



**Overview of the ICER value framework
and proposals for an update for 2017-2018**

February 1, 2017

Introduction

This paper presents proposed updates to the ICER value assessment framework, including refinements of its conceptual structure and modifications to the specific methods used to gather and assess evidence of different types. The process for stakeholder engagement during report development and public meetings is also being updated and will be described briefly here; greater detail will be available in separate guides to engagement for patients and manufacturers. Drafts of these guides will also be posted for further public comment.

This update to the ICER value assessment framework follows upon several years of experience using the current framework in the evaluation of drugs, devices, tests, and delivery system innovations. During that time ICER has actively sought the input of all stakeholders and made iterative changes to its methods and overall procedures to enhance their transparency and to seek to improve the ability of all parties to participate meaningfully in the process. ICER has also benefitted from the submission of over 300 pages of comments and suggestions from more than 50 organizations and individuals during a national public comment period in late 2016.

This paper reflects this combined experience, public input, and many additional discussions with stakeholders in various settings. With the posting of this document ICER will open a new 60-day period of public comment and will consider this additional input in making further revisions before a final framework update is posted. This finalized update to the ICER value framework and associated methods will be in place to guide reports launched during the two year period of April 2017- April 2019, with the next formal update scheduled for April 2019.

Overarching purpose and principles of the ICER value assessment framework

For more than ten years ICER has been active in developing methods for evidence assessment. Evidence assessment, however, is only one component of ICER's broader effort to provide mechanisms through which all stakeholders and the general public can engage in discussions on how best to use evidence as the foundation for a more effective and sustainable health care system. A formal effort was undertaken between 2014-2015 to gain input through a multi-stakeholder advisory group on ways to define with greater detail the conceptual and methodological underpinnings of ICER reports. Ultimately, the purpose of the value framework is to form the backbone of rigorous, transparent evidence reports that, within a broader mechanism of stakeholder and public engagement, will help the United States evolve toward a health care system that provides sustainable access to high-value care for all patients.

In this effort ICER is guided by several key underlying principles. One is that we act with respect for all, in concordance with a presumption of good will on the part of all participants and stakeholders in the health care system. ICER does not intend to target any particular interest group or organization. There are many areas in which the US health system fails to serve patients well, in which access to care is suboptimal, waste and inefficiency pose major problems, and costs to patients and the health system fail to align with added value. ICER believes that only through collaborative efforts, built upon a foundation of civil discourse and

honest consideration of evidence on effectiveness and value, can lasting progress be made on behalf of patients today and those of the future.

The ethical vision inherent in ICER's work recognizes that many choices that are made in health care – choices in clinical care, insurance coverage, pricing, payment, and allocation of resources within health systems – must address the basic reality that societal resources for health care are not unlimited, and that there will always be trade-offs and dilemmas over how to organize and pay for the services provided within a health system. Too often, these decisions are made without rigorous evidence and with little transparency. Too often there is little chance for reflection or public engagement in managing the tensions that can arise between innovation, access, and costs. ICER's value assessment framework seeks to place scientific methods of evidence analysis at the heart of a clearer and more transparent process. The value framework reflects our strong underlying belief that rigorous thinking about evidence can prevent the kind of waste that strains our ability to provide patient-centered care. The framework also is intended to support discussions about the best way to align prices for health services with their true added value for patients. While considering value and linking it to pricing and insurance coverage cannot solve every dilemma, nor satisfy every need, ICER believes it offers the best hope of avoiding rationing of care by the ability of patients to pay for care, and that it can promote a more dynamic, innovative health care system that will make the best use of available resources in caring for all patients.

The population perspective and intended uses of the ICER value framework

The ICER value framework describes the conceptual framework and set of associated methods that guide the development of ICER evidence reports. ICER reports are intended to support deliberation on medical policies related to health services (e.g. tests or treatments) and delivery system interventions (e.g. preventive programs, changes to the organization of medical personnel). To inform these kinds of medical policies the ICER value framework takes a “population” level perspective as opposed to trying to serve as a shared decision-making tool to be used by individual patients and their clinicians. Taking a population perspective implies that the ICER value framework seeks to analyze evidence in a way that supports population-level decisions and policies, such as broad guidelines on appropriate care, pricing, insurance coverage determinations, and payment mechanisms. A value framework intended to support decisions about the care of individual patients requires a structure that invites weighting of benefits, harms, and costs from the individual patient's perspective. There is a very important need for better evidence-based guides for individual decision-making, and ICER reports may be helpful in providing some of the substrate for these kinds of decision guides, but this is not the primary intended purpose of the ICER value framework or of ICER reports.

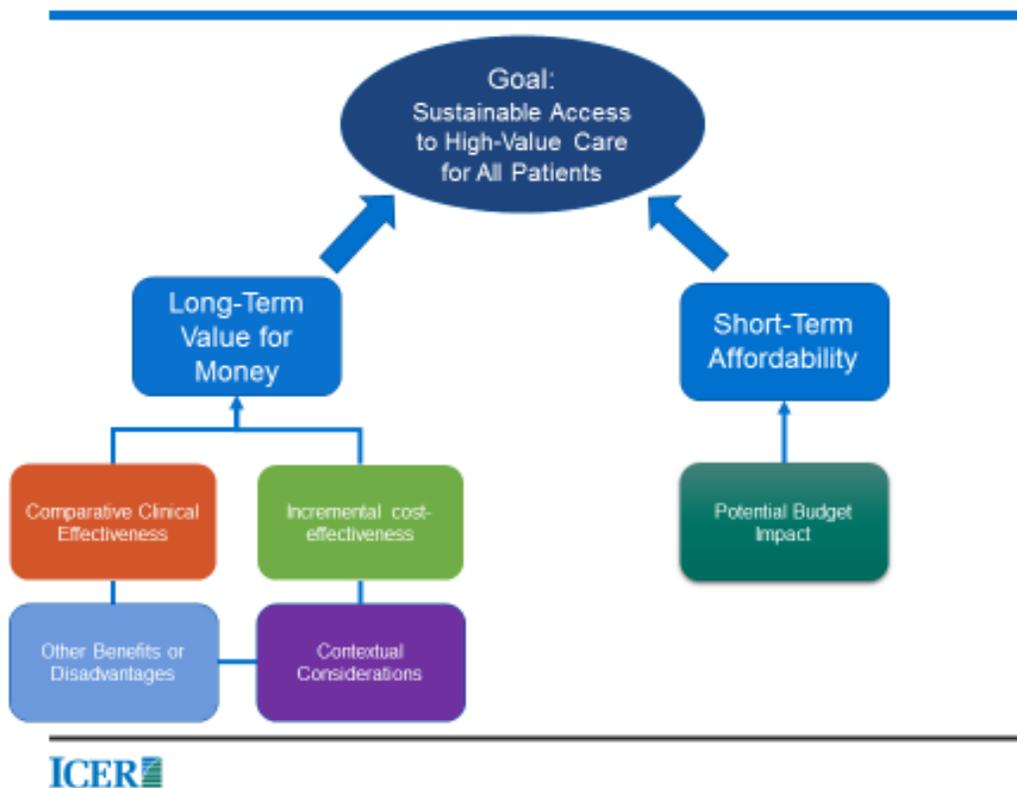
Even with its population-level focus, however, the ICER value framework seeks to encompass and reflect the experiences and values of patients. Representing the diversity of patient outcomes and values in a population-level framework is difficult because there will always be an inherent tension between average findings in clinical studies and the uniqueness of every patient. There will also always be diversity in the way that patients view the balance of risks

