ANNUAL REVIEWS

Annual Review of Public Health

Meta-Analysis of Complex Interventions

Emily E. Tanner-Smith[1,2] and Sean Grant[3]

[1]Peabody Research Institute, Vanderbilt University, Nashville, Tennessee 37203, USA

[2]Current affiliation: Department of Counseling Psychology and Human Services, University of Oregon, Eugene, Oregon 97403-1215, USA; email: etanners@uoregon.edu

[3]RAND Corporation, Santa Monica, California 90407-2138, USA; email: sgrant@rand.org

Annu. Rev. Public Health 2018. 39:135–51

First published as a Review in Advance on January 12, 2018

The *Annual Review of Public Health* is online at publhealth.annualreviews.org

https://doi.org/10.1146/annurev-publhealth-040617-014112

Keywords

complex intervention, meta-analysis, research synthesis, systematic review

Abstract

Meta-analysis is a prominent method for estimating the effects of public health interventions, yet these interventions are often complex in ways that pose challenges to using conventional meta-analytic methods. This article discusses meta-analytic techniques that can be used in research syntheses on the effects of complex public health interventions. We first introduce the use of complexity frameworks to conceptualize public health interventions. We then present a menu of meta-analytic procedures for addressing various sources of complexity when answering questions about the effects of public health interventions in research syntheses. We conclude with a review of important practices and key resources for conducting meta-analyses on complex interventions, as well as future directions for research synthesis more generally. Overall, we argue that it is possible to conduct meaningful quantitative syntheses of research on the effects of public health interventions, though these meta-analyses may require the use of advanced techniques to properly consider and attend to issues of complexity.

INTRODUCTION

Even the highest-quality primary research rarely provides sufficient evidence for making strong recommendations for public health policy or practice, given within-study sampling error or potential limitations inherent in any single study. Systematic reviews involving meta-analysis are therefore increasingly considered the gold standard for synthesizing and summarizing the best available evidence on the effects of public health interventions. Systematic reviews improve on traditional literature reviews by minimizing bias and error in the review process through the use of systematic, transparent, and more replicable data collection and synthesis procedures (15). Meta-analysis refers to the specific stage of the systematic review process in which statistical techniques are used to combine or synthesize quantitative findings from multiple primary studies (62, 102). By synthesizing the current best evidence on an entire body of research on intervention effects, systematic reviews involving meta-analysis play a crucial role in evidence-based public health.

This article focuses on the use of meta-analytic techniques to summarize the effects of public health interventions through a complexity lens. We first provide a brief overview of using complexity frameworks in public health intervention research and then discuss how to incorporate considerations of complexity in systematic reviews of public health interventions using meta-analytic techniques.

PUBLIC HEALTH INTERVENTIONS THROUGH A COMPLEXITY LENS

Interventions can be generally defined as activities, techniques, or strategies (i.e., intentional actions) intended to effect positive change (i.e., outcomes of action) by modifying determinants of targeted outcomes (i.e., mechanisms of action) (42). Specific types of intervention can be classified in a variety of ways across these domains of "action," "mechanism of action," and "outcome of action." Public health interventions are distinguished by their objective to improve health outcomes among large population groups (79), typically in one of the following ways:

1. Some public health interventions have mechanisms of action involving upstream determinants of population health—such as distal social environments and macro environmental factors—that are modified via community- and/or policy-level actions (99). Examples of these interventions include restriction or banning of alcohol advertising (78), regulation of fast-food outlets in geographic catchment areas (49), and housing improvements for health and associated socioeconomic outcomes (95).
2. Alternatively, other public health interventions have mechanisms of action involving downstream determinants of population health—such as individual characteristics and proximal social environments—that are modified via scalable individual- and group-level actions (85). Examples of these interventions include group-based parent training programs for parental health (4) and brief alcohol interventions for adolescents and young adults (91).

Public health interventions—both upstream and downstream—are increasingly conceptualized as complex owing to the actions involved and their corresponding mechanisms. Although there is no universally agreed on definition for the term "complex intervention" (7, 57), two sources of complexity are prominent in intervention research literature: complexity of interventions themselves and complexity of the systems in which interventions are implemented. Each source consists of various dimensions on which a public health intervention could be considered more or less complex.

Complexity of the Intervention

The UK Medical Research Council (MRC) guidance on developing and evaluating complex interventions (24) is arguably the most influential document conceptualizing sources of complexity arising from interventions themselves. The MRC guidance identifies several dimensions on which interventions can range in their complexity, including (*a*) the number of interacting intervention components, (*b*) the number and difficulty of behaviors required by those delivering and receiving interventions, (*c*) the number of groups or organizational levels targeted, (*d*) the number and variability of outcomes targeted, and (*e*) the permitted degree of flexibility or tailoring of interventions.

The Brief Alcohol Screening and Intervention for College Students (BASICS) is an example of a downstream public health intervention that could be considered complex owing to the number of interacting intervention components, the number of behaviors required by those delivering and receiving the intervention, and the degree of flexibility or tailoring of the intervention that is permitted (30). BASICS aims to reduce alcohol consumption and alcohol-related negative consequences among undergraduate students who already drink heavily or are at risk of experiencing problems because of their alcohol consumption. In two 50-minute counseling sessions, a health professional uses a motivational enhancement therapy/motivational interviewing therapeutic style to enhance students' motivations and skills to change their drinking behaviors. The core components include an initial screening to assess the student's drinking habits; a discussion with the student about alcohol, its effects, and risk factors for drinking and alcohol problems (based on the student's screening results); and delivery of personalized feedback and cognitive-behavioral strategies that target the student's motivation and capacity to change. Since its original development, BASICS has been modified for scalability, for instance, by being delivered by peers instead of health professionals (59), in group versus individual formats (88), and in online formats (25). BASICS can thus be considered inherently complex owing to its content and delivery, including provider tailoring and modification of the exact therapeutic content of each session depending on a student's unique screening results, motivation, and skills capacity to change.

Complexity of the System

Complexity can arise not only from interventions themselves, but also from important features of the contexts or systems in which interventions are implemented (65, 73). Public health interventions address health issues with diverse etiological origins, which are often produced by an interplay of biological, psychological, sociological, and ecological processes (2). Consequently, it is essential to consider the complexity of the systems into which public health interventions are implemented and integrated—often ultimately modifying the systems themselves (45).

