The ICER Appraisal Process:  
Comparisons with AHRQ’s Methodology

The U.S. Agency for Healthcare Research & Quality (AHRQ) developed a draft methods reference guide in 2007 to provide a clear and transparent picture of how the agency and its constituent evidence-based practice centers (EPCs) evaluate the evidence and make judgments on new and emerging healthcare technologies. This “living” document, which is intended to evolve over time as new topics are considered and the methodological state of the art changes, has set an important standard for the conduct of comparative effectiveness research in the U.S.

The Institute for Clinical and Economic Review (ICER) follows many of the principles highlighted in AHRQ’s document in the conduct of its own technology appraisals. There are several instances, however, in which ICER’s methods differ in important ways. A comparison of the key methodologies of the two organizations follows below, with a focus on the rationale for ICER’s approach where the methods differ.

**Topic Development**

AHRQ’s Scientific Resource Center (SRC) collates and categorizes nominated topics on a quarterly basis. Topics are nominated from a variety of sources, including the general public (via the Web site or letter), key stakeholder groups, and program partners. The SRC then summarizes the issues for each topic. AHRQ then prioritizes the topics for review, based on multiple criteria:

- The prevalence and burden of disease
- Quality of evidence on the interventions in question and for the key measures of interest
- Current controversy and/or key uncertainties regarding the condition and its treatment
- The potential impact of the topic and value of a comparative effectiveness review (e.g., high costs, over- or under-utilization)

ICER follows a similar approach to topic selection, inviting ongoing public input on topics of interest. ICER’s prioritization process differs somewhat in that a formal Topic Selection Committee is convened twice yearly to prioritize topics for review. This committee is comprised of representatives from four clinical societies (American College of Physicians, American College of Surgeons, American College of Cardiology,
and American College of Radiology) as well as individuals representing the diverse stakeholders that work with ICER (private and public payers, patient advocacy groups, manufacturers, employers). In addition to AHRQ's considerations for prioritization, ICER also considers the following in its own efforts:

- Variation in treatment selection and/or approach in current practice
- Multiple treatment choices available to patients/clinicians
- Questions regarding the comparative costs and/or cost-effectiveness of alternative treatment options
- Reasonable scope for timely appraisal completion (6-9 months)

ICER follows AHRQ's processes for topic development, including focus on populations, interventions, comparators, outcome measures, timing and settings (PICOTS) constructs\(^2\) for formulating key questions, development of analytic frameworks,\(^3\) and refining key questions. In similar fashion to AHRQ, ICER convenes an independent and diverse advisory group, known as the Evidence Review Group (ERG), to assist in formulating key questions and refining the project scope. Because the ERG is carefully constructed to include relevant experts as well as key stakeholders, however, their involvement is perhaps more intense in the ICER process. For example, the ERG is also asked to comment on issues and concerns throughout the appraisal cycle, review preliminary methods and findings, and debate and discuss the evidence at a final in-person meeting prior to report publication.

**Finding & Selecting Evidence**

ICER adheres to AHRQ's guidance in casting a relatively wide net for selecting evidence, with a priority focus on study designs that are generalizable to typical clinical practice as well as the specific patient populations of interest. As with any rigorous systematic review, priority is placed on randomized controlled trials as well as head-to-head comparisons of the interventions under study. While subject to a number of attendant biases, observational studies are an important component of ICER reviews because of (a) follow-up duration that may be longer than in a typical clinical trial; (b) larger sample sizes, enhancing the detection of differences in rates of relatively rare events; and (c) conduct in broad and varied practice settings. It is also recognized that much of the evidence base may come from cohort studies and case series, particularly in the appraisal of non-pharmaceutical interventions.

