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AHRQ series on complex intervention systematic reviews—paper 5: advanced analytic methods

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Abstract

Background and Objective: Advanced analytic methods for synthesizing evidence about complex interventions continue to be developed. In this paper, we emphasize that the specific research question posed in the review should be used as a guide for choosing the appropriate analytic method.

Methods: We present advanced analytic approaches that address four common questions that guide reviews of complex interventions: (1) How effective is the intervention? (2) For whom does the intervention work and in what contexts? (3) What happens when the intervention is implemented? and (4) What decisions are possible given the results of the synthesis?

Conclusion: The analytic approaches presented in this paper are particularly useful when each primary study differs in components, mechanisms of action, context, implementation, timing, and many other domains.

Keywords: Systematic review; Qualitative synthesis; Meta-analysis; Decision analysis; Meta-regression; Bayesian analysis; Finite mixture models

1. Introduction

This is the fifth of a seven-part series of papers providing tools and approaches for conducting reviews of complex interventions. This paper presents advanced analytic methods that can be applied to systematic reviews of complex interventions.

This paper seeks to update earlier work [1,2,3] with an overview of analytic methods that can address synthesis

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questions involving complex interventions. Reviews of complex interventions (defined by Guise et al. [4]) where complexity is considered important frequently seek to address several questions within a single review about the intervention and the health system within which it is implemented.

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).

As described in the fourth paper in this series by Viswanathan et al. [5], decisions about how to conduct a review of a complex intervention depend on a number of factors such as the nature and extent of the existing evidence and the resources available for the review.

In this paper, we emphasize the nature of the decision or, in other words, the specific research question posed in the review as a guide to the appropriate analytic method to address that question. We focus on methods that address four broad questions about complex interventions: (1) How effective is the intervention? (2) For whom is the intervention effective and in what contexts? (3) What happens when the complex intervention is implemented? and (4) What decisions are possible given the results of the synthesis? Given space limitations, the discussion will introduce analytic methods that can address these questions about complex interventions and provide pointers to resources for interested readers to gain expertise. Table 1 provides a summary of the types of questions asked about complex interventions and analytic strategies used to support these questions. The analytic techniques discussed here are not unique to reviews of complex interventions. They do, however, address the most common questions for reviews concerned with complexity.

2. How effective is the intervention?

Systematic reviews of complex interventions may start with a relatively simple question that does not necessarily explore complexity: Does the intervention, in general, work? Although each example of the intervention may differ from others in components, mechanism of action, context, implementation or other major domains, policy makers may still be interested in whether the complex intervention works better than, say, usual care. Methods for assessing the overall effectiveness of an intervention are well established in the literature and are covered in detail elsewhere [6]. We note, however, that new analytic approaches continue to be developed to address questions focused on the overall effectiveness of an intervention, or the comparative effectiveness of interventions, for example, network meta-analysis [7,8], and single-case designs [9,10]. Some interventions are so complex (such as slum upgrading, see Turley et al. [23]) that multiple effects and impacts are determined at different levels of the health system to provide a suite of different options to consider.

When studies of complex interventions examine multiple outcomes, methods such as multivariate meta-analysis [11] can be used to examine the average effect for a number of dependent outcomes. Another alternative is to use weighted least-squares estimates of average effect sizes with robust estimation for standard errors [12] when studies collect multiple outcomes on the same sample.

No matter what analytic strategy is used to examine the average effect of a complex intervention, full reporting of results is particularly important. Studies of complex interventions typically collect a range of outcomes, both beneficial and harmful, at a number of levels of the system. Estimates of effect size for all outcomes along with their associated confidence intervals should be provided for each analysis conducted. When appropriate, the consistency and heterogeneity of these estimates should also be presented. The literature on the effects of complex interventions is emerging, and thus, there may not be a large number of studies to use in a synthesis. Reporting on all the results helps inform the design of future studies on the intervention.

