward interventions. This paper provides conceptual and operational guidance for these early stages of scope formulation to assist authors of systematic reviews of complex interventions. 

*Keywords:* Complex interventions; Evidence-based medicine; Review literature as topic; Systematic review; Qualitative research; Research design

## 1. Introduction

This is the second of a seven-part series of papers providing tools and approaches for conducting reviews of complex interventions. This paper focuses on the initial stages of a review on complex interventions which involve understanding whether and how the review topic is complex, methods and approaches to generating and refining review questions without oversimplifying, and introduces novel approaches to exploring complexity such as scoping the reviews and use of theories as a potential organizational approach for complex interventions.

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Conventional methods of systematic review have been developed and tested over time and offer a reliable and consistent way to evaluate the evidence for medical tests and treatments. However, when applied to complex interventions that depend on multiple factors and changes, these systematic review methods may unintentionally oversimplify the complex nature of the intervention; especially those involving multiple components or which are implemented across multiple settings [1]. To provide a relevant and useful assessment of the evidence, systematic reviews of complex interventions need to consider how the complex nature of an intervention affects the outcomes of that intervention. This paper offers guidance on how to frame a systematic review on complex interventions, particularly on formulating the scope and key questions. Specifically, we describe points to consider before undertaking a systematic review in which the topic of interest involves interventions, contexts, human behaviors, outcomes, or mechanisms of action that might be described as complex. Problem formulation in the context of a systematic review of complex interventions is an iterative and emergent process that requires careful articulation before the literature review. At all points in the process, the activities described are team activities and involve joint decision making. Examples are given from Cochrane and the US Evidence-based Practice Centers program to help the reader understand how these concepts can be applied to reviews.

## 2. Determining whether and how the review topic and questions are complex

Defining the complexity of the area of interest is the initial step in understanding the topic and developing the key questions to be addressed in the review. Interventions that involve human behavior and interactions in organizations and institutions or that are about policy are typically complex [1].

Complexity has been defined in various ways [2,3]. A consolidated definition for complex interventions and a ''rule of thumb'' for when to consider a topic complex are proposed by the first paper of this series [4]. The definition is included in this paper as well for clarity as this paper elaborates on the definition and guidance.

Definition of complex interventions [4]

All complex interventions have two common characteristics: they have multiple components (intervention complexity) and complicated/multiple causal pathways, feedback loops, synergies, and/or mediators and moderators of effect (pathway complexity). In addition, they may also have one or more of the following three additional characteristics: target multiple participants, groups, or organizational levels (population complexity); require multifaceted adoption, uptake, or integration strategies (implementation complexity); or work in a dynamic multidimensional environment (contextual complexity).

Complexity may occur in the following overarching domains: intervention, pathway, population, implementation, and context [5]. Complexity may result when an intervention involves multiple components and internal arrangements [3]. It may reflect treatment heterogeneity. It also occurs when the intervention depends on a variety of contextual or environmental factors; takes place in a complex population, health system, organizational, or institutional setting; or requires iterative flexibility or tailoring of the intervention to adapt to changing environmental or other contextual conditions. Clarifying how these externalities influence the outcome is critical to developing a comprehensive understanding of the causal pathways that will guide the review questions and subsequent steps of the systematic review. In the following, we distinguish interventional complexity from implementation and contextual complexity.

Interventional complexity refers to situations in which the effects of an intervention are expected to be modified by characteristics of the intervention itself [5]. It may involve interacting components in the intervention and/or control. In complex systems, what constitutes an intervention may be vague. In public health, for example, interventions for smoking cessation [3], slum-upgrading [4], preventing alcohol misuse [6], preventing excess winter deaths [7], the integration of mental health treatment and primary care [8,9], and early childhood education programs [10], may involve an array of different actions that may be taken simultaneously and at multiple levels (eg, individual and community).

Implementation complexity [5] describes how the effects of an intervention or responses to it may be modified by implementation processes. For example, the intervention may require multifaceted adoption, uptake, or integration strategies, and factors such as administrative support and payment mechanisms may need to be altered to the ease of implementation of a new process [11].

