

Portland State University

**PDXScholar**

---

OHSU-PSU School of Public Health Faculty  
Publications and Presentations

OHSU-PSU School of Public Health

---

10-1-2017

# AHRQ Series on Complex Intervention Systematic Reviews-Paper 1: An Introduction to a Series of Articles that Provide Guidance and Tools for Reviews of Complex Interventions

Jeanne-Marie Guise  
*OHSU-PSU School of Public Health*

Christine Chang  
*Agency for Healthcare Research & Quality*

Mary E. Butler  
*University of Minnesota*

Meera Viswanathan  
*RTI International*

Peter Tugwell  
*University of Ottawa*

Follow this and additional works at: [https://pdxscholar.library.pdx.edu/sph\\_facpub](https://pdxscholar.library.pdx.edu/sph_facpub)



Part of the [Medicine and Health Sciences Commons](#)

**Let us know how access to this document benefits you.**

---

## Citation Details

Guise, J. M., Chang, C., Butler, M., Viswanathan, M., & Tugwell, P. (2017). AHRQ series on complex intervention systematic reviews—paper 1: an introduction to a series of articles that provide guidance and tools for reviews of complex interventions. *Journal of clinical epidemiology*, 90, 6-10.

This Article is brought to you for free and open access. It has been accepted for inclusion in OHSU-PSU School of Public Health Faculty Publications and Presentations by an authorized administrator of PDXScholar. Please contact us if we can make this document more accessible: [pdxscholar@pdx.edu](mailto:pdxscholar@pdx.edu).

SERIES: AHRQ SERIES ON COMPLEX INTERVENTION SYSTEMATIC REVIEWS

AHRQ series on complex intervention systematic reviews—paper 1: an introduction to a series of articles that provide guidance and tools for reviews of complex interventions

Jeanne-Marie Guise<sup>a,b,c,d,\*</sup>, Christine Chang<sup>e</sup>, Mary Butler<sup>f</sup>, Meera Viswanathan<sup>g</sup>, Peter Tugwell<sup>h</sup>

<sup>a</sup>Department of Obstetrics & Gynecology, Oregon Health & Science University School of Medicine, 3181 SW Sam Jackson Park Road, Portland, OR 97239, USA

<sup>b</sup>Department of Medical Informatics & Outcomes Research School of Medicine, Oregon Health & Science University, 3181 SW Sam Jackson Park Road, Portland, OR 97239, USA

<sup>c</sup>Department of Emergency Medicine, Oregon Health & Science University School of Medicine, 3181 SW Sam Jackson Park Road, Portland, OR 97239, USA

<sup>d</sup>Oregon Health & Science University, Portland State University School of Public Health, 3181 SW Sam Jackson Park Road, Portland, OR 97239, USA

<sup>e</sup>Agency for Healthcare Research & Quality, 5600 Fishers Lane, Mailstop 06E53A, Rockville, MD 20857, USA

<sup>f</sup>University of Minnesota School of Public Health, 420 Delaware Street SE, Minneapolis, MN 55455, USA

<sup>g</sup>RTI International, 3040 East Cornwallis Road, Research Triangle-Park, NC 27709, USA

<sup>h</sup>Department of Medicine, University of Ottawa, 43 Bruyère Street, Annex E, Room 304, Ottawa, Ontario, Canada K1N 5C8

Accepted 8 June 2017; Published online 15 July 2017

**Keywords:** Complex interventions; Health care interventions; Evidence-based medicine; Systematic review; Research design; Review literature as topic; Guidance as topic

## 1. Introduction

Issues of complexity are taking primacy as research increasingly reflects the complexity of the world around us. Although advances in science have resulted in dramatic improvements in health and longevity worldwide, there is increasing recognition that the effectiveness even of apparently simple interventions is often influenced by complex interplays of individual characteristics, social determinants, the health care delivery system, and the interventions themselves. Systematic reviews of topics, such as slum upgrading [1,2], behavioral interventions for autism [3,4], smoking cessation in pregnancy [5], and the integration of mental health in primary care [6,7], illustrate that the boundaries of traditional reviews and review methods are being expanded and that reviewers are in need of guidance and tools to address this new approach.

When the methods for conducting systematic reviews were originally developed, the process of reviewing the

literature was treated as relatively straightforward. Complexity existed, but reviewers often tried to simplify this complexity to group studies and in attempts to make comparative claims. In general, the systematic reviews and primary research included in systematic reviews approached research from a classic reductive philosophic and methodologic stances. Increasingly, people interested in adopting published interventions from reviews have found that this reductive stance eliminates details that are critical for them to understand whether the intervention is feasible and likely to work in their context, with their populations, and at what cost. As the fundamentals of evidence-based practice are now established, complexity has moved to the forefront.