3. For whom is the intervention effective and in what contexts?

More often, we are focused on the question of whether the effectiveness of the intervention varies because of differences among studies in their context, participant samples, or elements of the intervention actually implemented. This question centers on the heterogeneity of the intervention's effects. Given the nature of a complex intervention, we expect that treatment effects and impacts will vary because of reasons related to the complexity of the intervention itself. There are a number of methods that a reviewer could use to examine how treatment effects from a complex intervention vary across studies. Here, we will present two general statistical modeling strategies that could be used to examine heterogeneity: meta-regression and finite mixture models.

4. Meta-regression

Meta-regression is a commonly used technique in meta-analysis [13] and can prove useful in exploring heterogeneity in the context of complex interventions. Reviewers should begin with an a priori theory about how the effectiveness of a complex intervention may vary as a function of intervention components, the context, the

Table 1. Analytic strategies for complex interventions

Complex intervention question	Analytic strategies
How effective is the intervention?	Single outcomes • Random- and fixed-effects estimates of average effect [6] • Network meta-analysis [7,8] • Single-subject studies meta-analysis [9] Multivariate outcomes • Multivariate meta-analysis, using methods such as multilevel modeling [10,11] • Robust variance estimation [12]
For whom is the intervention effective and in what contexts?	Meta-regression • Frequentist [13] • Bayesian [14] Finite mixture models (structural equation models or latent class models) [15–17] Qualitative comparative analysis [18–21]
What happens when the complex intervention is implemented?	Choice of a wide range of designs, methodologies, and methods of evidence synthesis
What decisions are possible given the results of the synthesis?	Decision analysis [22]

implementation of the intervention, the participants, the caregivers, and so on. A priori theory guards against capitalizing on chance and issues of multiplicity which are serious problems in meta-analysis [24]. Reviewers then test a model using study and intervention characteristics as predictors for variation in effect size.

Reviewers can take either a frequentist or Bayesian approach to fitting a meta-regression model. In frequentist meta-analytic models, the effect sizes we observe are assumed to come from a process of sampling from a distribution of effect sizes. Parameters are estimated only from our sample at hand. In contrast, Bayesian methods for meta-analysis [14] represent a different philosophical approach to statistical inference. Specifically, Bayesian inference applies Bayes' theorem to a fully specified probability model, and the model includes two primary components: (1) choosing prior distributions for each unknown parameter such that it describes the uncertainty before the analysis and (2) choosing appropriate sampling distribution to describe the data. Bayes' theorem then combines the prior distributions of the parameters with the sampling distributions of the data to yield posterior distributions of the model parameters. Thus, we use evidence from the data to update what is known about our parameters, summarizing the new information state using probability distributions. Bayesian analysis can incorporate prior knowledge about a complex intervention such as the likely extent of between-study variation that we might have from other sources.

5. Finite mixture modeling

Although meta-regression under either a frequentist or Bayesian model is best used when the researcher has an a priori model for heterogeneity, finite mixture modeling takes a more exploratory approach. Reviewers may find that not all of the relevant, observable characteristics are reported in studies, and much unexplained heterogeneity remains. A researcher might wish to explore whether there are distinct groupings of intervention effects using finite mixture modeling [15] in a manner similar to exploratory factor analysis.

Finite mixture modeling, also known as latent class modeling, falls within the structural equation modeling framework. When researchers apply a finite mixture model to the analysis of effect sizes, they assume that there are distinct, latent classes or subpopulations of effect sizes [16]. The researcher prespecifies the number of subpopulations of effect sizes that need to be extracted and then uses the results to make sense of the extracted latent classes [17]. For example, a researcher may find that effect sizes measuring the effectiveness of a complex intervention are heterogeneous. Using finite mixture modeling, the researcher finds that effect sizes cluster into two classes, and this grouping of effect sizes into two classes accounts for much of the heterogeneity. The researcher's next task is to examine potential reasons for the clustering of the effect sizes into two groups to arrive at hypotheses for the observed heterogeneity. Perhaps, the studies in one cluster all include much younger and healthier patients than those in the second cluster.