Contextual complexity, a closely related concept, refers to the characteristics of the settings or contexts where the intervention is implemented. For example, the integrated care approach for mental health in primary care noted earlier was more easily implemented in situations where medical and mental health professionals had a history of collaboration [8,9].

In contrast, population complexity occurs when intervention effects are modified by variant characteristics of the participants (individuals, groups, or organizations) receiving the intervention [5]; these may involve physical conditions such as comorbidities or social factors. For example, patient-level literacy or numeracy issues affecting medication adherence [12] or socioeconomic differences affecting smoking cessation interventions [13]. Interactions between variables affiliated with two or more distinct dimensions of the intervention need to be addressed [3,5,14–19].

## 3. Formulating the questions: engaging stakeholders to understand the complexities of a topic

Engaging stakeholders, people who will use, be affected by, or have an interest in the topic of the evidence review, is an important step in improving the relevance and usefulness of any systematic review. For this reason, many programs that produce systematic reviews now engage stakeholders early in the process of conducting a review. Reviewers from the Agency for Healthcare Research and Quality's (AHRQ) Evidence-based Practice Center (EPC) Program, for example, develop systematic reviews for clinicians, consumers, and policymakers while routinely engaging stakeholders across the spectrum of the Program's activities; including the selection of topics for systematic review and systematic review development (Fig. 1). Stakeholders may include people with expertise in delivering the complex intervention, and their knowledge and skills will also be drawn upon at all phases of the work.

Investigators are guided by principles described in Program guidance documents to ensure a balanced, unbiased, and rigorous process. AHRQ provides guidance and educational modules for the selection and engagement of stakeholders spanning nomination, development, review, and future research [20–23]. This process has been traditionally depicted as a linear one, although it does in reality encompass iterative engagement with stakeholders (Fig. 2). This engagement process can add new dimensions to a topic and is particularly important for complex topics. The EPC Program engaged individuals of diverse perspectives to prioritize research gaps identified in a comparative effectiveness review on medications to reduce the risk of breast cancer [24]. This group was interested in a range of interventions beyond medications such as diet, behavioral changes, and physical activity; a significant emphasis was placed on contextual influences including family, environment, economic, education, social, and health system influences. Furthermore, an AHRQ white paper addressed the benefits of stakeholder engagement in the systematic review process [25]. The white paper asked a number of EPC directors about the benefit of stakeholder engagement in their work; these added dimensions are described in Box 1.

Explicitly incorporating complexity into the topic scope and stakeholder discussions may prevent oversimplification of the topic area and review questions and ensure a shared understanding of the breadth and depth of review most helpful for the end user. Reviewers assessing complex interventions may require broad and deep engagement with a variety of stakeholders to understand complexity, the utilization of different methods of engagement to communicate complexity clearly, and provision of specific information outlining complexity to elicit and inform stakeholder input on the scope of the review. Communicating complexity in a way that elicits helpful input may require reviewers to consider how and where different stakeholder perspectives may be informative. In a review on teenage pregnancy prevention, for example, the reviewers created an a priori knowledge map (sometimes referred to as a scoping review) to understand the facets of complexity to describe the streams of evidence for effectiveness, risk factors and effect modifiers, implementation, acceptability, contextual factors, and barriers and facilitators to uptake of interventions