In order for systematic reviews to address this complexity, all stages of the review, including question formulation, framework development, selection of review and analytic methods, and synthesis, need to account for

Funding: Agency for Healthcare Research & Quality (HHS290201200004C, HHS290201200016I, and HHS290201500011I).

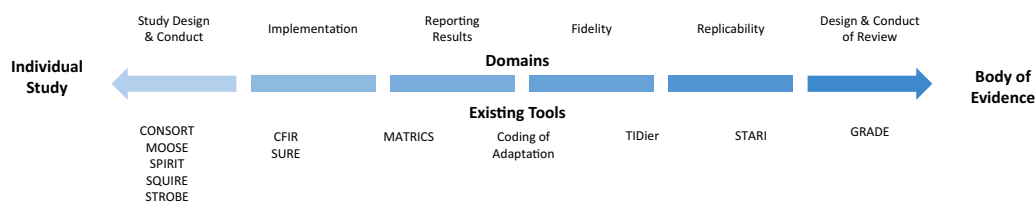
Conflict of interest: The authors have no conflicts of interest to report. The authors alone are responsible for the content and writing of the article. This project was funded under Contracts from the AHRQ, US Department of Health and Human Services. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the AHRQ or the US Department of Health and Human Services.

\* Corresponding author. Tel.: +1-503-494-2101; fax: +1-503-494-5296.

E-mail address: guisej@ohsu.edu (J.-M. Guise).

<http://dx.doi.org/10.1016/j.jclinepi.2017.06.011>

0895-4356/© 2017 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



**Fig. 1.** Existing tools for complex interventions. CONSORT, Consolidated Standards of Reporting Trials [8]; MOOSE, Meta-analysis Of Observational Studies in Epidemiology [9]; SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials [10]; SQUIRE, Standards for QUality Improvement Reporting Excellence [11]; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology [12]; CFIR, Consolidated Framework for Implementation Research [13]; SURE, Supporting the Use of Research Evidence [14]; MATRICS, Method for Aggregating the Reporting of Interventions in Complex Studies [15]; Coding of Adaptations [16]; TIDier, template for intervention description and replication [17]; STARI, Standards for Reporting Implementation studies of complex interventions [18]; GRADE, Grading of Recommendations, Assessment, Development and Evaluations [19].

these sources of complexity. Although several tools offer guidance for research on complex interventions, implementation of complex interventions, or specific aspects of conducting reviews (Fig. 1), until now, there has been no source of overarching guidance specific to systematic reviews of complex interventions [8–19].

### 1.1. Series approach

Against this backdrop, in 2013, the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center Program launched a methods development program around systematic reviews of complex interventions. Initial efforts focused on outlining high-level approaches and challenges in conducting reviews of complex interventions [20,21]. Around the same time, the Montebello series was published, which included several articles describing the theoretical foundations of complexity in systematic reviews of interventions [22–24]. Building on these efforts, we undertook a three-staged process to develop practical guidance and tools for reviews of complex interventions: in-person meeting establishing the complex interventions working group; international Delphi process of reporting elements of reviews of complex interventions; and ongoing expert workgroup consensus.

A six-person steering committee invited representatives from international evidence review groups, methodologists, funders, and systematic review publishers to attend an in-person conference. The committee identified five areas in need of guidance: (1) formulating review questions and scope; (2) Population, Intervention, Comparator, Timing, Setting as well as frameworks; (3) selecting analytic approaches; (4) best practices in analytic approaches for complex interventions; and culminating in (5) Preferred Reporting Items for Systematic Reviews and Meta-analyses for Complex Interventions (PRISMA-CI) checklist; and (6) PRISMA-CI explanation and elaboration. On June 18–19, 2015, 57 experts in quantitative and qualitative approaches to systematic reviews of complex interventions attended a conference at AHRQ's Eisenberg Building in Rockville, Maryland. The conference format included

presentations, moderated discussions, brainstorming, and writing roundtables. After the meeting conference attendees participated in designated workgroups via twice-monthly teleconference calls to draft documents providing guidance for systematic reviewers of complex interventions in the five outlined areas: (1) scope and questions; (2) frameworks, (3) selecting analytic methods; (4) advanced analytic methods and matching methods to review questions; and (5) reporting standards for reviews of complex interventions.