Finite mixture modeling offers a flexible framework for meta-analytic data analyses. It is possible to accommodate missing data and model random effects while testing meta-analytic mixture models (including intervention effects on univariate or multivariate outcomes as well as moderator analyses) all within the single framework [16]. Most user-friendly structural equation modeling software programs (including, e.g., the frequently used Mplus software) allow testing and estimation of finite mixture models and of more typical meta-analytic research hypotheses.

Meta-regression and finite mixture modeling are two methods used to explore heterogeneity of effect sizes in the synthesis of complex interventions. Another method under development for exploring heterogeneity is qualitative comparative analysis [18,19]. Used within a systematic review context, each individual study within the review represents a case, and qualitative comparative analysis is used to identify the combinations of intervention components, implementation features, or contextual

characteristics (e.g., population, setting, etc.) that are associated with effectiveness of an intervention, or alternatively, ineffectiveness. Because qualitative comparative analysis is a relatively new technique, and few examples exist, specific standards for using the approach, conducting the analysis, and reporting results are in evolution [20,21].

The use of any analytic method described previously has limitations in the synthesis of complex interventions. One issue involves the interpretation of the results from these strategies. Models examining effect size heterogeneity can only suggest associations among characteristics of studies and variation in effect sizes. Causal inferences about how or why effect sizes vary cannot be supported by the use of these models. In addition, Berlin et al. [25] and Schmid et al. [26] warn about the potential of aggregation bias when interpreting meta-regression, and, by extension, finite mixture modeling results. Relationships that hold at the study level may not apply to how the intervention operates at the level of the individual patient, and interpretation of meta-regression should be restricted to the study level. Careful use of these models can help researchers explore the potential reasons for heterogeneity in treatment effectiveness but may have limited use with small numbers of studies of complex interventions coupled with many potential sources of heterogeneity.

When examining heterogeneity in complex interventions, results from all analyses should be reported, particularly any sensitivity or subgroup analyses. This information is particularly important in the synthesis of complex interventions as there are likely many different outcomes and subgroups to examine. Given the number of decisions about the number and types of analyses conducted, full and transparent reporting helps inform future syntheses and primary studies on the complex intervention.

6. What happens when the complex intervention is implemented?

For many complex interventions where heterogeneity makes it difficult to undertake any meaningful synthesis of intervention effects, the more important question is what happens when the complex intervention is implemented [27]. Understanding the intended and unintended impacts of complex interventions in different contexts can provide vital information to inform decision making. Evidence to address questions about ‘‘what happens’’ is typically qualitative, quantitative, or mixed method (such as interviews, focus groups, stakeholder surveys, etc.). In addition, Turley et al. [23] suggest that synthesizing other types of quantitative studies (e.g., controlled after intervention and uncontrolled before and after studies) not usually included in traditional reviews can help understand the wider impacts of interventions such as the association between interventions and outcomes. Guidance is available to support reviewers in designing reviews to address ‘‘what happens’’ questions. Noyes et al. [27] have produced guidance on choice of social theory to systematize review processes and inform interpretation of evidence. The UK Medical Research Council [28] has recently produced detailed guidance on designing theory-informed process evaluations to explore implementation, stakeholder experiences, and impacts. The Medical Research Council’s process evaluation guidance provides a clear framework of the types of social theories that may be helpful and the types of evidence that can be synthesized to better understand what happens when a complex intervention is implemented. One emerging strategy is the synthesis of trial-sibling studies. Trial-sibling studies are studies of the implementation of an intervention, which are linked with a randomized controlled trial. If trial-sibling studies are not available, Cochrane guidance recommends searching for and synthesizing qualitative studies of similar interventions in similar contexts unrelated to the included trials [29].