and benefits of different treatment options. The ICER value framework does not solve these tensions, but neither does it obscure them. Population-level decisions and policies have always been made by life science companies, insurers, and clinical organizations looking at evidence in the same general way. One important goal of the ICER value framework is to provide an evidence report that does a better job of analyzing the strengths and limitations of the available evidence, including what is or is not known about the variation in response to different treatments among patients with different personal and clinical characteristics. The ICER value framework also creates an explicit place and role for consideration of elements of value that are important to individual patients but that fall outside traditional clinical measures. Guided by the value framework, ICER reports analyze evidence and incorporate input from patients and other stakeholders to help explore the potential tension between population-level policies and the perception of value by individual patients.

General overview of the value framework

As shown in the new proposed structure of the ICER value framework, it seeks to inform decisions that are aimed at achieving sustainable access to high-value care for all patients (see Figure 1 below). This goal requires consideration of two general concepts: “long-term value for money” and “short-term affordability.”

Figure 1. New proposed conceptual structure of the ICER value assessment framework



Long-term value for money

Long-term value for money serves as the primary anchor of the ICER value framework. It is itself a concept that is comprised of multiple domains: 1) comparative clinical effectiveness; 2) incremental cost-effectiveness; 3) other benefits or disadvantages; and 4) contextual considerations. Updates to how these domains are measured and integrated into an ultimate judgment of long-term value for money will be described in detail in the “updates” section of this paper. There are several high-level points about this element of the value framework that bear highlighting here:

1. Long-term perspective.

Even though most of the clinical data available on health care services come from studies of relatively short duration, the grounding of any evaluation of value should recognize the long-term perspective on both outcomes for patients and costs. The ICER value framework recognizes this principle by grounding the methods of incremental cost-effectiveness analysis in simulations that estimate outcomes and costs at the longest feasible time horizon, usually the full lifetime of patients. Benefits for patients and potential cost offsets for new treatments that might take many years to be seen are therefore estimated and included as a core element of the value framework.

2. Foundation in the evaluation of evidence on comparative clinical effectiveness.

The ICER value framework is rooted in an objective evaluation of the evidence on the comparative clinical effectiveness of different care or care delivery options. This element of the framework serves as the primary source of information to inform cost-effectiveness analysis, and includes a systematic review of available evidence performed according to the highest academic methodological standards. As part of the evaluation of comparative clinical effectiveness, ICER reports include a clear description of the sources of evidence, the strengths and limitations of individual studies, and a summary judgment of the net health benefit of different care options along with a statement explaining the relative certainty that the body of evidence is able to provide. The detailed methods used by ICER in its evaluation of comparative clinical effectiveness are available on the ICER website (<https://icer-review.org/methodology/icers-methods/>). The ICER rating system for evidence has been published in a peer-reviewed journal and has been endorsed by the AMCP-NPC-ISPOR Comparative Effectiveness Research Collaborative.^{1,2}

3. Acceptance of multiple forms of evidence.

Patients, clinicians, and policymakers are most interested in evidence on the comparative clinical effectiveness of care options, but this does not mean that ICER’s value framework limits the type of evidence to be considered to the results of randomized controlled trials (RCTs). When available, high-quality RCTs provide evidence that is least susceptible to certain scientific biases, but the best evidence on longer-term benefits and side effects often comes from other sources, such as observational analyses based on cohort studies, patient reported data, and

¹ Ollendorf DA, Pearson SD. An integrated evidence rating to frame comparative effectiveness assessments for decision makers. *Med Care*. 2010 Jun;48(6 Suppl):S145-52.

² <https://www.cercolaborative.org/global/default.aspx?RedirectURL=%2fhome%2fdefault.aspx>.

long-term registries. When head-to-head trials have not been performed, rigorous insights into comparative clinical effectiveness also often require indirect comparisons through the method of formal network meta-analysis. In short, ICER has a flexible and ecumenical approach to sources of evidence and, while stressing the importance of the rigor of clinical trial data in any assessment, the value framework and ICER's methods incorporate multiple sources and types of evidence, seeking the evidence that is most helpful in understanding the long-term net health benefits for patients of different care options.

4. Recognition that what matters to patients is not limited to measured "clinical" outcomes.

The inclusion of an explicit domain of value labeled "other benefits or disadvantages" demonstrates that the ICER value framework fully acknowledges that all too often what matters most to patients is poorly captured in the available clinical trial data. Sometimes this occurs because surrogate outcome measures do not reflect true patient-centered outcomes; but even when trials do capture the clinical outcomes that matter most to patients, there are other aspects of value related to the complexity of the treatment regimen or the impact of care options on the ability to return to work, on family and caregiver burden, on public health, or on other aspects of the health system or society.³ The ICER value framework identifies these "other benefits or disadvantages" as important elements of any overall judgment on long-term value for money, and all ICER reports have separate sections in which evidence and information pertaining to these elements are presented. As part of the update proposals later in this paper we will describe our proposal for making the integration of this domain of value in the public deliberation and voting process at ICER meetings even more tangible.

5. Acknowledgment of the role of contextual considerations.

Decisions about the value of care options do not happen in a vacuum. There may be broader contextual issues related to the severity of the condition, whether other treatments are available or soon will be, and ethical, legal or other societal priorities that are important to acknowledge as part of any discussion on value. The ICER value framework includes this element and it is explored in a separate section of each ICER report. In addition, contextual considerations often feature prominently in the deliberation on value between independent expert committees and all stakeholders that is a central feature of the public meetings convened by ICER on each report. Linked to the update proposals for "other benefits or disadvantages," proposals to revise the methods used to integrate contextual considerations into the ICER meeting and voting process are described later in this paper.

