Comparison of Value Assessment Frameworks Using the National Pharmaceutical Council’s Guiding Practices for Patient-Centered Value Assessment

Final White Paper

HEALTHCARE AND HUMAN SERVICES POLICY, RESEARCH, AND CONSULTING—WITH REAL-WORLD PERSPECTIVE.

Prepared for: National Pharmaceutical Council

Submitted by: The Lewin Group, Inc.

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I. Introduction

The development of value assessment frameworks in the U.S. has emerged in the broader context of a shift in emphasis from volume to value of health care. Among other important contributing factors to the interest in such frameworks are: public attention to therapies with high or steeply increased prices, alternative payment models intended to incentivize value, increased focus on patient- and consumer-centered care, advances in personalized medicine, growing capacity for the generation of real-world evidence pertaining to value (e.g., through the use of claims and electronic health data), and the general absence in the US of an explicit cost-effectiveness criterion for payers and policymakers.

In the U.S., five value assessment frameworks and related tools that have recently emerged into prominence include the following:

- American College of Cardiology and American Heart Association (ACC-AHA) Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures
- American Society of Clinical Oncology (ASCO) Conceptual Framework to Assess the Value of Cancer Treatment Options
- Memorial Sloan Kettering Cancer Center’s (MSKCC) DrugAbacus
- Institute for Clinical and Economic Review (ICER) Value Framework
- National Comprehensive Cancer Network (NCCN) Evidence Blocks™

While these frameworks generally focus on assessing the value of different treatments and overlap in some ways, their respective intended purposes and target users differ. Table 1 summarizes the intended purpose, audience, and treatments or other interventions addressed by these frameworks. Three of the frameworks focus on cancer treatments (mostly drugs and biologics), including the ASCO framework, MSKCC’s DrugAbacus, and NCCN’s Evidence Blocks™. The ACC-AHA framework focuses on cardiovascular care. The ICER framework is not limited to any specific conditions or types of intervention.

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II. Overview of the Frameworks

These five frameworks are in different stages of development, and all of their developers consider them to be works in progress, including two (ACC-AHA and ASCO) that are not ready for widespread use. Developers of all five express that their frameworks are open to refinement in response to stakeholder feedback.

A. American College of Cardiology and American Heart Association

ACC-AHA currently is still developing the methodology for its framework. The ACC-AHA framework assigns one of five value levels to an intervention based on the available evidence on the magnitude of benefit as well as explicit ranges of cost-effectiveness using cost per quality-adjusted life year (QALY) gained.

The five levels of value designated by ACC-AHA are:

- High value: better outcome at lower cost or incremental cost-effectiveness ratio <$50,000 per QALY gained
- Intermediate value: $50,000 to <$150,000 per QALY gained
- Low value: ≥$150,000 per QALY gained
- Uncertain value: value examined but data are insufficient to draw a conclusion because of no studies, low-quality studies, conflicting studies, or prior studies that are no longer relevant
- Not assessed: value not assessed by the writing committee

ACC-AHA defined these levels according to the World Health Organization Choosing Interventions that are Cost-Effective (WHO-CHOICE) project, which provides an approach for setting cost-effectiveness thresholds that can be applied globally across a range of health interventions. The three WHO-CHOICE categories of cost-effectiveness are derived from gross domestic product (GDP) as a proxy for relative national wealth: highly cost-effective (less than GDP per capita), cost-effective (1 to 3 times GDP per capita), and not cost-effective (>3 times GDP per capita). Using 2012 GDP data, the WHO-CHOICE thresholds for the US correspond roughly to the thresholds cited above.

These value assessments are to be incorporated into ACC-AHA clinical practice guidelines and performance measures. To date, the ACC-AHA framework has not been applied to any cardiovascular interventions. As such, the extent to which this framework aligns with the NPC guiding practices reflects how ACC-AHA has described, though not yet implemented, that framework.

B. American Society of Clinical Oncology

ASCO assesses cancer treatments based on data from clinical trials, typically comparing a treatment to a standard of care. ASCO’s framework yields a composite net health benefit (NHB) score based on the clinical benefits (e.g., improvement in overall survival, progression-free survival, and response rate), toxicity, and bonus points for symptom palliation and treatment-free
survival. The ASCO framework also includes drug acquisition costs, which are reported separately from the NHB score.

The first published iteration of the framework included assessments of treatments for four clinical conditions that ASCO used to demonstrate the calculations for the NHB score. Each of these examples relied on data from single clinical trials. Following a public comment period, ASCO revised the framework and published an updated version in June 2016. The most notable revisions include the following:

- the use of hazard ratios (where available), rather than absolute improvements in survival, in calculating treatment efficacy
- consideration of more reported side effects, not just the most severe, high-grade toxicities
- addition of bonus points for improvement in quality of life (QoL) and significant improvement in survival at the tail end of the curve.  