The Cochrane Qualitative and Implementation Methods group provides guidance and signposting to appropriate searching, appraisal, and synthesis methods to address ‘‘what happens’’ questions [30]. There are numerous methodologies and methods from which to select an approach to address specific types of ‘‘what happens’’ questions; far too many to summarize here. The forthcoming update of the Cochrane Handbook contains a new chapter on methods for complex intervention synthesis. The key issue for review authors to consider when selecting an appropriate design, methodology, and method(s) is the ‘‘fit’’ with the review questions and the type and quality of available evidence as discussed in Viswanathan et al. in this series [5]. The ‘‘fit’’ of review questions with review design and methodology may not become apparent until the pool of evidence is known and understood. Reviews of different types of evidence may be undertaken separately and then combined in an overarching synthesis or integrated within a single review process. Table 2 outlines various approaches and examples for integrating qualitative and quantitative evidence.

High-quality methodological exemplars exploring ‘‘what happens when complex interventions are implemented’’ are increasingly available; see for example, the Cochrane qualitative evidence synthesis of the barriers and facilitators to implementation of lay health worker programs [30,36] that is then integrated with the corresponding effectiveness review using a logic model.

7. What decisions are possible given the results of the synthesis?

Often researchers undertake a review of a complex intervention to make a decision or take an action. In the context of evidence synthesis to inform decision making about clinical or public health interventions, ‘‘decision analysis’’ typically refers to the use of mathematical computer models to

Table 2. Qualitative and quantitative evidence integration approaches

Integrative approach	Definition and citations for examples
1. Qualitative comparative analysis	Quantification of qualitative evidence in a single review [20,21]
2. Bayesian synthesis	Quantification of qualitative evidence in a single review [31]
3. Oliver's framework for the synthesis of qualitative and quantitative evidence	Creating matrices to juxtapose quantitative and qualitative evidence in original form [32]
4. Logic models	Developing explanatory lines of logic to integrate evidence of effect with qualitative synthesized hypotheses
5. Thematic synthesis	Qualitizing quantitative findings
6. Realist review, critical interpretive synthesis, meta-study/meta-summary	Uses data in its original form [31,33,34]
7. Narrative synthesis guidance	Provides a theory-informed framework for the synthesis of quantitative and qualitative evidence that draws on a tool box approach from the aforementioned methods [35]

estimate the probability of specific outcomes of interest of two or more competing interventions. Based on the probabilities of these outcomes and the implicit or explicit value that the decision maker places on each outcome, the optimal decision can be identified if there is consensus on the definition of "optimal." In the setting of decisions where the cost of the interventions are considered, this can be formally defined as the decision maker's "willingness to pay" for a given level of health benefit [37]. In settings where costs are not considered, estimates of the expected number of harms and benefits with each option can be used, although there has been much less consideration of the definition of an acceptable "harm/benefit" ratio [38].

The real power of the method lies in the ability to quantify the effect of uncertainty in the underlying probability estimates that are included in the model—clinical effectiveness, probability of adverse events, costs of specific outcomes [37]. Although decision modeling can be used in the evaluation of simple interventions, such a framework is especially powerful in the evaluation of complex interventions where the available interventions may not be studied in a single study, or where specific combinations of interventions may not ethically be examined by an RCT. A decision model allows the user to bring together evidence from diverse sources, to explore novel combinations of interventions, and to evaluate the gaps in the evidence and needs for further data. Through sensitivity analysis (systematically varying the value of specific parameters, either across a range defined by the literature or expert opinion, or stochastically using distributions obtained from the available evidence), the impact of uncertainty in probabilities can be illustrated, and the relative contributions of specific aspects of uncertainty can be identified [22]. This, in turn, can be very useful for identifying future research needs [39–41]. The method can still be useful even if no direct estimates of a parameter are available. For example, in the setting of a complex intervention where there is uncertainty about uptake among patients outside of a trial setting, the proportion of the population accepting the intervention, as well as the potential impact of additional components of the intervention on acceptability, can be varied to illustrate the impact of acceptability on overall health outcomes [40].

This flexibility also allows the model to predict outcomes under different scenarios. For example, if there is evidence of differential effectiveness in specific subgroups, this can be modeled by changing the relevant parameters. Subgroup-specific outcome probabilities can be combined to estimate the population-level effect under different subgroup distributions. In the setting of complex interventions, the effect of differences in specific subgroups can be modeled relatively easily.