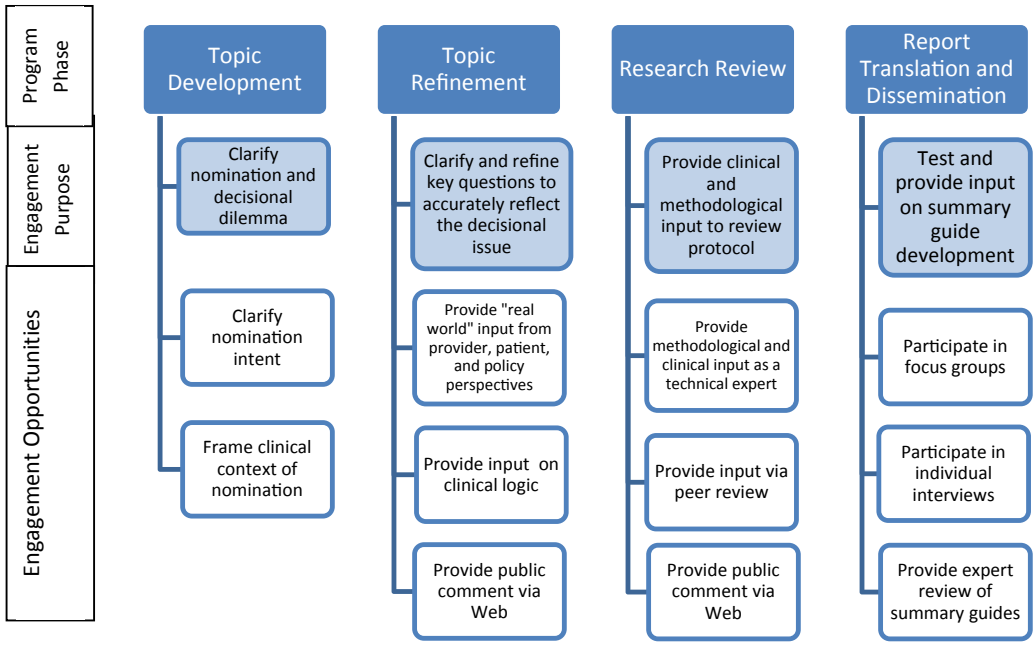


**Fig. 1.** Engagement of stakeholders in the US Evidence-based Practice Center Program.

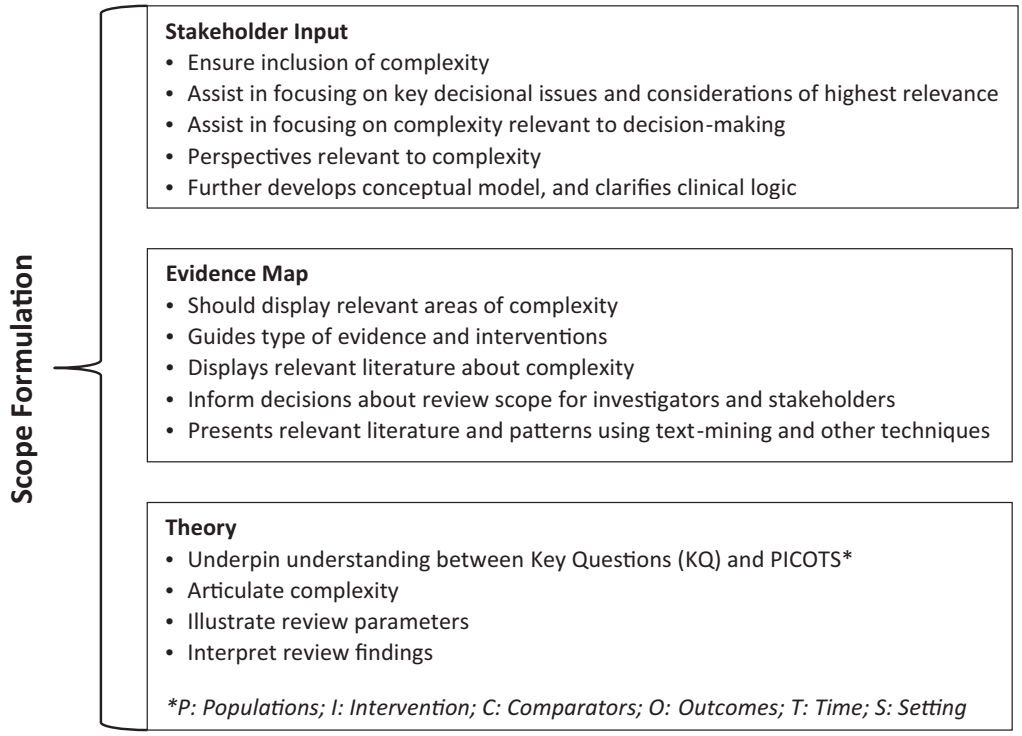


**Fig. 2.** Approach to scope formulation for systematic reviews of complex interventions.

(see Box 2 below for brief definitions). This mapping exercise, in addition to informing the review, was used to engage with the advisory group, including stakeholders in the field, on the areas of focus and further investigation, refinement, and prioritization in the subsequent review [29]. Guidance on the production of knowledge maps is available from the EPPI-Centre, London [30,31].