Short-term affordability

With long-term value for money being the dominant element in considerations of value, a complementary perspective is provided by an evaluation of short-term affordability. The ICER value framework includes an explicit evaluation of the short-term affordability of different care options by analyzing the potential short-term budget impact of changes in health expenditures

³ For further insight and examples a useful resource is the FasterCures and Avalere Health work on "Integrating the Patient Perspective into the Development of Value Frameworks" available at <http://www.fastercures.org/assets/Uploads/value-coverage-framework-March-2016.pdf>

with the introduction of a new test, treatment, or delivery system process. Among the update proposals presented later in this paper there are several related to potential budget impact analyses, but here it is important to note two high-level aspects of this part of the ICER value framework.

1. Potential budget impact analyses estimate the net budget impact across all elements of the health system.

ICER's methods have never sought to estimate the potential budget impact of treatments within "silos" of a payer budget, such as the expenses only on pharmaceuticals, devices, or hospital costs. It remains a core principle of ICER's value framework that it should evaluate both short and long-term costs across the entire health system, so that care options that might increase spending for one type of service (e.g. drugs) while reducing other spending (e.g. hospital costs) receive full credit for cost offsets and are not penalized in any way.

2. At 5 years, the time frame for considering "short-term" affordability is stretched as far as possible without losing relevance for identifying new care options that may require special measures – in pricing, payment mechanisms, coverage criteria, or budgeting – to maintain patient access without serious financial strain throughout the health care system.

Public insurers in the US, such as Medicaid, and private insurers manage health care use and expenses within relatively short 1-2 year budget timeframes. Any new added costs to the health system must therefore be estimated and planned for within that timeframe. At one time ICER reports used 1-2 year budget timeframes, but with feedback from stakeholders an iterative change was introduced in 2015 to push the time frame out to 5 years. Doing so reduces the utility of the analysis for most insurers but helps accommodate some of the important potential clinical benefits and cost offsets that may not occur immediately with the adoption of a new care option. With the primary anchor of the ICER value framework being the long-term perspective represented by long-term value for money, the time horizon for short-term affordability has been extended as far as it seems possible in order for it to serve the important purpose of providing information to inform discussions on whether special efforts need to be taken to manage the introduction of a new care option so that access and affordability can both be maintained.

Justification for short-term affordability as part of the ICER value framework

Critics of including budget impact assessment as part of a value framework often ignore a key question: What type of economic perspective and information currently influences decision-making by insurers in the US? Without a doubt---and insurers are the first to admit this---it is budget impact. Considerations regarding budget impact, and not measures of long-term cost-effectiveness, have dominated the way that insurers assess the economic impact of all health care services, not just drugs. There is a logic to this perspective but also obvious perverse outcomes.

Budget impact is a reasonable consideration because insurers work in rapid cycles with purchasers and individual subscribers, translating short-term cost projections into planned insurance premiums for the coming year. Rapid cost growth in the short-term, especially when

it increases beyond anticipated inflation rates, pushes quickly upstream to purchasers and policymakers who have to make their own short-term decisions about how to find the needed resources. This may lead to decisions to increase deductibles or otherwise reduce health benefits for employees; for example, state governments might need to consider reducing next year's education budget to find the funds to keep a Medicaid program afloat.

In addition, for provider groups that bear financial risk, budget impact analyses inform very real short-term decisions about how to allocate resources to maximize the quality of health care within a given budget. A rapid increase in costs resulting from the significant budget impact of a new drug might lead to decisions to forgo hiring of needed new staff, or delay of introduction of other new services. Quite simply: budget impact, and not long-term cost-effectiveness, determines how affordable health care insurance will be in coming years and shapes what health care can be provided with the resources available.

And yet, the perverse influence of an undiluted focus on budget impact cannot be overstated. A narrow short-term perspective blinds policy makers, insurers, and providers to the need to forge efforts to reshape the delivery system and reframe payment mechanisms to "make room" for new, and potentially expensive interventions that will help patients and pay off in the end. Therefore, if an economic analysis of new interventions is focused only on the short term, relying solely on budget impact estimates, patients and the health care system will be the ultimate losers.

But our nation cannot make advances in managing the potential tension between long-term value for money and short-term budget impact by keeping budget impact assessment out of value frameworks and value assessment reports. The idea that having analyses of long-term value and budget impact in the same report will somehow taint decisions can only be imagined if budget impact were not already dominating the playing field. The ICER value framework includes budget impact analysis because leaving it out would only reinforce its silent power over too many decisions.

Thus, ICER's value framework represents the conviction that keeping budget impact considerations off the table, to be factored in only post-hoc by insurers or provider groups in ways unknown, would be a mistake. It would rob our nation of the chance to bring the public directly into the critical discussions about health care and health insurance that we need to have if we are going to achieve sustainable access for all patients to the kind of innovative new tests, treatments, and delivery system interventions that add value to their lives.

Specific Update Proposals

What follows below are specific update proposals for the ICER value assessment framework and associated methods of evidence analysis and stakeholder engagement. These proposals are generally applicable to ICER reviews of all health care services, including tests, drugs, devices/procedures, and delivery system interventions such as prevention programs, alterations in the organization and composition of health care teams, etc. However, please note several important exceptions and modifications relevant to specific types of interventions:

Ultra-orphan Drugs

An assessment of the value of ultra-orphan drugs will follow the general outlines of the ICER value framework, but there are reasons to consider the possibility of modifications to the evaluation of strength of evidence and value given the unique features of the development and evaluation of ultra-orphan drugs, as well as the size of the potential patient population for such therapies. In particular, questions exist about the composition of factors and their weighting in the categories of “other benefits or disadvantages” and “contextual considerations.” ICER is working with stakeholders to develop specific guidance on how the ICER value framework methods will be adapted for ultra-orphan drugs, but that work has not proceeded far enough to present specific proposals at this time. ICER anticipates posting guidance on its methods for ultra-orphan treatments later this year.