The PRIME trial provides an example of a public health intervention that requires complex systems thinking (75). The PRIME intervention was designed to reduce malaria-related illnesses in rural Uganda by improving the quality of care in public health centers. The intervention included workshops that provided training to health centers on topics related to the management of funds and supplies, clinical procedures for fever case management and rapid diagnostic tests, interpersonal interactions between patients and providers, and the improvement of supply chains for health centers. Although the PRIME intervention was designed with input from community members and contextualized within the political, economic, and historical systems of public health centers in rural Uganda (16), the developers noted that the beneficial effects of the intervention were overshadowed by larger systemic limitations in other health services available to community members. Okwaro and colleagues (75) thus concluded that public health interventions embedded within complex systems, like the PRIME intervention, will require attention to local health

Table 1 Summary of meta-analysis approaches for synthesizing evidence on complex public health interventions

Analysis approach	Scenarios in which the approach may be useful
Traditional pairwise estimate of average intervention effect	Estimating the average effect of an intervention across a sample of intervention trials.
Subgroup analysis	Estimating and comparing average effects of interventions across discrete categories of intervention trials, e.g., comparing effects across intervention categories, settings or contexts, regions, countries, or patient populations.
Meta-regression analysis	Comparing intervention effect magnitude across trial characteristics (discrete or continuous). Explaining or predicting effect size heterogeneity with measured trial characteristics.
Individual participant data meta-analysis	Comparing intervention effect magnitude across trial- or patient-level characteristics (discrete or continuous). Explaining or predicting effect size heterogeneity with measured trial- or patient-level characteristics.
Network meta-analysis	Estimating and comparing average effects of interventions across a network of discrete categories of intervention trials. Estimating indirect comparisons that have not been directly examined in any primary trial.
Multilevel meta-analysis	Explaining or predicting effect size heterogeneity with trial- or cluster-level characteristics, where trials are nested within larger clusters (e.g., provider organization, health care system, region, country).
Path analysis and meta-analytic structural equation modeling	Examining mediators or mechanisms of change in intervention effects. Testing theory-based nomological networks.

priorities, political and historical contexts, and the larger health systems in which the interventions are embedded.

META-ANALYTIC TECHNIQUES FOR ESTIMATING EFFECTS OF COMPLEX PUBLIC HEALTH INTERVENTIONS

As public health researchers and practitioners increasingly embrace (rather than ignore) complexity perspectives, several distinct methodological challenges arise when conducting meta-analyses of intervention effects (26). In addition to questions about whether and to what magnitude an intervention yielded intended effects, consideration of complexity warrants questions regarding for whom and in which contexts interventions are more (or less) effective, which intervention components are most (or least) essential, and how and why the intervention yielded effects (or not). These additional questions provide opportunities for innovative statistical techniques when meta-analyzing evidence on the effects of public health interventions (see **Table 1**).

Traditional Pairwise Meta-Analysis of Overall Intervention Effects

Meta-analysis of overall intervention effects is still possible for many complex interventions, whereby effect sizes using a common metric—such as Cohen's d, Pearson's r, odds ratios, and risk ratios—are used to measure the magnitude and direction of intervention effects. Most meta-analyses synthesize effect sizes using standard statistical approaches, such as estimating means and variances of effect size distributions (62). There is a common misperception that the inherent heterogeneity in a body of evidence on complex interventions always threatens the validity of traditional pairwise meta-analyses intended to estimate overall intervention effects. This misperception likely arose from the explicit focus of many early meta-analyses on estimating the precise magnitude of a mean effect size. When conducting a fixed-effect meta-analysis to estimate the common mean effect size across primary studies, it is indeed critical for those studies to be as homogeneous as possible (e.g., in terms of populations, outcomes, interventions, comparators, study designs) to ensure that the resulting mean effect size is substantively meaningful. A meta-analysis estimating a fixed-effect mean effect size across multiple studies often assumes that there is one true common effect size in the population (10, 47), and thus substantial heterogeneity could reflect a potential violation of the underlying assumptions of the statistical model (80).

Over the past several decades, many public health researchers have shifted emphasis away from fixed-effect models to random-effects meta-analysis models, which assume that there may be multiple true effect sizes in the population and that heterogeneity around the average of those population effect sizes can be quantified and potentially explained with measured study characteristics. In these random- or mixed-effects meta-analyses, heterogeneity in effect sizes does not violate the underlying assumptions of the model. Rather, heterogeneity is itself a parameter of interest that can be quantified and potentially explained by other measured characteristics (62). Consequently, heterogeneity plays a central role in meta-analyses of complex interventions, and numerous statistical methods are available for investigating and explaining heterogeneity that will be useful for researchers embracing a complexity perspective.

Subgroup Analyses

One of the most common meta-analytic strategies for examining heterogeneity in a meta-analysis is the use of subgroup analysis, whereby mean effect sizes (and corresponding confidence intervals, prediction intervals, and heterogeneity statistics) are estimated for subgroups or subsets of the included trials (11). Any data collected on the intervention or context that can be operationally defined as a categorical measure can be used to subgroup the meta-analysis, such as the presence/absence of intervention components, the importance of different intervention components, organizational setting, and implementation quality or fidelity. Conducting meta-analyses on smaller, more homogeneous subsets of studies can then yield mean effect estimates for "clinically meaningful units" (68) or subgroups of trials. Ideally, these subgroups match units of interest to clinical and policy decision makers, such as the expected effect of an intervention with specific features, targeting specific types of participants, or provided in a specific setting.

For instance, in a meta-analysis examining media-delivered self-help therapies for anxiety disorders, Mayo-Wilson & Montgomery (67) investigated whether average intervention effects differed according to anxiety disorder type, intervention technique, and format of delivery. The subgroup analysis approach allowed the researchers to determine that trials with interventions targeting patients with the same anxiety disorder had larger effects than did interventions designed for populations with a variety of anxiety disorders and that trials with interventions delivered over the Internet yielded larger effects than did those delivered through books or telephone calls. Conducting subgroup analyses on these clinically meaningful units identified effect estimates specific to client populations and intervention modalities relevant for practitioners. Subgroup analysis approaches thus offer substantial intuitive appeal, particularly for translation and dissemination purposes.

Nonetheless, the subgroup analysis approach does have limitations. Subgroup analyses in meta-analyses yield strictly observational/correlational evidence, given that the included trials were not randomly allocated to subgroups; thus, even if all included trials in a meta-analysis are randomized controlled trials, the subgroup analysis approach does not permit causal inferences about differences across subgroups, given that this analytic strategy breaks the randomization from the original trial. Furthermore, subgroup analyses can suffer from poor statistical power and inefficient estimates of mean effect sizes and heterogeneity statistics, particularly when the subgroups of interest have only a small number of included studies (96). For this reason, meta-analysts should always present mean effect estimates along with confidence or credibility intervals and include prediction intervals for any random-effects meta-analyses (12). When the number of included studies in a subgroup is small, the meta-analyst may also consider supplementing the quantitative subgroup analysis with thick narrative descriptions of the variability and range of observed effects across the subgroups examined.