8. Summary

The analytic methods discussed here provide tools for addressing four of the key questions commonly asked about a complex intervention: (1) How effective is the intervention? (2) For whom is the intervention effective and in what contexts? (3) What happens when the complex intervention is implemented? and (4) What decisions are possible given the results of the synthesis? The methods discussed here can be used in the synthesis of any intervention but are particularly useful when each primary study of the complex intervention differs in components, mechanisms of action, context, implementation, and many other domains. Future methodological research is needed in developing methods that fit or match the kinds of questions most important to stakeholders.

References

[1] Anderson LM, Oliver SR, Michie S, Rehfuess 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.

[2] Noyes J, Gough D, Lewin S, Mayhew A, Michie S, Pantoia 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.

[3] Petticrew M, Rehfuess E, Noyes J, Higgins JP, Mayhew A, Pantoia T, et al. Synthesizing evidence on complex interventions: how meta-analytical, qualitative, and mixed-method approaches can contribute. J Clin Epidemiol 2013;66:1230–43.

[4] Guise JM, Chang C, Butler M, Viswanathan M, Tugwell P. AHRQ series on complex intervention systematic reviews—paper 1: an introduction to a series of articles provides guidance and tools for reviews of complex interventions. J Clin Epidemiol 2017;96:6–10.

[5] 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.
[6] Higgins JPT, Green S, Eds., Cochrane handbook for systematic reviews of interventions Vol. 5.1.0. The Cochrane Collaboration; 2011. Available at http://handbook.cochrane.org.
[7] Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. Res Synth Methods 2012;3:80−97.
[8] Welton NJ, Caldwell D, Adamopoulos E, Vedhara K. Mixed treatment comparison meta-analysis of complex interventions: psychological interventions in coronary heart disease. Am J Epidemiol 2009;169:1158−65.
[9] Shadish WR, Rindskopf DM. Methods for evidence-based practice: quantitative synthesis of single-subject designs. New Dir Eval 2007;2007:95−109.
[10] Moeyaert M, Ferron JM, Beretvas SN, Van den Noortgate W. From a single-level analysis to a multilevel analysis of single-case experimental designs. J Sch Psychol 2014;52:191−211.
[11] Jackson D, Riley R, White IR. Multivariate meta-analysis: potential and promise. Stat Med 2011;30:2481−98.
[12] Hedges LV, Tipton E, Johnson MC. Robust variance estimation in meta-regression with dependent effect size estimates. Res Synth Methods 2010;1:39−65.
[13] Borenstein M, Hedges LV, Higgins J, Rothstein HR. Introduction to meta-analysis. West Sussex, UK: Wiley Online Library; 2009.
[14] Smith TC, Spiegelhalter DJ, Thomas A. Bayesian approaches to random-effects meta-analysis: a comparative study. Stat Med 1995; 14:2685−99.
[15] Gagné P. Mean and covariance structure mixture models. In: Hancock GR, Mueller R, editors. Structural equation modeling: A second course. Greenwich, CT: Information Age; 2006:197−224.
[16] Cheung M. Meta-analysis: a structural equation modeling approach. West Sussex, UK: John Wiley & Sons; 2015.
[17] Allua S, Stapleton LM, Beretvas SN. Testing latent mean differences between observed and unobserved groups using multilevel factor mixture models. Educ Psychol Meas 2008;68:357−78.
[18] Ragin CC. Redesigning social inquiry: fuzzy sets and beyond. Chicago, IL: The University of Chicago Press; 2008.
[19] Rihoux B, Ragin CC. Configurational comparative methods: qualitative comparative analysis (QCA) and related techniques. Thousand Oaks, CA: SAGE Publications, Inc; 2009.
[20] Schneider CQ, Wagemann C. Standards of good practice in qualitative comparative analysis (QCA) and fuzzy-sets. Int J Comp Sociol 2010; 9(3):397−418.
[21] Schneider CQ, Wagemann C. Set-theoretic methods for the social sciences: a guide to qualitative comparative analysis. Cambridge, UK: Cambridge University Press; 2012.