ICER accesses all of the major electronic publications databases cited in the AHRQ Methods Guide to retrieve relevant publications (e.g., MEDLINE, EMBASE, Web of
Science), as well as databases of prior systematic reviews (e.g., Cochrane Collaboration, University of York Centre for Reviews and Dissemination) that may be valuable in replacing all or part of de novo review processes. In addition, manual review of references is conducted to supplement electronic searches, and ERG members are queried for relevant published or unpublished data, including data that manufacturer representatives may be willing to supply.

**Evidence Synthesis**

ICER employs modern techniques for quantitative synthesis of evidence, and follows AHRQ guidance on the specific techniques to employ. The decision to perform meta-analysis is generally comparable to the AHRQ process, as it is guided by conclusions regarding the similarity of patient populations, outcome measures employed, duration of follow-up, and other structural concerns, rather than statistical heterogeneity alone. However, if candidate studies are deemed to be similar enough, ICER performs meta-analysis even in cases of substantial heterogeneity, in order to serve two major purposes: (a) to explore, through stratified analyses, meta-regression, or other techniques, study or population features that are major contributors to heterogeneity; and (b) to produce parameter estimates for use in sensitivity analyses of companion decision-analytic models, as a means of exploring the potential for these estimates to affect how the value of multiple interventions compares.

**Grading Strength of Evidence**

The key domains in AHRQ’s approach to assigning a level of confidence to the evidence obtained are (a) risk of bias; (b) consistency; (c) directness; and (d) precision. While these domains are also considered in ICER’s examination of the evidence, there are key differences in approach and ultimate output of this process. First, the inputs to ICER’s assessment of the strength of evidence include both data accumulated through the systematic review and key clinical outputs from decision-analytic modeling. For example, in ICER’s recent appraisal of coronary computed tomographic angiography (CCTA) for coronary artery disease (CAD), it was recognized that the diagnostic accuracy of CCTA has primarily been tested in populations with a relatively high underlying prevalence of CAD; in practice, however, CCTA is often used as a testing strategy in those at low-to-intermediate risk of CAD. ICER’s modeling effort illustrated changes in the balance of benefits and harms at different levels of underlying CAD prevalence, which ultimately affected ICER’s consideration of strength of evidence.
Second, ICER’s approach to grading evidence strength is related, but not identical, to AHRQ’s “confidence” rubric. For each intervention under study, a rating for “comparative clinical effectiveness” is assigned that compares the intervention to a common referent and incorporates two constructs: (a) the level of certainty in the net benefit of the intervention as compared to the referent; and (b) the likely magnitude of the net benefit of interest. ICER’s rating is therefore assigned based on a summary consideration of all effects of the intervention (e.g., effectiveness, harms, quality of life), while AHRQ’s evaluation of evidence strength is typically specific to each key question identified in the review. More information on ICER’s rating system can be found at: http://www.icer-review.org/index.php/rating-system.html.

**Comparative Value**

A final key difference between AHRQ’s and ICER’s approach is consideration of comparative value. ICER’s appraisal process includes the development of a de novo decision-analytic model to accompany the systematic review. These models are aligned closely with the parameters of the systematic review to ensure that model outputs are generalizable to the appropriate patient populations and treatment settings. Model findings are used to inform an assessment of comparative value between interventions, which is then incorporated in the integrated evidence rating described above. Comparative value is typically defined in multiple ways for different stakeholders; for example, patients may be most concerned with visit/testing requirements or out-of-pocket expenses, while policymakers may be most interested in traditional summary measures such as incremental cost-effectiveness ratios. In contrast, AHRQ reviews may summarize the current literature on the economic impact of interventions, but do not typically include a companion model.

**Summary**

AHRQ’s methodologic approach to the conduct of comparative effectiveness research is comprehensive and highly-regarded. The modifications to this approach that ICER has incorporated are intended to maintain the standard for scientific rigor that AHRQ has set while attempting to enhance the interpretation of appraisal findings. ICER believes that these methodological modifications improve the usefulness of the appraisals for a variety of stakeholders while also stimulating implementation of relevant changes in clinical practice, medical policy, and payment reform.
REFERENCES