Meta-Regression Modeling

Another common meta-analytic technique for examining heterogeneity is meta-regression modeling, which can examine whether measured trial-level characteristics are associated with effect size magnitude and explain any observed heterogeneity in effects. Meta-regression is typically conducted using weighted regression models where effect sizes are the dependent variable and the trial-level characteristics are independent variables (94). Random- or mixed-effects inverse–variance weighted meta-regressions are typically preferred over fixed-effect meta-regressions because they allow for residual heterogeneity, i.e., remaining variability in effect sizes that is unexplained by predictors in the model. As with subgroup analyses, meta-regression can be used to examine whether a range of measured trial characteristics explain heterogeneity. In addition, multivariable meta-regression models can examine the effects of several trial-level characteristics simultaneously after adjusting for (holding constant) other potential confounding variables, such as participant characteristics or trial quality.

For instance, Jonkman et al. (53) conducted a meta-analysis to examine the effects of self-management interventions on health-related quality of life in chronically ill patients. They used meta-regression to examine whether different intervention features (e.g., intensity, duration, training, and components) explained heterogeneity, while controlling for the age of participants. In a different meta-analysis examining the effects of brief interventions on alcohol use among youth, Tanner-Smith & Lipsey (91) used a combination of meta-regression modeling and subgroup analysis techniques to examine whether the presence or absence of different intervention components (e.g., personalized normative feedback, decisional balance exercises) was associated with effects, after adjusting for the methodological quality of included trials.

A common criticism of reviews of interventions that are complex due to multiple or flexible components is the lack of attention to interacting intervention components, especially considering that most complex interventions are composed of interdependent ingredients (60). Meta-regression approaches can be used to model these complicated relationships and interactions between components. In scenarios where components may not be linearly additive or independent, the researcher can include multiplicative interaction terms in the regression model to explore these complex relationships. These interaction terms (and all meta-regression model specifications to be examined) should be specified a priori in a review protocol, particularly when meta-analysts are conducting hypothesis-driven confirmatory analyses. For meta-analysts conducting exploratory analysis of interactions in meta-regression models, classification and regression trees can be used to explore and identify potential interactions (61).

Despite the great flexibility and appeal of meta-regression approaches for examining heterogeneity, these approaches can also suffer from poor statistical power and imprecision when the number of included trials is small. Furthermore, all the standard cautions about regression modeling in primary research apply to meta-regression modeling (19), such as recognizing the observational/correlational nature of the regression analysis, attending to issues of multicollinearity among predictors, and attending to issues of confounding and potentially omitted variables. The latter is particularly important when considering the methodological quality and/or risk of bias in the included trials and how those features may be confounded with any observed study characteristics examined in the meta-regression model.

Individual Participant Data Meta-Analysis

Although standard meta-regression modeling techniques can be used to examine whether effect sizes are associated with trial-level characteristics, interest often surrounds the relationship between intervention effects and participant-level characteristics such as age, gender, race/ethnicity, or baseline symptom severity. Traditional meta-analyses that rely on aggregate trial-level data will always be limited in examining participant-level moderators of intervention effects because participant-level variables would be measured at the aggregate trial level, making inferences about participant-level characteristics at the risk of the ecological fallacy (6). Individual participant data (IPD) meta-analysis is therefore considered the gold standard approach for examining participant-level moderators of intervention effects.

IPD meta-analysis refers to a range of analytic techniques that can be used to synthesize individual-level participant data across multiple trials (27, 89), including syntheses combining individual participant data with aggregate data from trials for which individual-level data may not be available (82, 83, 90). A range of statistical methods can be used in IPD meta-analyses to examine participant-level effect modifiers. One of the most powerful approaches is the use of a one-stage model that pools both within- and across-trial effects using multilevel regression modeling techniques (37, 38, 48). For instance, Kuyken et al. (58) conducted an IPD meta-analysis examining the efficacy of mindfulness-based cognitive therapy (MBCT) for preventing relapse in patients' remission from recurrent major depressive disorder. The authors used one-stage models to examine the overall efficacy as well as modification of effects by numerous sociodemographic and psychiatric variables, and they found that MBCT was efficacious overall and for patients with a greater severity of baseline depressive symptoms.

A barrier to implementing IPD meta-analytic techniques, however, is the required access to individual-level data for some or all trials—a requirement that may be unrealistic or unfeasible in some situations. In addition, collecting and harmonizing IPD across numerous trials can be time- and cost-intensive (81), may require collaborative data-sharing agreements across sites, and may require additional considerations regarding data confidentiality and protection of human subjects.

Multilevel Meta-Analysis

Multilevel meta-analytic techniques allow for synthesizing hierarchical or clustered evidence on intervention effects (5, 17, 55, 98). These techniques have been employed, for example, when multiple effect sizes are available from a single study and the researcher wishes to synthesize those dependent effect sizes (97), though there are other meta-analytic techniques for handling dependent effect sizes as well (51, 93). In meta-analyses of complex public health interventions, however, investigators may use a more common hierarchical data structure wherein primary study participants (level 1) provide effect sizes within trials (level 2) that are nested within some larger cluster (level 3) such as organizations, health systems, regions, or countries. In these instances, multilevel models account for within-cluster dependencies by decomposing the effect size variance into between- and within-cluster variance components. For example, Fischer & Boer (36) examined predictors of national well-being using a three-level multilevel meta-analysis model to handle the clustering of data within countries and to examine country-level predictors of well-being. The authors reported that national levels of individualism were better predictors of well-being than was wealth, even after adjusting for a range of potential confounding factors. Although this meta-analysis was not focused on synthesizing evidence of intervention effectiveness, it nonetheless illustrates the utility of multilevel meta-analysis for examining the importance of contextual characteristics. For complex public health interventions embedded within complex settings or systems, multilevel meta-analysis techniques can therefore be useful for partitioning variance in effects across these relevant clustering variables.

As with all statistical techniques we discuss, meta-analyses that synthesize results from only a small number of included studies will be limited in their ability to use multilevel approaches. A small number of included studies can preclude reliable estimation of the within- and between-cluster variance component estimates, which may lead to biased or inefficient standard errors (55, 98). Researchers interested in examining cluster-level predictors in a multilevel meta-analysis (i.e., level 3 variables such as organization, health system, or regional characteristics) will thus need access to a reasonable number of units at the larger cluster level to ensure reliable estimation of variance components (55).