[22] Saramago P, Cooper NJ, Sutton AJ, Hayes M, Dunn K, Manca A, et al. Cost-effectiveness of interventions for increasing the possession of functioning smoke alarms in households with pre-school children: a modelling study. BMC Public Health 2014;14:459.
[23] 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 2013;35:171−5.
[24] Polanin JR, Pigott TD. The use of meta-analytic statistical significance testing. Res Synth Methods 2015;6:63−73.
[25] Berlin JA, Santanna J, Schmid CH, Szczech LA, Feldman HI. Individual patient-versus group-level data meta-regressions for the investigation of treatment effect modifiers: ecological bias rears its ugly head. Stat Med 2002;21:371−87.
[26] Schmid CH, Stark PC, Berlin JA, Landais P, Lau J. Meta-regression detected associations between heterogeneous treatment effects and study-level, but not patient-level, factors. J Clin Epidemiol 2004; 57:683−97.
[27] Noyes J, Hendry M, Booth A, Chandler J, Lewin S, Glenton C, et al. Current use and Cochrane guidance on selection of social theories for systematic reviews of complex interventions. J Clin Epidemiol 2015; 75:78−92.
[28] Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. Br Med J 2015;350:h1258.
[29] Noyes J, Hannes K, Booth A, Harris J, Harden A, Popay J, et al. Chapter 20: Qualitative research and Cochrane reviews. In: Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions, Version 5.3.0. The Cochrane Collaboration 2015. Available at http://qim.cochrane.org/supplemental-handbook-guidance
[30] Glenton C, Colvin CJ, Carlsen B, Swartz A, Lewin S, Noyes J, et al. Barriers and facilitators to the implementation of lay health worker programmes to improve access to maternal and child health: qualitative evidence synthesis. Cochrane Database Syst Rev 2013; CD010414.
[31] Dixon-Woods M, Cavers D, Agarwal S, Annandale E, Authur A, Harvey J, et al. Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. BMC Med Res Methodol 2006;6:35.
[32] Oliver S, Harden A, Rees R, Shepherd J, Brunton G, Garcia J, et al. An emerging framework for including different types of evidence in systematic reviews for public policy. Evaluation 2005;11(4): 428−46.
[33] Pawson R, Greenhalgh T, Harvey G, Walshe K. Realist review−a new method of systematic review designed for complex policy interventions. J Health Serv Res Policy 2005;10:21−34.
[34] Sandelowski M, Barroso J, Voils CI. Using qualitative metasummary to synthesize qualitative and quantitative descriptive findings. Res Nurs Health 2007;30:99−111.
[35] Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M, et al. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. Version 1 2006.
[36] Lewin S, Munabi-Babigumira S, Glenton C, Daniels K, Bosch-Capblanch X, van Wyk BE, et al. Lay health workers in primary and community health care for maternal and child health and the management of infectious diseases. Cochrane Database Syst Rev 2010; CD004015. http://dx.doi.org/10.1002/14651858.CD004015.pub3.
[37] Hunink MM, Weinstein MC, Wittenberg E, Drummond MF, Pliskin JS, Wong JB, et al. Decision making in health and medicine: integrating evidence and values. Cambridge, UK: Cambridge University Press; 2014.
[38] Havrilesky LJ, Chino JP, Myers ER. How much is another randomized trial of lymph node dissection in endometrial cancer worth? A value of information analysis. Gynecol Oncol 2013;131:140−6.
[39] Claxton KP, Sculpher MJ. Using value of information analysis to prioritise health research. Pharmacoeconomics 2006;24:1055−68.
[40] Fenwick E, Claxton K, Sculpher M. The value of implementation and the value of information: combined and uneven development. Med Decis Making 2008;28:21−32.
[41] Pei P, Weinstein M, Li X, Hughes MD, Paltiel DA, Hou T, et al. Prioritizing HIV comparative effectiveness trials based on value of information: generic versus brand-name ART in the US. HIV Clin Trials 2015;16:207−18. 1945577115Y0000000009.