Devices

There are many important unique aspects to the development, early evaluation, regulatory approval, and patterns of use and iterative evidence generation for devices. Therefore, although the conceptual elements of the ICER value framework remain the same for any health care intervention, the specific methods for incorporating and judging evidence will differ for devices. For example, ICER methods acknowledge the practical and ethical considerations that may make it impossible to use RCTs in the early evaluation of clinical effectiveness, while iterative changes to devices, along with the learning curve for practitioners, also raise special considerations about how to judge the available evidence.⁴ Evaluations of long-term cost-effectiveness are made challenging because of the potential for evolution of devices and the attendant changes in cost, effectiveness, and the types of patients that will be treated. These complexities are also relevant to estimations of potential budget impact, and, as noted in sections below, it is very difficult to identify the current baseline costs of all device use in the US health care system in order to calculate a growth target for a budget impact threshold. For these reasons the conceptual elements of the ICER value framework remain relevant for devices but within that framework ICER will continue to incorporate specific unique approaches to evidence evaluation for devices that reflect their unique features.

⁴ See for example the discussion of strength of evidence for devices in the ICER reviews on proton beam therapy, depression, prostate cancer, migraine management, and congestive heart failure (<https://icer-review.org/topics/>).

Tests

Similarly, different approaches to evidence evaluation are required for diagnostic interventions and tests used to monitor patients or provide information on disease prognosis. For example, the general hierarchy in the types and strength of evidence for tests is different than that for therapeutic interventions.⁵ As with devices, tests will continue to be evaluated using the overall conceptual approach of the ICER value framework but there will be important modifications based on the distinctive nature of the evidence and the system for the development, evaluation, and use of diagnostic interventions. Further work will be needed to develop a method for estimating a threshold for potential budget impact that should trigger additional policy maker consideration of short-term affordability.

Delivery System Interventions

There are also many distinctive challenges to evaluating the evidence on the effectiveness and value of delivery system interventions. Chief among these is that in most cases a delivery system intervention will be highly variable in its implemented form across different settings, raising great questions about the generalizability of results from studies of one institution or one system of care. RCTs can be difficult to perform, increasing concerns about the internal validity of study findings. ICER will use the same general value assessment framework to guide its reviews of delivery system interventions, but as with devices and tests, some of the specific methods for judging evidence and for determining thresholds for potential budget impact analysis will reflect the unique nature of these kinds of health service innovations.⁶

Specific ICER value framework update proposals

1. Conceptual structure of the ICER value framework

- 1.1 As shown in Figure 1 earlier in this paper, ICER proposes to replace the conceptual term “care value” with “long-term value for money” as the term for the summary judgment of value that incorporates evaluation of comparative clinical effectiveness, incremental cost-effectiveness, other benefits or disadvantages, and contextual considerations.
- 1.2 The original value framework included a second framing of value, “provisional health system value,” to reflect the formal integration of “care value” with consideration of potential short-term budget impact. Interim changes had already dispensed with a vote on provisional health system value, and ICER now proposes to eliminate this term entirely. The ICER value framework is now structured (and depicted) without a formal

⁵ See for example the discussion of the Fryback and Thornbury evidentiary model used as part of the ICER review on cardiac nuclear imaging, coronary computed tomographic angiography, CT colonography, breast cancer screening, and diagnostic tests for Alzheimer’s disease (<https://icer-review.org/topics/>).

⁶ See for example ICER reviews on Community Health Workers, Integration of Behavioral Health Care into Primary Care, Management of Opioid Addiction, and Diabetes Prevention Programs, and Outpatient Palliative Care (<https://icer-review.org/topics/>).

integration of long-term value for money and short-term affordability. Instead, the value framework suggests that consideration of these two elements is necessary to inform decisions seeking “sustainable access to high-value care for all patients.”

2. Comparative Clinical Effectiveness

2.1 ICER re-states its intent to evaluate evidence arising from multiple sources, not just randomized controlled trials (RCTs), that can be useful in judging the comparative clinical effectiveness of different care options.

RCT data and results of rigorous systematic reviews of high-quality evidence will remain critical elements of ICER evidence reviews, but evidence from non-RCT sources will continue to be included according to transparent quality stipulations (e.g. size, duration, eligibility criteria, etc.) in the scoping document and final evidence report. ICER also continues to include evidence from the “grey literature” as per its stated criteria available at <https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework/grey-literature-policy/>.

2.2 Whenever possible from available data or data provided by manufacturers, ICER proposes to include an evaluation of the heterogeneity of treatment effect for key clinical outcomes.

3. Incremental cost-effectiveness analysis

3.1 The primary measure by which the incremental cost-effectiveness of different care options will be compared will remain the cost per quality-adjusted life year (QALY). The QALY is the established benchmark for capturing benefits for patients through lengthening life and/or improving the quality of life, and it is the standard used by academics, manufacturers, patient groups, and governments around the world. ICER participates in the global dialogue around the best methods for evaluating the value of health services and is always attuned to new developments that might provide a better and fairer system of measuring benefits across different kinds of interventions and patients. Several refinements to ICER’s use of the QALY are described below.

3.2 ICER will use a broader range of cost-effectiveness thresholds between \$50,000 and \$150,000 per QALY to guide considerations of long-term value for money. The range used by ICER for several years has been \$100,000 to \$150,000 per QALY. However, reconsideration of empiric evidence, academic literature, and discussion with stakeholders lead us to propose a broader range. Current benchmarks for cost-effectiveness thresholds are frequently justified by estimates of “societal willingness to pay,” which are commonly cited as approximately 1-3 times the per capita GDP of the country per additional QALY. For the US this range is approximately \$50,000 to

\$150,000.⁷ Among others, the World Health Organization recommends this range for lower and middle income countries, and it has also been adopted the American College of Cardiology for its methods of incorporating value judgments in clinical guidelines.⁸ Secondly, studies of individual willingness to pay (by trading off salary for additional years of life) have widely varying results but many are in the range of two times the individual's salary. Given the mean personal income in the US in 2015 was \$44,510, this would suggest a threshold of approximately \$90,000 per QALY.⁹ The third, and in many ways most relevant information to guide the setting of cost-effectiveness thresholds is information on the true opportunity cost at the margin of health spending. Recently, empiric studies have been performed in upper and medium countries in Europe and Latin America that have found that to reflect true opportunity costs the cost-effectiveness threshold should be set closer to 1-2 times the per capita national GDP (approximately \$50,000-\$100,000 per QALY in the US).¹⁰

With these considerations in mind, ICER proposes to expand its cost-effectiveness range by incorporating \$50,000 per QALY as the lower bound and maintaining \$150,000 as an upper bound. This entire range will be used in the calculation of a range for the ICER value-based price benchmark, but as is described later in section 4.1.6 we are proposing to use a weighting of other benefits or disadvantages and contextual considerations given by an independent appraisal committee to select a single cost-effectiveness threshold from within this broader range as the anchor for a final, single value-based price benchmark.