Network Meta-Analysis

Network meta-analysis involves the comparison of multiple interventions simultaneously in the same model to determine their comparative effectiveness (41). This meta-analytic technique can be used to estimate mean effect sizes for any range of combinations of categorical subgroups of complex public health intervention trials (14). A unique benefit of network meta-analysis is its ability to synthesize both direct effects (i.e., pairwise contrasts between subgroups reported in one or more trials) and indirect evidence to increase the precision of effect estimates even when particular interventions have never been directly compared in trials (50, 101). For instance, Pandor et al. (76) examined the effects of remote monitoring strategies for improving health outcomes among adults recently discharged from hospitals after unplanned admissions for heart failure. They used network meta-analysis to compare effects according to the different types of remote monitoring strategies used and found that structured telephone support with human-to-human contact as well as tele-monitoring reduced all-cause mortality.

Barriers to network meta-analysis involve some important statistical assumptions that may be unreasonable or untenable in some meta-analyses of complex public health interventions (33, 66). First, as with traditional pairwise meta-analysis of direct effects, using network meta-analysis to estimate mean effect sizes for subgroups of trials assumes homogeneity (or residual homogeneity) within the subgroups of trials of interest (33). Network meta-analysis also assumes transitivity (sometimes called similarity or exchangeability), which implies that any effect modifiers are comparably distributed across any pairs of trials being compared within the network. The statistical manifestation of the transitivity assumption is consistency, which implies that the direct and indirect effects in the network are in agreement (13). Consistency may be difficult to establish in meta-analyses of public health interventions, given the inherent and expected complexity in the evidence being synthesized. Researchers conducting network meta-analyses should therefore always attend carefully to issues of homogeneity and consistency and employ a range of available methods for assessing the tenability of these assumptions (28, 31, 66).

Path Analysis and Structural Equation Modeling

Meta-analytic path analysis and structural equation modeling can be used to test patterns of effects in nomological networks of constructs, which may be particularly useful for exploring and testing hypothesized mechanisms of action or theories of change underlying complex public health interventions (18, 52). Path analysis—a useful extension to regression modeling—can be used to assess linear, additive, and asymmetric relationships among a set of observed variables assumed to be associated through a set of linear causal pathways (32). Structural equation modeling similarly allows assessment of mechanisms and causal pathways while also permitting inclusion of latent constructs and correlated measurement error (64). For instance, Hagger et al. (46) used meta-analytic path analysis to examine the nomological validity of the theory of planned behavior for predicting alcohol consumption and dietary behaviors—specifically, examining the roles of past behavior, attitudes, subjective norms, and perceived behavioral control as they relate to behavioral intentions and actual behavior. Through path analysis approaches, the authors modeled the processes by which these theoretical constructs were associated with patient behavior and tested for mechanisms and pathways of effects using mediation analysis.

IMPORTANT CONSIDERATIONS FOR META-ANALYSES OF COMPLEX INTERVENTIONS

Successful use of the abovementioned meta-analytic approaches depends on several procedural and interpretational practices. Below we outline four particularly important considerations when conducting meta-analyses of complex intervention effects.

Stakeholder Engagement

Engaging stakeholders throughout the review process is an effective practice for increasing the relevance, awareness, and ultimate use of review findings in public health policy and practice decision making (54). Identifying which stakeholders to include, which tasks to assign stakeholders, and which methods of engagement to use are three essential considerations for creating a stakeholder engagement plan. For instance, in addition to other researchers, a review team may consider engaging stakeholders representing the public, policy makers, practitioners, and those involved in purchasing or paying for interventions in real-world contexts (21). In addition, chosen stakeholders can be engaged at various stages of the review process, such as when defining research questions, setting eligibility criteria, identifying potentially relevant studies, interpreting findings, and disseminating and applying results (20). Regarding meta-analyses on the effects of complex public health interventions, stakeholders may be particularly helpful in identifying factors to examine as effect modifiers in statistical analyses (65). Various modes and methods exist to engage stakeholders in review processes (1, 56). Although little evidence to date has measured the benefits and trade-offs of specific approaches (23), chosen approaches should be properly resourced and supported to obtain the full benefits of engaging stakeholders (22, 72).

Preregistration of Review Protocols

Researchers conducting systematic reviews and meta-analyses should develop and preregister protocols for each review prior to completing formal screening of search results against eligibility criteria (69). As with the rationale for preregistering trials prior to participant recruitment (29), preregistration of systematic reviews is essential for minimizing the risk of reporting biases (e.g., selective reporting of positive outcomes), facilitating transparency in the review process (e.g., by allowing tracking of major changes in planned methods), and informing interested stakeholders of both ongoing and completed reviews (8). Preregistration is particularly important when reviews involve meta-analyses, given the numerous analytic options available and the risks associated with post hoc data mining (39). Ideally, researchers should prespecify all meta-analytic statistical analyses to be conducted in a review protocol and fully define all outcomes to be meta-analyzed so as to ensure transparency in data analysis approaches. Policies of preeminent organizations conducting research syntheses that include reviews on public health interventions, such as the Cochrane and the Campbell Collaborations, require authors to publish protocols publicly prior to assessing studies for eligibility. Protocols for other systematic reviews and meta-analyses that include a health-related outcome can also be published in PROSPERO, an international and publicly available database of protocols produced by the Centre for Reviews and Dissemination at the University of York. In addition, several peer-reviewed journals, such as *Systematic Reviews* and *BMJ Open*, accept submissions of systematic review protocols for publication online.

Use of Logic Models

Systematic reviews of complex interventions can also benefit greatly from the use of logic models for visually depicting the complex theories of change underlying interventions. To assist in exploring heterogeneity and mechanisms of action via meta-analysis, logic models can be used to specify the causal system of interest, the core components of a complex intervention, and potential mechanisms or pathways of the intervention (2, 74). That is, using logic models can help identify which factors are core components of the intervention and, therefore, should be extracted from trials during data collection and potentially examined during data analysis (3). Logic models can also be useful for complex interventions that may have multiple or competing theories about how and why the intervention may produce effects; for example, see Welch et al. (100) for a use of logic models in a meta-analysis examining the effects of mass deworming for soil-transmitted helminths. It is important that researchers use logic models to help guide meta-analytic data collection and analysis decisions so that they do not engage in a blind or atheoretical exploration of heterogeneity. In many cases, logic models should be developed during the review-planning stage and used to develop a priori data analysis plans to protect against risks associated with post hoc data mining (65), although iterative logic modeling approaches may also be used (84).