### 1.2. Defining complexity

To date, there is no single agreed on definition of complex interventions. For this series, we build on prior definitions and posit this consolidated definition for complex interventions [20,21,23–29].

#### Definition of complex interventions

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*).

### 1.3. How do I know if an intervention is complex?

To judge whether an intervention is simple or complex, systematic reviewers should specify clearly what the intervention is. Depending on how the intervention is framed, the same core component could potentially be reviewed as a simple or complex intervention. A complex intervention involves, at minimum, multiple components and a complex pathway. For example, if the focus of the review is the efficacy of taking aspirin after a myocardial infarction compared with another pill, placebo, or no treatment, this would not be a complex intervention. Although aspirin may act through complex biologic pathways, biologic or

**Table 1.** Description of article in the *Journal of Clinical Epidemiology* series on complex interventions

Key concept	Article title	Topic
Introduction	AHRQ series on complex intervention systematic reviews—paper 1: an introduction to a series of articles that provide guidance and tools for reviews of complex interventions	Provides an introduction and overview of the AHRQ series on complex intervention systematic reviews. This article discusses the process used to develop the series, provides a consolidated definition of complex interventions, and provides questions systematic reviewers can ask to determine whether the subject of their review is a complex intervention
Developing protocols for systematic reviews and meta-analyses of complex interventions Scoping questions	AHRQ series on complex intervention systematic reviews—paper 2: defining complexity, formulating scope, and questions [30]	Offers guidance on the earliest stages of a review, particularly on stakeholder engagement and scope and key question formulation. Complex intervention problem formation is an iterative and emergent <i>process</i> that requires careful articulation before the literature review
Developing frameworks	AHRQ series on complex intervention systematic reviews—paper 3: adapting frameworks to develop protocols [31]	Examines how to use frameworks to elaborate the research questions and define the study eligibility criteria (i.e., whether and why/how it works) and an analytic framework (or other visual model) to clearly depict how the analysis will address the key research questions, taking into account how the interventions may affect outcomes of interest
Developing analytic plans for systematic reviews of complex interventions Best practice analytic methods	AHRQ series on complex intervention systematic reviews—paper 4: selecting analytic approaches [32]	Describes important considerations for choosing analytic approaches for review questions about complex interventions
Selecting analytic approaches	AHRQ series on complex intervention systematic reviews—paper 5: advanced analytic methods [33]	Introduces analytic methods that can address four broad questions about complex interventions: (1) How effective is the intervention?; (2) How well does the intervention work for whom in what contexts?; (3) What happens when the intervention is implemented?; and (4) What decisions are possible given the results of the synthesis?
PRISMA-CI PRISMA-CI checklist	AHRQ series on complex intervention systematic reviews—paper 6: PRISMA-CI extension statement & checklist [34]	Provides a template for authors to use when reporting systematic reviews of complex interventions. It is intended to improve the transparency and scientific merit of systematic reviews of complex interventions
PRISMA-CI explanation and elaboration	AHRQ series on complex intervention systematic reviews—paper 7: PRISMA-CI elaboration & explanation [35]	Explains the meaning and rationale for each PRISMA-CI checklist item and provides examples for further clarity on their use

*Abbreviations:* AHRQ, Agency for Healthcare Research and Quality; PRISMA-CI, Preferred Reporting Items for Systematic Reviews and Meta-analyses of Complex Interventions.

physiologic complexity is not considered sufficient to categorize an intervention as complex for the purposes of a systematic review. However, a review question about how to increase adherence with daily aspirin after a myocardial infarction would be complex. Because behavioral interventions often use multiple approaches and target systems or multiple agents (e.g., providers, patients, family members, etc), they are commonly considered complex. A second example of a complex intervention would be personal protective equipment. A systematic review of the efficacy of one type of mask compared with another may reasonably

treat the intervention as simple. In contrast, systematic reviews focusing on effectiveness in public health settings and feasibility of uptake should consider the intervention to be complex: the effectiveness of the intervention depends on the context in which the personal protective equipment will be implemented, whether agents are available to perform fittings and testing, whether there are mechanisms available to disseminate the personal protective equipment items, whether training is required, and the ability of people to get to a place for training, and others. Each of these considerations can be deemed a component in this system

intervention. Commonly, public and population health, community and system-level interventions, and those aimed at behavior change are more likely to be complex than simple.

#### 1.4. Series overview

The seven articles in this series reflect and distill the discussions from the in-person meeting and follow-up workgroups on tools and approaches to systematic reviews of complex interventions (Table 1).