## 4. Scoping complex interventions: organizing without oversimplifying

The process of scoping the review requires a different way of thinking. Formulating questions within the context of a systematic review typically begins with a broad overarching topic that is then gradually focused into more precise problem formulation, using input from stakeholders and the literature base. That is, review questions are scoped through gradual and iterative stages, with input from the literature, stakeholders, and the content expertise of the review team. In scoping decisions, the review team may consider issues including fidelity to the intent of the original question, feasibility of a systematic review, responsiveness to stakeholder input, and relevance to the intended end user [32].

However, a different way of thinking about question formulation that goes beyond the standard approach of conventional systematic reviewing is required for complex interventions. Approaches such as a mapping/scoping review and the use of theory may assist in articulating complexity during the question formulation process (Fig. 2) [33]. A mapping/scoping review can be used to map (but not systematically review) the literature in a field at the outset. A knowledge map can be helpful in determining the amount and type of evidence available and the different types of interventions. Some interventions are targeted at whole populations, some at communities, and others at neighborhoods or family settings; they are not just about outcomes or effects in individuals.

In complex interacting systems, causal pathways involve integrated biological, psychological, and social mechanisms [34]. As current interest moves on to include not only "what works" but also to "what happens" when an intervention is implemented [35], a more flexible approach to conceptualizing the review scope, question(s) and the

**Box 1 Engaging stakeholders throughout the systematic review process**

Stakeholder involvement early in the review process leads to a better "understanding [of] the context and history of a given topic, including areas of scientific uncertainty or debate and politically charged or "hot button" issues from a consumer or advocacy perspective." Some directors described "instances when stakeholders were able to uncover 'blind spots' including issues of current debate or concern that impacted what questions were asked or how the report's findings were communicated" [25].

**Box 2 Glossary of terms**

Knowledge mapping/scoping review—Reports a wide search for evidence on a topic to demonstrate the amount and type of evidence. The purpose is to look for what is published from which you can generate more specific review questions. This has also been referred to by some as an evidence inventory [26,27].

Logic models—"A logic model is a graphic description of a system and is designed to identify important elements and relationships within that system" [28].

review design [36] is required. Text-mining techniques, which use computer learning to aid in the retrieval and distillation of information from unstructured text, may be useful at this stage [32]. Other techniques such as automatic term recognition, document clustering, automatic document classification, and document summarization can help to speed the process of identifying relevant literature and recognizing emergent patterns and relationships in the literature [37]. The iCAT_SR tool has been designed to help reviewers categorize intervention complexity as a typology that can be used to visually map intervention complexity to gain a more detailed understanding to support data extraction and data interpretation [38,39].

### *4.1. Use of theory*

Social and epidemiologic theories can be especially helpful in delineating core components of a multicomponent intervention and defining the nature of interacting components [40]. The Cochrane Collaboration has produced guidance on the selection and use of social theories in reviews of complex interventions that reviewers can use as a resource [40]. Theory can aid in understanding how contextual factors, such as the physical, social, and economic environment, can affect an intervention's success. Theory can also help reviewers think beyond the usual clinical and sociodemographic patient-level characteristics to include organizational, cultural, and psychosocial factors [28,41]. Finally, theory can be used to help identify interactions between the different dimensions of complexity (Box 3).

**Box 3 Social theories successfully used to identify parameters in systematic reviews of complex interventions [28]**

An example of a Cochrane protocol for a mixed-methods review that incorporates social theory to develop the review parameters, phenomenon of interest, and questions is as follows: "Exercise for chronic hip and knee pain" [42]. Detailed logic models are commonly used to show diagrammatically the causal pathway and interactions and required behaviors between components, people, and the health system. The team developed a priori logic models (which are discussed in paper 3 of this series [43]) using their experiential knowledge, previous research, and integration of key concepts and models from literature to explore the complex, reciprocal relationship between pain, physical and psychosocial functioning, social support, rehabilitation, and a second model explored the effects of erroneous health beliefs on participation in exercise programs. Their initial proposition was that people's reactions to pain are highly variable and influenced by the beliefs, meanings, and explanations they attach to it. They subsequently interpreted evidence using the logic models to better understand these complex behavioral responses to interventions.