Data Collection Strategies for Investigating Heterogeneity

Investigating heterogeneity using meta-analytic techniques requires careful consideration as early in the review process as when the research questions are defined and the eligibility criteria are developed. At these stages, it is critical to develop a clear definition of the complex intervention(s) to be reviewed, including conceptual and operational definitions for all key concepts. Although the same is true in any meta-analysis, defining the key concepts relevant to public health interventions can be particularly difficult given the potential number of sources of complexity (87). Most meta-analyses of complex public health interventions will aim to examine heterogeneity in effects across the different components, active ingredients, or "kernels" of the complex intervention (35). Thus, in addition to collecting data related to aspects of complexity in terms of study setting and context, implementation features, and participant characteristics, the meta-analyst must consider how best to operationally define and measure the components of the complex intervention itself. When defining the critical components of a complex intervention, researchers should draw first on existing theoretical or empirical typologies of the intervention but should also consider surveying trialists conducting research in the area, reviewing policy or procedures documents, examining findings from prior descriptive and/or qualitative studies of the complex intervention, and seeking stakeholder input on definitions (86). As mentioned above, these core components can also be identified a priori on the basis of a logic model or contact with stakeholders or experts in the field, as well as through supplementary syntheses of evidence from qualitative studies or nonrandomized intervention trials (45).

One of the most common approaches for measuring intervention component data to be used in a meta-analysis is to develop a checklist of all potential components that may be present in a complex intervention. During data collection, the meta-analyst can then collect detailed information regarding the presence/absence of each of those components and/or the strength or level of each component in any given trial. Collecting these data will be particularly important for meta-analyses that synthesize evidence on interventions that do not follow strict standardized implementation approaches, which will be the case for many complex public health interventions.

Meta-analysts collecting data on complex intervention components must often rely on primary trial authors' reporting of these data. This approach can present challenges, however, if trialists are unclear or inconsistent in their descriptions of the complex intervention and its implementation (often an unfortunate by-product of limited word space in journal manuscripts). It is thus critical for trial authors and journal editors to follow new reporting guidelines such as the Criteria for Reporting the Development and Evaluation of Complex Interventions (CReDECI) (70) and the Consolidated Standards of Reporting Trials Statement for Social and Psychological Interventions (CONSORT-SPI) (71) to ensure consistent and transparent reporting of key characteristics of the complex intervention. When primary trial authors' reporting is insufficient or lacking, meta-analysts should consider collecting supplementary data from intervention manuals and program materials and/or contacting trial authors to request more detail about intervention components and implementation procedures (92). Given the difficulties in collecting intervention component and implementation data via checklist approaches (43), meta-analysts can also consider supplementing these data with additional qualitative and narrative data, which can be used to provide thicker descriptions of the types of components and ingredients present in a complex intervention (34). Although such narrative data would not be used as variables in the meta-analysis, they can be used to help clarify to readers exactly which activities and strategies are involved in the complex intervention and can also be useful in assessing the external and ecological validity of the meta-analysis results.

CONCLUSION

This article provides an introduction to meta-analyses of complex interventions and describes a menu of statistical options available for researchers conducting these types of meta-analyses. In the behavioral, social, and health sciences, meta-analyses of interventions should no longer focus solely on examining whether an intervention works. We support the adoption of complexity thinking, lenses, and frameworks for conceptualizing public health interventions. These complexity considerations have important implications for public health researchers conducting research syntheses on the effects of public health interventions: Attention to sources of complexity in the interventions themselves and the systems in which they are implemented necessitates a range of meta-analytic techniques to meaningfully examine intervention effects in research syntheses. Fortunately, there are numerous established and promising meta-analytic approaches, such as subgroup analysis, meta-regression modeling, individual participant data meta-analysis, network meta-analysis, multilevel meta-analysis, and meta-analytic path analysis and structural equation modeling, to address the complexity of public health interventions.

These types of syntheses do require careful consideration of issues of heterogeneity, active ingredients, and potential mechanisms of action, and researchers conducting meta-analyses of complex public health interventions will likely need to consider complementary qualitative and mixed-methods approaches for synthesizing evidence as well (2, 44, 45, 77). Several comprehensive texts regarding meta-analytic and research synthesis methods are available and offer more technical details, which interested readers may find useful (9, 40, 62, 63). In addition, the sidebar titled

KEY RESOURCES FOR CONDUCTING META-ANALYSIS OF COMPLEX INTERVENTIONS

Organizations

- Campbell Collaboration: **https://campbellcollaboration.org/**
- Cochrane Collaboration: **https://www.cochrane.org/**
- Cochrane Public Health Group: **http://ph.cochrane.org/**
- Collaboration for Environmental Evidence: **https://www.environmentalevidence.org/**
- EPPI-Centre: **https://eppi.ioe.ac.uk/cms/**
- Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group: **https://www.gradeworkinggroup.org/**
- Joanna Briggs Institute: **https://joannabriggs.org/**

Additional Resources

- Centre for Evaluation, London School of Hygiene & Tropical Medicine: **http://evaluation.lshtm.ac.uk/evidence-synthesis/**
- Centre for Reviews and Dissemination Guidance: **https://www.york.ac.uk/crd/guidance/**
- Cochrane Handbook for Systematic Reviews of Interventions: **http://handbook.cochrane.org/**
- EPPI-Centre Resources: **https://eppi.ioe.ac.uk/cms/Default.aspx?tabid=88**
- Joanna Briggs Institute Resources: **http://joannabriggs.org/**
- *Journal of Clinical Epidemiology*, AHRQ Series on Complex Intervention Systematic Reviews: **http://www.jclinepi.com/article/S0895-4356(17)30630-3/fulltext**
- *Journal of Clinical Epidemiology*, Special Issue: Considering Complexity in Systematic Reviews of Intervention: **http://www.jclinepi.com/content/jce-considering-complexity-in-systematic-reviews-of-intervention**
- Methodological Expectations of Cochrane Intervention Reviews: **http://methods.cochrane.org/mecir**
- Methodological Expectations of Campbell Collaboration Intervention Reviews: **https://www.campbellcollaboration.org/mec2ir**
- PRISMA Reporting Guidelines for Systematic Reviews and Meta-Analyses: **http://www.prisma-statement.org/**
- PROSPERO Prospective Trial Registry for Systematic Reviews: **https://www.crd.york.ac.uk/PROSPERO/**
- World Health Organization Meeting on Retrieval, Synthesis, and Assessment of Evidence on Complex Health Interventions: **http://www.who.int/maternal_child_adolescent/guidelines/development/complex-health-interventions/en/**

Key Resources for Conducting Meta-Analysis of Complex Interventions provides links to online resources that may also be useful to researchers conducting meta-analyses of complex public health interventions. As public health researchers increasingly embrace a complexity perspective, these and other methodological approaches may offer great promise for identifying and understanding mechanisms and effects of public health interventions.