The first three articles address how systematic reviews for complex interventions are conceptualized and operationalized for the protocol [30,31]. The next two articles discuss how to choose appropriate analytic methods to implement analyses of complex interventions [32,33]. The final two articles [34,35] describe proposed reporting elements for systematic reviews of complex interventions.

Methods and approaches described in this series are intended to help researchers design and conduct systematic reviews of complex interventions to better answer important clinical, policy, and research questions; improve their usefulness; and improve health care and health outcomes. However, as the number of methods and approaches for reviewing complex interventions proliferate in a rapidly evolving field, unanswered questions remain about the relative value of these methods. Widespread adoption of new methods and transparency of reporting can help solidify our understanding of the best methods for complex interventions, advance the field, and help better answer pressing real-world questions. Recognizing that this is a rapidly evolving field, the complex interventions working group intends to monitor the application of these tools and modify them as needed.

#### Acknowledgments

The authors thank Terri Pigott for her participation and valuable contributions in planning the conference and this collection of work, all members of the complex interventions working group for their participation, and valuable intellectual discussions and contributions to this series; Karli Kondo and Kelly Vander Ley for their assistance with planning the in-person conference, Makalapua Motu'apuaka for her tireless work coordinating all planning committee meetings, in-person conferences, and all workgroup activities, and both Makalapua Motu'apuaka and Lyndzie Sardenga for their assistance on all documents and coordinating external reviews and comments. We thank Stephanie Chang and Arlene Bierman from AHRQ for their continued support and valuable input.

#### References

- [1] Turley R, Saith R, Bhan N, Rehfuess E, Carter B. Slum upgrading strategies involving physical environment and infrastructure interventions and their effects on health and socio-economic outcomes. *Cochrane Database Syst Rev* 2013;(1):CD010067. <http://dx.doi.org/10.1002/14651858.CD010067.pub2>.
- [2] Turley R, Saith R, Bhan N, Doyle J, Jones K, Waters E. Slum upgrading review: methodological challenges that arise in systematic reviews of complex interventions. *J Public Health (Oxf)* 2013;35:171–5.
- [3] Kay N, Pennucci A. Early childhood education for low-income students: a review of the evidence and benefit-cost analysis (doc. no. 14-01-2201). Olympia, WA: Washington State Institute for Public Policy; 2014.
- [4] Weitlauf AS, McPheeters ML, Peters B, Sathé N, Travis R, Aiello R, et al. Therapies for children with autism spectrum disorder: behavioral interventions update. Comparative effectiveness review no. 137. (Prepared by the Vanderbilt Evidence-based Practice Center under contract no. 290-2012-00009-I.) AHRQ publication no. 14-EHC036-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2014.
- [5] Likis FE, Andrews JC, Fonnesebeck CJ, Hartmann KE, Jerome RN, Potter SA, et al. Smoking cessation interventions in pregnancy and postpartum care. Evidence report/technology assessment no. 214. (Prepared by the Vanderbilt Evidence-based Practice Center under contract no. 290-2007-10065-I.) AHRQ publication no. 14-E001-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2014.
- [6] Butler M, Kane RL, McAlpine D, Kathol R, Fu SS, Hagedorn H, et al. Does integrated care improve treatment for depression?: a systematic review. *J Ambul Care Manage* 2011;34:113–25.
- [7] Butler M, Kane RL, McAlpine D, Kathol RG, Fu SS, Hagedorn H, et al. Integration of mental health/substance abuse and primary care. Evidence reports/technology assessments, no. 173. Rockville, MD: Agency for Healthcare Research and Quality (US); 2008.
- [8] Moher D, Schulz KF, Altman DG, Group C. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet* 2001;357:1191–4.
- [9] Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *J Am Med Assoc* 2000;283:2008–12.
- [10] Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200–7.
- [11] Davidoff F, Batalden P, Stevens D, Ogrinc G, Mooney S. Publication guidelines for improvement studies in health care: evolution of the SQUIRE project. *Ann Intern Med* 2008;149:670–6.
- [12] Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Prev Med* 2007;45:247–51.
- [13] Breimaier HE, Heckemann B, Halfens RJ, Lohrmann C. The Consolidated Framework for Implementation Research (CFIR): a useful theoretical framework for guiding and evaluating a guideline implementation process in a hospital-based nursing practice. *BMC Nurs* 2015;14:43.
- [14] World Health Organization. SURE guides for preparing and using evidence-based policy briefs. *Evidence-informed policy-making* 2011. Available at <http://www.who.int/evidence/sure/guides/en/>. Accessed June 2015.
- [15] Hutchings HA, Thorne K, Jerzembek GS, Cheung W-Y, Cohen D, Durai D, et al. Successful development and testing of a method for aggregating the reporting of interventions in complex studies (MATRICS). *J Clin Epidemiol* 2016;69:193–8.
- [16] Stirman SW, Miller CJ, Toder K, Calloway A. Development of a framework and coding system for modifications and adaptations of evidence-based interventions. *Implement Sci* 2013;8:65.
- [17] Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: Template for Intervention Description and Replication (TIDieR) checklist and guide. *BMJ* 2014;348:g1687.