3.3 ICER will include cost per life-year gained and additional measures of clinical benefit in the presentation of the results of incremental cost-effectiveness analyses.

In order to increase the transparency to the cost per QALY estimates, ICER proposes to include in its reports analyses of cost per life-year gained and certain other "cost per consequences" when relevant. For example, treatments intended to prevent strokes might be compared by a "cost per stroke averted" analysis as a complement to the cost per QALY analysis.

3.4 ICER will perform scenario analyses that examine the influence of lower utilities for individuals with chronic severe conditions on cost per QALY findings.

When the major impact of a treatment is to extend the life of patients with a chronic and

⁷ <http://data.worldbank.org/indicator/NY.GDP.PCAP.CD>

⁸ See ACC/AHA Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures. Available at <http://circ.ahajournals.org/content/129/22/2329>.

⁹ Figures based on "Selected Characteristics of People 15 Years and Over, by Total Money Income, Work Experience, Race, Hispanic Origin, and Sex". US Census Bureau. 26 August 2016. Available at <https://www.census.gov/data/tables/time-series/demo/income-poverty/cps-pinc/pinc-01.html>.

¹⁰ Claxton, K., Martin, S., et al., 2015. Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. *Health Technol Assess.* 2015 Feb;19(14):1-503.

severe condition, the lower utility (quality of life) assigned to these health states will diminish the overall QALY gain relative to the QALY gain that would be calculated for the same extension of life for patients with a higher baseline quality of life. Under these conditions ICER will actively compare the cost per life-year-gained with the cost per QALY and will also perform scenario analyses using a standardized baseline QALY for the general population in order to examine the degree to which assumed poor quality of life for individuals with chronic severe conditions and disabilities affects the incremental cost-effectiveness ratio of new treatments. When the impact of lower utilities for baseline chronic conditions makes a substantive difference in the calculated incremental cost-effectiveness ratios for treatments, ICER will seek patient input and public comment on which scenario analysis should serve as the base case within the ICER report.

- 3.5 ICER proposes to continue with a recent change to its benchmark for prices used in cost-effectiveness and potential budget impact analyses. Instead of using wholesale acquisition cost (WAC), whenever possible ICER reports will use estimates of prices net of discounts, rebates, and other price concessions.

ICER has long sought a benchmark for pricing that could reliably and with relative transparency provide an estimate for net prices in the US market. With the recent report on treatments for psoriasis ICER has begun a collaboration with SSR Health, a consultancy which combines data on net US dollar sales with information on unit sales to derive net pricing at the unit level across all payer types. Further details on the mechanism used to estimate net prices are available in the methods section of each ICER report.

- 3.6 ICER will continue to calculate incremental cost-effectiveness from the health system perspective as its base case, but will perform a scenario analysis including work productivity when feasible, and will use a new template to give greater detail and transparency to the perspective taken in all cost-effectiveness analyses.

ICER will continue to use the health system perspective as the “base case” of its cost-effectiveness analyses for two reasons. First, full consideration of the societal perspective often requires inclusion of broad and uncertain assumptions regarding the impact of health care on productivity, income tax generation, educational outcomes, the criminal justice system, and disability and social security benefits. Finding reliable estimates for long-term effects of health interventions on these broader outcomes is usually not possible. Second, the health system perspective is the most relevant for decision-making by public and private insurers, risk-bearing provider groups, and health care policymakers. Whenever feasible, however, the relative impact of different care options on work productivity will be estimated and included as a scenario analysis in all ICER reports. This information will be considered by ICER independent public appraisal committees as part of their weighing of “other potential benefits and disadvantages” as described later in this paper. To emphasize the important distinctions

among perspectives, ICER will use the template recently promulgated by the Second Panel on Cost-Effectiveness to describe the elements of health system and societal perspectives included in ICER cost-effectiveness analyses.

3.7 ICER's cost-effectiveness analyses will not routinely make estimates of price changes across comparator treatments linked to patent and exclusivity time horizons. However, when high likelihood of a major change to pricing can be anticipated within 12-24 months, a scenario analysis may be developed to explore the impact of price changes on long-term cost-effectiveness ratios.

Including assumptions about price changes is not currently the standard in academic or health technology assessment agency cost-effectiveness analyses. In part this is because it is very difficult to predict the pricing landscape many years into the future, and even when patents and exclusivity expire prices may not drop substantially. When they do it may be because prices have increased rapidly in the preceding few years, and prices of relevant comparator drugs may drop as well. Changes in the competitive landscape anticipated within 12-24 months, however, may be considered if there are consistent historical findings of price changes that can be applied to the topic under review.

4. Other Benefits or Disadvantages and Contextual Considerations

Many comments were received related to these two domains within the ICER value framework. In general, many commentators felt that greater transparency was needed in the way that other benefits or disadvantages and contextual considerations were integrated into the voting of the independent committees and linked to value-based price benchmarks. Most health technology assessment groups around the world do not attempt to quantify these domains of value, believing that their relative weight in any overall judgment of value should be left qualitative and subject to public discussion. Given the comment from various stakeholders, however, ICER has considered several methodological options that could enhance the transparency and explicit integration of these considerations.

Formal multi-criteria decision analysis (MCDA) has been considered but rejected because we do not believe that the methods for weighting individual elements are robust enough to add to reliability of value judgments. ICER has attempted formal MCDA with its independent committees on several occasions in the past and found the technique too complicated for reliable use.

Other approaches were explored for quantifying some considerations within "other benefits or disadvantages" and "contextual considerations." For example, ICER considered use of proportional and absolute QALY shortfall methods to measure "burden of illness" and create a weighted QALY. However, we are not proposing to adopt these methodologies given the risk of unintended consequences that favor some conditions/treatments over

others and in light of the lack of consensus on these techniques in the academic community and among national health technology assessment agencies worldwide.

We also explored recently proposed methods in Norway in which broader societal considerations, including burden of illness, would be used to assign a treatment to one of 3 step-wise cost-effectiveness thresholds. Norway has decided not to adopt this approach, and our own investigation, including discussion with multiple patient groups and other stakeholders, suggests that this approach would be likely to create ethically problematic distinctions between types of patients and conditions.