DISCLOSURE STATEMENT

Sean Grant's spouse is a salaried employee of Eli Lilly and Company and owns stock in the company; he has accompanied his spouse on company-sponsored travel. The authors are not aware

of any other affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

LITERATURE CITED

1. Abelson J, Wagner F, DeJean D, Boesveld S, Gauvin FP, et al. 2016. Public and patient involvement in health technology assessment: a framework for action. *Int. J. Technol. Assess. Health Care* 32:256–64
2. Anderson LM, Oliver SR, Michie S, Rehfuess E, Noyes J, Shemilt I. 2013. Investigating complexity in systematic reviews of interventions by using a spectrum of methods. *J. Clin. Epidemiol.* 66:1223–29
3. Anderson LM, Petticrew M, Rehfuess E, Armstrong R, Ueffing E, et al. 2011. Using logic models to capture complexity in systematic reviews. *Res. Synth. Methods* 2:33–42
4. Barlow J, Smailagic N, Huband N, Roloff V, Bennett C. 2012. Group-based parent training programmes for improving parental psychosocial health. *Cochrane Database Syst. Rev.* (5):CD002020
5. Beretvas SN, Pastor DA. 2003. Using mixed-effects models in reliability generalization studies. *Educ. Psychol. Meas.* 63:75–95
6. Berlin JA, Santanna J, Schmid CH, Szczech LA, Feldman HI. 2002. Individual patient- versus group-level data meta-regressions for the investigation of treatment effect modifiers: Ecological bias rears its ugly head. *Stat. Med.* 21:371–87
7. Blackwood B. 2006. Methodological issues in evaluating complex healthcare interventions. *J. Adv. Nurs.* 54:612–22
8. Booth A, Clarke M, Dooley G, Ghersi D, Moher D, et al. 2012. The nuts and bolts of PROSPERO: an international prospective register of systematic reviews. *Syst. Rev.* 1:2
9. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. 2009. *Introduction to Meta-Analysis*. West Sussex, UK: Wiley
10. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. 2010. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res. Synth. Methods* 1:97–111
11. Borenstein M, Higgins JPT. 2013. Meta-analysis and subgroups. *Prev. Sci.* 14:134–43
12. Borenstein M, Higgins JPT, Hedges LV, Rothstein HR. 2017. Basics of meta-analysis: I2 is not an absolute measure of heterogeneity. *Res. Synth. Methods* 8:5–18
13. Caldwell DM. 2014. An overview of conducting systematic reviews with network meta-analysis. *Syst. Rev.* 3:109
14. Caldwell DM, Welton NJ. 2016. Approaches for synthesising complex mental health interventions in meta-analysis. *Evid. Based Ment. Health* 19:16–21
15. Cent. Rev. Dissem. 2008. *Systematic Reviews: CRD's Guidance for Undertaking Reviews in Health Care*. York, UK: Univ. York
16. Chandler CIR, Kizito J, Taaka L, Nabirye C, Kayendeke M, et al. 2013. Aspirations for quality health care in Uganda: How do we get there? *Hum. Resour. Health* 11:13
17. Cheung MW. 2014. Modeling dependent effect sizes with three-level meta-analyses: a structural equation modeling approach. *Psychol. Methods* 19:211–29
18. Cheung MWL, Chan W. 2009. A two-stage approach to synthesizing covariance matrices in meta-analytic structural equation modeling. *Struct. Equ. Model.* 16:28–53
19. Cohen J, Cohen P, West SG, Aiken LS. 2003. *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences*. Mahwah, NJ: Erlbaum. 3rd ed.
20. Concannon TW, Fuster M, Saunders T, Patel K, Wong JB, et al. 2014. A systematic review of stakeholder engagement in comparative effectiveness and patient-centered outcomes research. *J. Gen. Intern. Med.* 29:1692–701
21. Concannon TW, Meissner P, Grunbaum JA, McElwee N, Guise JM, et al. 2012. A new taxonomy for stakeholder engagement in patient-centered outcomes research. *J. Gen. Intern. Med.* 27:985–91
22. Coon JT, Gwernan-Jones R, Moore D, Richardson M, Shotton MC, et al. 2016. End-user involvement in a systematic review of quantitative and qualitative research of non-pharmacological interventions for attention deficit hyperactivity disorder delivered in school settings: reflections on the impacts and challenges. *Health Expect.* 19:1084–97

23. Cottrell E, Whitlock E, Kato E, Uhl S, Belinson S, et al. 2014. *Defining the Benefits of Stakeholder Engagement in Systematic Reviews*. AHRQ Publ. No. 14-EHC006-EF. Rockville, MD: Agency Healthc. Res. Quality (AHRQ)
24. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. 2008. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 337:a1655
25. Cronce JM, Bittinger JN, Liu J, Kilmer JR. 2014. Electronic feedback in college student drinking prevention and intervention. *Alcohol Res. Curr. Rev.* 36:47–62
26. Datta J, Petticrew M. 2013. Challenges to evaluating complex interventions: a content analysis of published papers. *BMC Public Health* 13:568
27. Debray TPA, Moons KGM, van Valkenhoef G, Efthimiou O, Hummel N, et al. 2015. Get real in individual participant data (IPD) meta-analysis: a review of the methodology. *Res. Synth. Methods* 6:293–309
28. Dias S, Welton NJ, Caldwell DM, Ades AE. 2010. Checking consistency in mixed treatment comparison meta-analysis. *Stat. Med.* 29:932–44
29. Dickersin K, Renne D. 2003. Registering clinical trials. *JAMA* 290:516–23
30. Dimeff LA, Baer JS, Kivlahan DR, Marlatt GA. 1999. *Brief Alcohol Screening and Intervention for College Students (BASICS): A Harm Reduction Approach*. New York: Guilford Press
31. Donegan S, Williamson P, D'Alessandro U, Tudur Smith C. 2013. Assessing key assumptions of network meta-analysis: a review of methods. *Res. Synth. Methods* 4:291–323
32. Duncan OD. 1966. Path analysis: sociological examples. *Am. J. Sociol.* 72:1–16
33. Efthimiou O, Debray TPA, van Valkenhoef G, Trelle S, Panayidou K, et al. 2016. GetReal in network meta-analysis: a review of the methodology. *Res. Synth. Methods* 7:236–63
34. Egan M, Bambra C, Petticrew M, Whitehead M. 2009. Reviewing evidence on complex social interventions: appraising implementation in systematic reviews of health effects of organisational-level workplace interventions. *J. Epidemiol. Community Health* 63:4–11
35. Embry DD, Biglan A. 2008. Evidence-based kernels: fundamental units of behavioral influence. *Clin. Child Fam. Psychol. Rev.* 11:75–113
36. Fischer R, Boer D. 2011. What is more important for national well-being: money or autonomy? A meta-analysis of well-being, burnout, and anxiety across 63 societies. *J. Pers. Soc. Psychol.* 101:164–84
37. Fisher DJ, Copas AJ, Tierney JF, Parmar MKB. 2011. A critical review of methods for the assessment of patient-level interactions in individual participant data meta-analysis of randomized trials, and guidance for practitioners. *J. Clin. Epidemiol.* 64:949–67
38. Goldstein H, Yang M, Omar R, Turner R, Thompson S. 2000. Meta-analysis using multilevel models with an application to the study of class size effects. *Appl. Stat.* 49:339–412
39. Goodman SN, Fanelli D, Ioannidis JPA. 2016. What does research reproducibility mean? *Sci. Transl. Med.* 8:341ps12
40. Gough D, Oliver S, Thomas J. 2017. *An Introduction to Systematic Reviews*. London: Sage
41. Grant ES, Calderbank-Batista T. 2013. Network meta-analysis for complex social interventions: problems and potential. *J. Soc. Soc. Work Res.* 4:406–20
42. Grant S. 2014. *Development of a CONSORT Extension for Social and Psychological Interventions*. Oxford, UK: University of Oxford
43. Grant SP, Mayo-Wilson E, Melendez-Torres GJ, Montgomery P. 2013. Reporting quality of social and psychological intervention trials: a systematic review of reporting guidelines and trial publications. *PLOS ONE* 8:e65442
44. Greenhalgh T, Robert G, Macfarlane F, Bate P, Kyriakidou O, Peacock R. 2005. Storylines of research in diffusion of innovation: a meta-narrative approach to systematic review. *Soc. Sci. Med.* 61:417–30
45. Guise JM, Chang C, Viswanathan M, Glick S, Treadwell J, et al. 2014. Agency for Healthcare Research and Quality Evidence-Based Practice Center methods for systematically reviewing complex multicomponent health care interventions. *J. Clin. Epidemiol.* 67:1181–91
46. Hagger MS, Chan DK, Protogerou C, Chatzisarantis NL. 2016. Using meta-analytic path analysis to test theoretical predictions in health behavior: an illustration based on meta-analyses of the theory of planned behavior. *Prev. Med.* 89:154–61