- [18] Pinnock H, Epiphaniou E, Sheikh A, Griffiths C, Eldridge S, Craig P, et al. Developing standards for reporting implementation studies of complex interventions (StaRI): a systematic review and e-Delphi. *Implement Sci* 2015;10(1):42.
- [19] Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. *J Clin Epidemiol* 2011;64:380–2.
- [20] Guise J-M, Chang C, Viswanathan M, Glick S, Treadwell J, Umscheid CA, et al. Agency for Healthcare Research and Quality Evidence-based Practice Center methods for systematically reviewing complex multicomponent health care interventions. *J Clin Epidemiol* 2014;67:1181–91.
- [21] Guise J-M, Chang C, Viswanathan M, Glick S, Treadwell J, Umscheid CA, et al. Systematic reviews of complex multicomponent health care interventions. Rockville, MD: Agency for Healthcare Research and Quality (US); 2014.
- [22] Noyes J, Gough D, Lewin S, Mayhew A, Michie S, Pantoja T, et al. A research and development agenda for systematic reviews that ask complex questions about complex interventions. *J Clin Epidemiol* 2013;66:1262–70.
- [23] Anderson LM, Oliver SR, Michie S, Rehfuss E, Noyes J, Shemilt I. Investigating complexity in systematic reviews of interventions by using a spectrum of methods. *J Clin Epidemiol* 2013;66:1223–9.
- [24] Petticrew M, Anderson L, Elder R, Grimshaw J, Hopkins D, Hahn R, et al. Complex interventions and their implications for systematic reviews: a pragmatic approach. *J Clin Epidemiol* 2013;66:1209–14.
- [25] Kühne F, Ehmcke R, Härter M, Kriston L. Conceptual decomposition of complex health care interventions for evidence synthesis: a literature review. *J Eval Clin Pract* 2015;21:817–23.
- [26] Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;337:a1655.
- [27] Burford B, Lewin S, Welch V, Rehfuss E, Waters E. Assessing the applicability of findings in systematic reviews of complex interventions can enhance the utility of reviews for decision making. *J Clin Epidemiol* 2013;66:1251–61.
- [28] Pigott T, Shepperd S. Identifying, documenting, and examining heterogeneity in systematic reviews of complex interventions. *J Clin Epidemiol* 2013;66:1244–50.
- [29] Squires JE, Valentine JC, Grimshaw JM. Systematic reviews of complex interventions: framing the review question. *J Clin Epidemiol* 2013;66:1215–22.
- [30] Kelly MP, Noyes J, Kane RL, Chang C, Uhl S, Robinson KA, et al. AHRQ series on complex intervention systematic reviews—paper 2: defining complexity, formulating scope and questions. *J Clin Epidemiol* 2017;90:11–8.
- [31] Butler M, Epstein RA, Totten A, Whitlock EP, Ansari MT, Damschroder LJ, et al. AHRQ series on complex intervention systematic reviews—paper 3: adapting frameworks to develop protocols. *J Clin Epidemiol* 2017;90:19–27.
- [32] Viswanathan M, McPheeters ML, Murad MH, Butler ME, Devine EE, Dyson MP, et al. AHRQ series on complex intervention systematic reviews—paper 4: selecting analytic approaches. *J Clin Epidemiol* 2017;90:28–36.
- [33] Pigott T, Noyes J, Umscheid CA, Myers E, Morton SC, Fu R, et al. AHRQ series on complex intervention systematic reviews—paper 5: advanced analytic methods. *J Clin Epidemiol* 2017;90:37–42.
- [34] Guise J-M, Butler ME, Chang C, Viswanathan M, Pigott T, Tugwell P. AHRQ series on complex intervention systematic reviews—paper 6: PRISMA-CI extension statement & checklist. *J Clin Epidemiol* 2017;90:43–50.
- [35] Guise J-M, Butler M, Chang C, Viswanathan M, Pigott T, Tugwell P. AHRQ series on complex intervention systematic reviews—paper 7: PRISMA-CI elaboration & explanation. *J Clin Epidemiol* 2017;90:51–8.