ICER could continue with a general approach that identifies other benefits or disadvantages and contextual considerations and invites independent committees to consider these factors in overall votes on what will now be called “long-term value for money.” As a potential alternative in response to public comment requesting some kind of quantitative approach, ICER proposes to adopt a modified form of MCDA. We propose a form of MCDA that will delineate the elements and use a weighting system to integrate their consideration as part of long-term value for money. But we do not believe deriving quantitative weights for each individual element is conceptually robust or practically feasible. The following specific methods for this proposed modified MCDA approach are as follows:

- 4.1 Based on ICER’s existing value framework, discussions with stakeholders, and benchmarking other value frameworks around the world, ICER reports will explicitly delineate other benefits or disadvantages and contextual considerations as the following 10 elements:
 1. Unmeasured patient health benefits
 2. Relative complexity of the treatment regimen that is likely or demonstrated to significantly affect adherence and outcomes
 3. Impact on productivity and ability of the patient to contribute to personal and national economic activity
 4. Impact on caregiver burden
 5. Impact on public health
 6. New mechanism of action that is likely to help patients who have not responded to other treatments
 7. Severity of the untreated condition
 8. Lifetime burden of illness
 9. Lack of availability of any previous treatment for the condition
 10. Other ethical, legal, or social considerations that might strongly influence the overall value of an intervention to patients, families and caregivers, the health system, or society

- 4.2 During the public meeting, ICER independent public appraisal committees will be asked to consider these 10 areas and indicate their relative score for each on a visual analogue scale from “least” to “most.” The ICER report will include evidence and other information relevant to these value elements, and before voting at the public meeting further input will be obtained from patient representatives, clinical experts, and other stakeholders. The independent appraisal committee will then be asked to give an overall ranking on a quantitative scale from 1-5 of the relative contribution to overall long-term value for money of all “other benefits or disadvantages and contextual considerations.”
- 4.3 Case studies will be prepared for each of the 10 elements to give examples of care options that would represent the high and low ends of the spectrum. These case studies would be intended to help calibrate and make more transparent the consideration of each of these value domains by ICER independent public appraisal committees.
- 4.4 The vote on the overall score on other benefits or disadvantages and contextual considerations will be recorded as part of the public meeting and incorporated in the final ICER report, making it clear that the weighting done by the committee reflects one group’s judgment and may not represent the same weighting that various decision-makers would assign.
- 4.5 The average weighting from 1-5 obtained from the vote of the independent committee will be used to assign a single incremental cost-effectiveness ratio from within the range of \$50,000-\$150,000 per QALY included in the draft evidence report. This single incremental cost-effectiveness ratio will be used as the threshold at which a single value-based price benchmark will be calculated for the care option under consideration.
- 4.6 To clarify how this would work, the Table below shows how the average of the independent committee scores on other benefits or disadvantages and contextual considerations would be translated into a cost-effectiveness threshold:

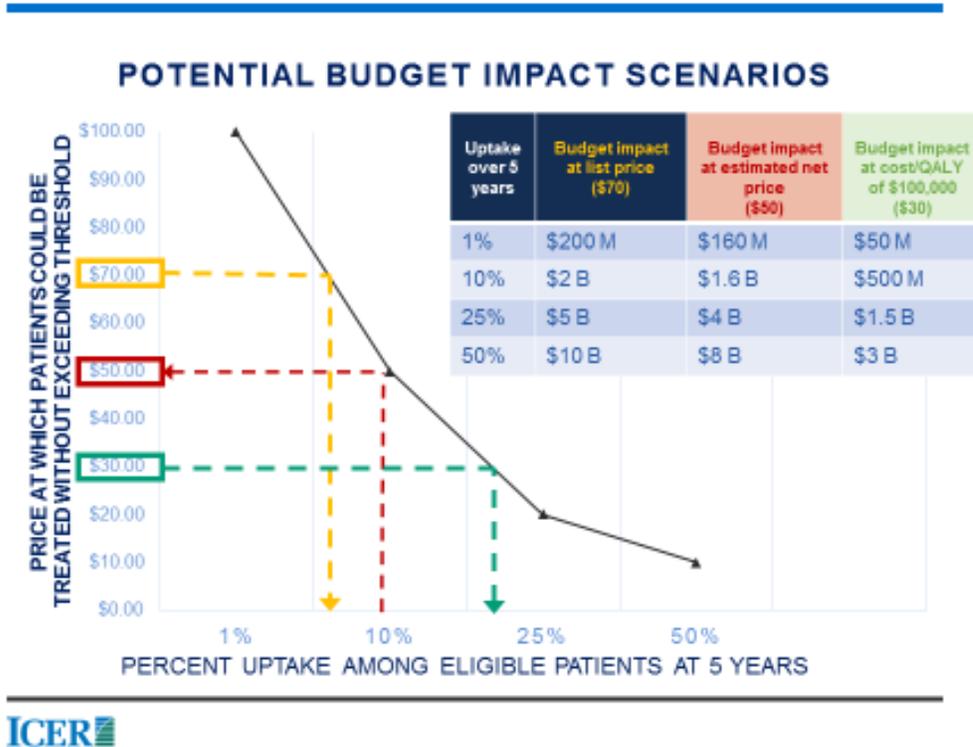
Other benefits/contextual considerations average score	Associated incremental cost-effectiveness ratio used as threshold for final value-based price benchmark
1	\$50,000 per QALY
2	\$75,000 per QALY
3	\$100,000 per QALY
4	\$125,000 per QALY
5	\$150,000 per QALY

- 4.7 Voting averages on other benefits/contextual considerations do not have to be integers to be translated into cost per QALY thresholds. For example, if six council members give a weighting of “3”, five vote for “4”, and two vote for “5” the summary cost-effectiveness ratio would be $[(6 \times 100) + (5 \times 125) + (2 \times 150)]/13 = \$117,000$ per QALY].
- 4.8 The final ICER value-based price benchmark will be a single price based on the price needed to achieve the weighted incremental cost-effectiveness ratio determined by the independent committee at the public hearing. ICER Final Reports and press releases will also include the broader price range needed to achieve thresholds of \$50,000-\$150,000 per QALY as a reference for all stakeholders and to emphasize that the single ICER value-based price benchmark reflects the weighting of other benefits and contextual considerations by the independent committee, value judgments that other observers might make differently.
- 4.9 In this new approach there would no longer be a separate committee vote on long-term value for money. However, stakeholders have commented that they wish ICER final reports to continue to include overall value ratings, so the following approach is proposed: once the committee vote has determined the “weighted” cost-effectiveness threshold, if the base case incremental cost-effectiveness ratio for the treatment is more than \$25,000 per QALY higher than this threshold the long-term value for money of the treatment will be identified as “low.” If the base case incremental cost-effectiveness ratio is more than \$25,000 lower than the weighted threshold the treatment will be labeled as having “high” long-term value for money. Otherwise the treatment will be identified as having “intermediate” long-term value for money.