Another example of the development of theory throughout the review to focus the interpretation of evidence is reported by the review team who undertook the Cochrane slum-upgrading review. They convened an expert advisory group to develop an initial logic model (theory) and identify the parameters of what constituted slum upgrading, together with outcomes, impacts, and phenomena of interest such as what happens when multiple slum-upgrading interventions are implemented together [44,45]. Patient-reported outcomes are measured with instruments, whereas patient-reported impacts are less tangible and usually captured through interviews (such as feeling less frightened). The logic model was then further developed over the course of the review as a midrange theory as to how slum-upgrading interventions worked in combination to improve the lives of slum dwellers.

## 5. Refining the review questions

It is important to resist the temptation to oversimplify when formulating questions. For reviews of clinical interventions, refining the effectiveness question by using the PICO (Population, Intervention, Comparator, Outcomes) framework typically provides sufficient guidance for searching the literature [43,46]. The basic principle is that the review question has to be defined in advance. It can be challenging, however, to set review questions and conduct reviews as application of systematic approaches to reviewing the evidence for complex interventions moves beyond clinical medicine. The nature of interactions involved within the empirical areas of interest and the diverse methods used to collect primary data in them require alternative approaches.

Outlining a definitive question or questions a priori will often not suffice when dealing with complexity [47]. The question(s) with which the work begins should seldom be reduced to ''is X effective?'' as ''X'' is frequently a multitude of different things. Complex intervention review questions must go beyond assessing whether or not an intervention works, to interrogating which components are essential, how and why an intervention works, for whom an intervention works or does not work, and under what circumstances an intervention works or not [36]. When preparing to search for and review evidence about complex interventions, questions must be iteratively refined as the complexity is elaborated and the evidence is explored. Inputs from stakeholders and the use of theory, as described previously, can contribute to this process by providing guidance on relevant or important types of complexity to enhance the usefulness and feasibility of a systematic review.

All of this is important because the a priori determination of the question(s) is not value neutral. The nature of the questions determines the kinds of evidence that will be searched for and indeed what can be considered as evidence at all. If the questions are wrong, or only partially right, the evidence that comes to light will almost certainly be only partially relevant to the complexity of the problem under consideration. It is important not to assume in advance that the kinds of evidence relevant to the problem and the methods used to produce it are already well understood. Instead, with complexity, judgment is required to interpret the emerging questions and the kinds of evidence needed to answer them [48]. The assumption that we know in advance what the relevant evidence is and have confidence in the methods used to find and evaluate it is true so long as there is a direct linear pathway between intervention and outcome, the pathway is short, all confounding factors can be known and controlled for, and the relationship between the dependent and the independent variables is real [34,48]. However, in complex interventions (especially social and organizational systems), binary linear relationships between single dependent and independent variables can exist only as analytic abstractions or simplified models, which cannot faithfully represent these complex multifaceted interacting systems [36].

## 6. Conclusions

Systematic reviews of complex interventions require substantial adaptation of conventional review methods, including the use of additional methods that incorporate different types of diverse evidence. The current process for scope formulation in traditional reviews has largely been conceived as a linear process with discrete phases. When conducting reviews of complex interventions, considerable effort needs to be frontloaded into the process to allow for the emergence of clear research questions to guide the review(s). This may require an approach that is more iterative and explicitly explores complexity in the literature and with stakeholders. This involves clarifying complexity and articulating which elements are complex (the intervention, its implementation, its setting and so on). In clarifying causal pathways, it may be helpful to use knowledge mapping and technologies such as text mining as innovative approaches to mapping the literature during problem formulation. Reviewers should consider the input of stakeholders and expert advisers, theory, and evidence mapping in the process of determining the review's scope. New methods and strategies for communicating and framing complexity may be needed to elicit informed and relevant stakeholder input. In addition to all, reviewers should resist the temptation of simple linear models, which can distort the reality under consideration and affect the relevance and usefulness of the review.

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