47. Hedges LV, Vevea JL. 1998. Fixed- and random-effects models in meta-analysis. *Psychol. Methods* 3:468–504
48. Higgins JPT, Whitehead A, Turner RM, Omar RZ, Thompson SG. 2001. Meta-analysis of continuous outcome data from individual patients. *Stat. Med.* 20:2219–41
49. Humphreys DK, Panter J, Sahlqvist S, Goodman A, Ogilvie D. 2016. Changing the environment to improve population health: a framework for considering exposure in natural experimental studies. *J. Epidemiol. Community Health* 70:941–46
50. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, et al. 2015. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann. Intern. Med.* 162:777–84
51. Jackson D, Riley R, White IR. 2011. Multivariate meta-analysis: potential and promise. *Stat. Med.* 30:2481–98
52. Jak S. 2015. *Meta-Analytic Structural Equation Modelling*. Dordrecht, Neth.: Springer
53. Jonkman NH, Schuurmans MJ, Groenwold RH, Hoes AW, Trappenburg JC. 2016. Identifying components of self-management interventions that improve health-related quality of life in chronically ill patients: systematic review and meta-regression analysis. *Patient Educ. Couns.* 99:1087–98
54. Keown K, Van Eerd D, Irvin E. 2008. Stakeholder engagement opportunities in systematic reviews: knowledge transfer for policy and practice. *J. Contin. Educ. Health Prof.* 28:67–72
55. Konstantopoulous S. 2011. Fixed effects and variance components in three-level meta-analysis. *Res. Synth. Methods* 2:61–76
56. Kreis J, Puhan MA, Schünemann HJ, Dickersin K. 2013. Consumer involvement in systematic reviews of comparative effectiveness research. *Health Expect*. 16:323–37
57. Kühne F, Ehmcke R, Härter M, Kriston L. 2015. Conceptual decomposition of complex health care interventions for evidence synthesis: a literature review. *J. Eval. Clin. Pract.* 21:817–23
58. Kuyken W, Warren FC, Taylor RS, Whalley B, Crane C, et al. 2016. Efficacy of mindfulness-based cognitive therapy in prevention of depressive relapse: an individual patient data meta-analysis from randomized trials. *JAMA Psychiatry* 73:565–74
59. Larimer ME, Turner AP, Anderson BK, Fader JS, Kilmer JR, et al. 2001. Evaluating a brief alcohol intervention with fraternities. *J. Stud. Alcohol* 62:370–80
60. Lenz M, Steckelberg A, Richter B, Mühlhauser I. 2007. Meta-analysis does not allow appraisal of complex interventions in diabetes and hypertension self-management: a methodological review. *Diabetologia* 50:1375–83
61. Li X, Dusseldorp E, Meulman JJ. 2017. Meta-CART: a tool to identify interactions between moderators in meta-analysis. *Br. J. Math. Stat. Psychol.* 70:118–36
62. Lipsey MW, Wilson DB. 2001. *Practical Meta-Analysis*. Thousand Oaks, CA: Sage
63. Littell JH, Corcoran J, Pillai V. 2008. *Systematic Reviews and Meta-Analysis*. New York: Oxford Univ. Press
64. Loehlin JC. 2004. *Latent Variable Models: An Introduction to Factor, Path, and Structural Equation Analysis*. Mahwah, NJ: Erlbaum. 4th ed.
65. Lorenc T, Felix L, Petticrew M, Melendez-Torres GJ, Thomas J, et al. 2016. Meta-analysis, complexity, and heterogeneity: a qualitative interview study of researchers' methodological values and practices. *Syst. Rev.* 5:192
66. Mavridis D, Giannatsi M, Cipriani A, Salanti G. 2015. A primer on network meta-analysis with emphasis on mental health. *Evid. Based Ment. Health* 18:40–46
67. Mayo-Wilson E, Montgomery P. 2013. Media-delivered cognitive behavioural therapy and behavioural therapy (self-help) for anxiety disorders in adults. *Cochrane Database Syst. Rev.* (9):CD005330
68. Melendez-Torres GJ, Bonell C, Thomas J. 2015. Emergent approaches to the meta-analysis of multiple heterogeneous complex interventions. *BMC Med. Res. Methodol.* 15:47
69. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, et al. 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst. Rev*. 4:1
70. Möhler R, Köpke S, Meyer G. 2015. Criteria for Reporting the Development and Evaluation of Complex Interventions in healthcare: revised guideline (CReDECI 2). *Trials* 16:204