5. Potential Budget Impact Analysis

- 5.1 As previously described, potential budget impact will no longer be included conceptually as one component of “provisional health system value.”
- 5.2 The new approach proposed for performing and presenting an analysis of potential budget impact for new drugs is shown in the Figure on the following page and described subsequently.

Figure 2. Proposed new approach to potential budget impact analysis. The black line indicates when the potential budget impact threshold is reached at each combination of price and percent uptake among eligible patients at 5 years.



5.3 ICER will no longer attempt to estimate the uptake of a new intervention. The intention of ICER’s current methods has been to estimate the potential uptake of a new intervention if insurers and provider groups exercise no restraint on utilization. This “unmanaged uptake” assumption has proven difficult to convey given the natural tendency to view an uptake estimation as an estimate of what will actually happen in the marketplace.

5.4 Rather than try to estimate real-world uptake, ICER will present information that will allow stakeholders to ascertain the potential budget impact of a new service according to a wide range of assumptions on price and uptake. Prices modeled in the potential budget impact analysis will include: WAC, estimated net price from SSR data, and prices to achieve cost-effectiveness thresholds of \$50,000, \$100,000, and \$150,000 per QALY. As part of this analysis for new drugs ICER will continue to present information allowing stakeholders to know when the combination of price and uptake at the national level would lead to a potential budget impact that would meet a threshold linked to a growth target for the overall health system.

- 5.5 This potential budget impact threshold for new drugs will continue to be calculated as double the average net budget impact for new drugs that would contribute to overall health care cost growth beyond the anticipated growth in national GDP plus an additional 1%. Extensive discussions with stakeholders have affirmed the relevance of linking the potential budget impact threshold to national GDP growth.
- 5.6 For services other than new drugs ICER has explored different ways to calculate a potential budget impact threshold linked to growth in existing use and overall growth targets, but has not arrived at an approach in which we have full confidence. After discussion with stakeholders, ICER proposes that for devices and other services a net budget impact threshold of \$500 million per year be used to indicate when special attention may be needed to address short-term affordability.
- 5.7 New calculations updating the potential budget impact threshold have been done for 2017-2018. The updated potential budget impact threshold is \$915 million per year, annualized over 5 years. Full calculations with sources for data are shown in the Figure following this section. The two most notable changes from the previous calculation are the estimates of total personal medical health care spending and the contribution of drug spending to total health care spending. For the former, personal health care less dental care is now used as a more relevant figure for health spending. For the latter, updated figures that capture drugs administered in hospital and physician offices are now used. The combined effect of these two changes, in combination with a lower projected GDP growth rate for the US, leaves the overall threshold for potential budget impact for drugs little changed from 2015-2016.
- 5.8 ICER will note in its reports the percent uptake of a new intervention, at its net price level, that would produce a potential budget impact that exceeds this threshold. Note that it is possible that the new intervention will not exceed the threshold regardless of uptake level; this will be noted as well.
- 5.9 As described earlier, the goal of integrating considerations of potential budget impact with appraisal of an intervention's "long-term value for money" will be clarified in the value framework as being: "sustainable access to high-value care for all patients." Given this goal, ICER will include as part of its final report an "affordability and access alert" if discussion among stakeholders at the meeting of ICER's independent appraisal committees suggests that utilization driven by clinical need, at estimated net pricing, would exceed the budget impact threshold without active intervention by insurers and others to limit access to the treatment. The purpose of an ICER affordability and access alert will be to signal to stakeholders and policy makers that the amount of added health care costs associated with a new service may be difficult for the health system to absorb over the short term without displacing other needed services or contributing to rapid growth in health care insurance costs that threaten sustainable access to high-value care for all patients.

Figure 3. Updated calculations deriving a threshold for potential budget impact for new drugs.

Item	Parameter	2015-2016 Estimate	2017-2018 Estimate	Source
1	Growth in US GDP, 2017 (est.) +1%	3.75%	3.20%	World Bank, 2016
2	Total personal medical health care spending	\$3.08 trillion	\$2.71 trillion	CMS NHE, 2016
3	Contribution of drug spending to total health care spending	13.3%	17.7%	CMS NHE, 2016; Altarum Institute, 2014
4	Contribution of drug spending to total health care spending	\$410 billion	\$479 billion	Calculation (Row 2 x Row 3)
5	Annual threshold for net health care cost growth for ALL drugs	\$15.4 billion	\$15.3 billion	Calculation (Row 1 x Row 4)
6	Average annual number of new molecular entity approvals	34	33.5	FDA, 2016
7	Annual threshold for average cost growth per individual new molecular entity	\$452 million	\$457.5 million	Calculation (Row 5 ÷ Row 6)
8	Annual threshold for estimated potential budget impact for each individual new molecular entity	\$904 million	\$915 million	Calculation (doubling of Row 7)

6. Report development and stakeholder engagement

Along with these proposals, ICER has posted updated versions of guides for patient and manufacturer engagement in the report development and meeting process. These engagement guides provide improved templates and suggestions to help the patient community participate in the scoping of the topic and contribute data and other information to the report. Timelines have all been reconsidered, with overall length of report development extended and every effort made to provide suitable response time to draft documents. Some of the highlights from these materials include the following changes, some of which have already been instituted in recent reports and meetings.

- 6.1 Preliminary report findings from the systematic review and economic modeling are now discussed with manufacturers and patient groups prior to posting of the first draft review for broader public comment.
- 6.2 Patient rep(s) and clinical experts will join the independent committee for the entire meeting, being available for questions and able to make comments during the presentation of the evidence and deliberation prior to voting.

- 6.3 Patient groups will be given the opportunity to present the results of their own evidence generation through patient-reported outcomes and surveys on other benefits or disadvantages.
- 6.4 At our next meeting in February 2017 we will pilot test a change to our meeting agenda that creates an expanded opportunity for manufacturer comment and discussion immediately following the presentation of the summary of the evidence review.
- 6.5 All ICER reports will have newly prominent language specifying that the review is time limited. A formal process for report updates is still under development.
- 6.6 All reports will include improved transparency in the listing of patient groups, clinical experts, and policy experts who have been consulted as part of the report development process. Formal peer review of the draft report by 1-2 clinical experts will be noted.

7. Economic model transparency

Many commenters suggested that ICER develop some approach to improving the transparency in the design of the economic models that are used to perform cost-effectiveness analyses. ICER will continue to work with its academic colleagues to explore various opportunities to create access to executable models, but suitable mechanisms have not yet been developed that can find the right balance between protecting the intellectual investment in the model by academic health economists, providing external users a model that can be run without extensive aid from the model developer, and the timelines for model development and interaction with all stakeholders within the overall report development process. With recent reports, however, ICER and our academic colleagues have made extensive efforts to provide sufficient detail in the draft report appendix to allow manufacturers and other stakeholders to seek to replicate the report findings and understand if and why results differ from other modeling efforts.

To try to make the model assumptions and outputs as transparent and reproducible as possible, ICER has adopted the following general statement and approach. We welcome further comment in this area from all stakeholders:

The Institute for Clinical and Economic Review (ICER) is committed to open and transparent engagement with all stakeholders that have an interest in each of its evidence reviews. This commitment to transparency extends to the development and/or modification of economic models. Such transparency helps to increase the public's confidence in model results. Without detailed descriptions of model structure and processes as well as estimates used, economic models run the risk of being considered "black boxes," with no way to evaluate the validity of model processes or accuracy of model inputs. Explicit delineation of model structure and flow gives stakeholders the ability to evaluate the model's face validity. Details on the point estimates and ranges used in sensitivity analyses allow for the explicit testing of alternative assumptions and model inputs, provide insight into the drivers of specific results, and allow

other interested parties to replicate or extend analyses conducted by ICER and its collaborators.

GENERAL APPROACH

Our general approach to model transparency is based on the Modeling Good Research Practices Task Force report on “Model Transparency and Validation” jointly produced by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and the Society for Medical Decision-Making (SMDM).[1] Our aim is to provide information on the model structure and processes, all major inputs and sources for data, and key assumptions used in our economic analyses, so that readers can judge their confidence in the results while preserving the intellectual property rights of those we collaborate with.

All model documents will note that funding for ICER’s analyses is unrestricted and publicly disclosed. In addition, ICER develops economic models in collaboration with academic researchers who are free from financial conflicts on any given project. In addition, ICER maintains a strict conflict-of-interest policy for its own employees, which can be accessed at: <https://icer-review.org/methodology/rules-that-apply-to-icer/interactions-with-external-partners/>.

POLICY

For each report, the interventions selected for study will be specified in detail. ICER and its collaborators will provide model documentation, including model structure, comparators, and specifications. When existing models are being used, ICER will provide references to prior publications that provide further details on the model. When new models are developed, this information will be provided as part of the technical report.

Following the publication of a final scope for each topic, ICER and its external collaborators will publish a modeling analysis plan with detailed specifications for the expected conduct of the work. The plan will be published on a public website used to share collaborative research known as the Open Science Framework (<https://osf.io/7awvd/>), approximately 10-12 weeks after a topic is publicly announced. Stakeholders will be notified when the analysis plan is posted. The plan may be updated following review of additional data sources, discussions with stakeholders, and other activities, and so is intended to be considered a “living document.” Detailed elements of the analysis plan will include:

- Analytic objectives
- Model structure, including a textual and/or graphic depiction of the model structure, process, and outputs
- Descriptions of interventions and comparators
- Perspective (generally health care system)
- Time horizon (generally lifetime)
- Discount rate
- Key assumptions to be used in the model

- Model input values, ranges, and sources of data
- Other variables crucial to understanding model transition and flow (e.g., risk equations for downstream events)

Sources for model inputs, risk equations, etc. will be provided as part of the documentation. In general, ICER's analyses will use data sources and information from published or publicly available sources, including peer-reviewed journals, supplementary appendices, briefing documents used by regulatory authorities, and conference proceedings. In specific instances, valid analyses may require the use of unpublished information, such as manufacturers' data on file. In such circumstances, explicit requests will be made to affected parties, and any reasonable documentation to protect patient and/or stakeholder confidentiality will be provided. The final version of the modeling analysis plan will be used in conducting the ICER's "long-term value for money" analyses.

Importantly, the modeling analysis plan is intended to provide enough information for an experienced researcher to be able to replicate the economic model and analyses. Actual executable models and associated computer code will not be provided as part of the deliverable, as such an effort would unduly compromise the intellectual property rights of ICER's external collaborators. As the ISPOR-SMDM Task Force has pointed out, without such protections, "the incentives and resources to build and maintain complex models could disappear."¹¹

Additionally, ICER and its collaborators will provide a summary of the results of these analyses in a model technical summary. This 10- to 15-page summary will be part of a larger report that ICER will produce that will include information on the available clinical evidence, current guidelines and payer coverage policies, and other relevant topics. The model summary will consist of the following sections:

- Methods, including key assumptions and key model inputs
 1. Overview, including description of model structure
 2. Perspective
 3. Patient Population
 4. Costs
 5. Quality of Life/Utility
 6. Primary, Alternative, and Sensitivity Analyses
 7. Budget Impact Analysis
 8. Appendices, including other assumptions and model inputs
- Results
 1. Primary (Base-Case) Analysis Results

¹¹ Eddy DM, Hollingworth W, Caro JJ, Tsevat J, McDonald KM, Wong JB, on behalf of the ISPOR-SMDM Modeling Good Research Practices Task Force. Model transparency and validation: A report of the ISPOR-SMDM Modeling Good Research Practices Task Force-7. *Value in Health* 2012;15:843-850.

2. Alternative and Sensitivity Analysis Results, including tornado diagram
 3. Budget Impact Analysis Results
 4. Appendices, including supporting tables/figures summarized in main text
- Summary and Comment, including limitations and comparison to other published models on the topic of interest

The model results become sections of an ICER-published report on the comparative clinical effectiveness, cost-effectiveness and budget impact of the specific interventions being evaluated. The initial draft report will be posted for a public comment period of four weeks, after which it may be revised. The revised draft report is then presented as part of a public assessment meeting. The modeling sections of the report are intended to provide enough information to evaluate the economic analysis, but not necessarily all of the information that would be required to replicate the analysis.

ICER endeavors to follow recommended best practices throughout our evaluations. By following the process outlined above, we hope to make our economic models and associated analyses more transparent and useful to the health care community.