71. Montgomery P, Grant S, Hopewell S, Macdonald G, Moher D, et al. 2013. Protocol for CONSORT-SPI: an extension for social and psychological interventions. *Implement. Sci.* 8:99
72. Morley RF, Norman G, Golder S, Griffith P. 2016. A systematic scoping review of the evidence for consumer involvement in organisations undertaking systematic reviews: focus on Cochrane. *Res. Involv. Engagem.* 2:36
73. Noyes J, Gough D, Lewin S, Mayhew A, Michie S, et al. 2013. A research and development agenda for systematic reviews that ask complex questions about complex interventions. *J. Clin. Epidemiol.* 66:1262–70
74. Noyes J, Hendry M, Booth A, Chandler J, Lewin S, et al. 2016. Current use was established and Cochrane guidance on selection of social theories for systematic reviews of complex interventions was developed. *J. Clin. Epidemiol.* 75:78–92
75. Okwaro FM, Chandler CIR, Hutchinson E, Nabirye C, Taaka L, et al. 2015. Challenging logics of complex intervention trials: community perspectives of a health care improvement intervention in rural Uganda. *Soc. Sci. Med.* 131:10–17
76. Pandor A, Gomersall T, Stevens JW, Wang J, Al-Mohammad A, et al. 2013. Remote monitoring after recent hospital discharge in patients with heart failure: a systematic review and network meta-analysis. *Heart* 99:1717–26
77. Petticrew M, Anderson L, Elder R, Grimshaw J, Hopkins D, et al. 2013. Complex interventions and their implications for systematic reviews: a pragmatic approach. *J. Clin. Epidemiol.* 66:1209–14
78. Petticrew M, Shemilt I, Lorenc T, Marteau TM, Melendez-Torres GJ, et al. 2017. Alcohol advertising and public health: systems perspectives versus narrow perspectives. *J. Epidemiol. Community Health* 71:308–12
79. Rehfuess EA, Akl EA. 2013. Current experience with applying the GRADE approach to public health interventions: an empirical study. *BMC Public Health* 13:9
80. Rice K, Higgins JPT, Lumley T. 2018. A re-evaluation of fixed effect(s) meta-analysis. *J. R. Stat. Soc. A* 181:205–27
81. Riley RD, Lambert PC, Abo-Zaid G. 2010. Meta-analysis of individual participant data: rationale, conduct, and reporting. *BMJ* 340:c221
82. Riley RD, Lambert PC, Staessen JA, Wang J, Gueyffier F, et al. 2008. Meta-analysis of continuous outcomes combining individual patient data and aggregated data. *Stat. Med.* 27:1870–93
83. Riley RD, Steyerberg EW. 2010. Meta-analysis of a binary outcome using individual participant data and aggregate data. *Res. Synth. Methods* 1:2–19
84. Rohwer A, Pfadenhauer L, Burns J, Brereton L, Gerhardus A, et al. 2017. Logic models help make sense of complexity in systematic reviews and health technology assessments. *J. Clin. Epidemiol.* 83:37–47
85. Rychetnik L, Hawe P, Waters E, Barratt A, Frommer M. 2004. A glossary for evidence based public health. *J. Epidemiol. Community Health* 58:538–45
86. Shepperd S, Lewin S, Straus S, Clarke M, Eccles MP, et al. 2009. Can we systematically review studies that evaluate complex interventions? *PLOS Med.* 6:e1000086
87. Squires JE, Valentine JC, Grimshaw JM. 2013. Systematic reviews of complex interventions: framing the review question. *J. Clin. Epidemiol.* 66:1215–22
88. Ståhlbrandt H, Johnsson KO, Berglund M. 2007. Two-year outcome of alcohol interventions in Swedish university halls of residence: a cluster randomized trial of a brief skills training program, twelve-step–influenced intervention, and controls. *Alcohol. Clin. Exp. Res.* 3:458–66
89. Stewart LA, Clarke M, Rovers M, Riley RD, Simmonds M, et al. 2015. Preferred reporting items for a systematic review and meta-analysis of individual participant data: the PRISMA-IPD statement. *JAMA* 313:1657–65
90. Sutton AJ, Kendrick D, Coupland CAC. 2008. Meta-analysis of individual- and aggregate-level data. *Stat. Med.* 27:651–69
91. Tanner-Smith EE, Lipsey MW. 2015. Brief alcohol interventions for adolescents and young adults: a systematic review and meta-analysis. *J. Subst. Abuse Treat.* 51:1–18
92. Tanner-Smith EE, Lipsey MW, Wilson DB. 2016. *Meta-Analysis of Research on the Effectiveness of Juvenile Drug Courts*. Nashville, TN: Peabody Res. Inst., Vanderbilt Univ.
93. Tanner-Smith EE, Tipton E, Polanin JR. 2016. Handling complex meta-analytic data structures using robust variance estimates: a tutorial in R. *J. Dev. Life-Course Criminol.* 2:85–112

94. Thompson SG, Higgins JPT. 2002. How should meta-regression analyses be undertaken and interpreted? *Stat. Med.* 21:1559–73
95. Thomson H, Thomas S, Sellstron E, Petticrew M. 2013. Housing improvements for health and associated socio-economic outcomes. *Cochrane Database Syst. Rev.* (2):CD008657
96. Valentine JC, Pigott TD, Rothstein HR. 2010. How many studies do you need? A primer on statistical power for meta-analysis. *J. Educ. Behav. Stat.* 35:215–47
97. Van den Noortgate W, López-López JA, Marín-Martínez F, Sánchez-Meca J. 2015. Meta-analysis of multiple outcomes: a multilevel approach. *Behav. Res. Methods* 47:1274–94
98. Van den Noortgate W, Onghena P. 2003. Multilevel meta-analysis: a comparison with traditional meta-analytical procedures. *Educ. Psychol. Meas.* 63:765–90
99. Waters E, Petticrew M, Priest N, Weightman A, Harden A, Doyle J. 2008. Evidence synthesis, upstream determinants and health inequalities: the role of a proposed new Cochrane Public Health Review Group. *Eur. J. Public Health* 18:221–23
100. Welch VA, Ghogomu E, Hossain A, Awasthi S, Bhutta Z, et al. 2016. Deworming and adjuvant interventions for improving the developmental health and well-being of children in low-and middle-income countries: a systematic review and network meta-analysis. *Campbell Syst. Rev*. 2016:7
101. Wilson DB, Tanner-Smith EE, Mavridis D. 2016. *Network Meta-Analysis*. Campbell Methods Ser. Policy Note 1 (Version 1.0). Oslo: Campbell Collab.
102. Wilson SJ, Tanner-Smith EE. 2014. Meta-analysis in prevention science. In *Defining Prevention Science, Advances in Prevention Science*, ed. Z Sloboda, H Petras, pp. 431–52. New York: Springer