ASCO is planning to use the updated framework as a basis for developing a user-friendly software tool for providers to share with their patients to help inform their treatment decisions. ASCO anticipates that the tool will undergo changes as it is tested and feedback is received from providers and patients, and as it is adapted to different clinical scenarios and new clinical evidence. Once the tool is developed, ASCO anticipates that the drug cost component of its framework may prompt discussion of a patient’s copayment and any implications for therapeutic options.

C. DrugAbacus

The MSKCC DrugAbacus is an interactive online instrument that contains data on a large, though not systematically selected, set of 52 cancer drugs approved between 2001 and 2015 by the US Food and Drug Administration for the treatment of cancer. Described by its developers as a draft tool, DrugAbacus yields a value-based price calculated using a formula that consists of a set of domain parameters that are weighted based on the user’s preferences. The resulting DrugAbacus price is presented in comparison to an actual market monthly price (i.e., cost to Medicare).

Until July 2016, DrugAbacus accounted for the following six domains: efficacy, tolerability, novelty, research and development costs, rarity, and population burden. The updated tool accounts for two additional domains – unmet need and prognosis – which can also be weighted based on the user’s preferences. This update was in response to stakeholder feedback requesting inclusion of these additional domains. The updated tool also includes an indication-specific pricing feature, which allows users to compare the DrugAbacus price and actual price for multiple, different indications for some selected drugs (i.e., Abraxane, Avastin, Nexavar, and Tarceva). According to its developers, although DrugAbacus is often compared to value assessment frameworks, it is primarily a research tool meant to explore and test different concepts that could affect a drug’s value. Also according to DrugAbacus’ developers, there are no plans to add drugs to the tool unless there is a need to test new concepts.

6 Tail-of-the-curve bonus points are awarded if: (1) the test regimen results in at least a 50% relative improvement in the proportion of patients who are alive with the test regimen at the time point on the survival curve that is at twice the median overall survival (OS) or progression-free survival (PFS) point for the control regimen and (2) at least 20% of patients receiving the control regimen are alive at this time.
D. Institute for Clinical and Economic Review

ICER’s value assessment framework evaluates care value over the long term and potential health system budget impact over the short term. Care value accounts for comparative clinical effectiveness, incremental cost per outcomes achieved, other benefits or disadvantages, and contextual considerations. One of ICER’s three advisory panels votes on the results of care value at three levels:

- High value: <$100,000 per QALY gained
- Intermediate value: $100,000-$150,000 per QALY gained
- Low value: >$150,000 per QALY gained

The potential budget impact accounts for potential net changes in overall health spending over an initial five-year timeframe. In assessing the potential budget impact of a new treatment, ICER presents four potential uptake patterns based on health condition/market considerations (e.g., what treatments a new treatment may be replacing). The uptake rates range from what ICER considers a low of 10% over five years to a very high uptake rate of 75% over five years, all in an unmanaged environment. According to its developers, ICER does not intend these to be estimates or projections of actual uptake rates. Instead, the ICER framework presents potential budget impact levels along with a threshold that is intended to serve as an “alarm bell” for thinking about affordability of treatments at particular price points. ICER also calculates value-based price benchmarks based on the care value determination and potential levels of budget impact. ICER does not consider these benchmarks to be a formal part of its value assessment.

ICER has made changes to its framework in response to stakeholder feedback. ICER presented these changes in June 2016, describing them as part of “version 1.5” of the framework. Among the changes was the elimination of a separate vote by the assessing panel on “provisional health system value.” The potential budget impact is now discussed during the policy roundtable, which is a part of the public meeting that follows the panel’s vote on care value.

In addition to these updates, ICER made a national call for suggestions to improve its value assessment framework in July 2016. ICER plans to use the suggestions to guide internal review and further discussions with stakeholders for informing the development of an update to the framework planned for 2017 (version 2.0).

E. National Comprehensive Cancer Network

NCCN presents “Evidence Blocks” that accompany its oncology clinical practice guidelines. These five-by-five depictions represent five domains: efficacy, safety, quality of evidence, consistency of evidence, and affordability. Each domain is graded by members of an expert panel on a scale of 1 (least favorable) through 5 (most favorable). The average of their votes for each domain is used to build the blocks. Affordability is rated using the panel members’ knowledge of overall cost of the regimen. This is intended to include drug acquisition, administration, in-patient vs. out-patient care, supportive care, infusions, toxicity monitoring, antiemetics and growth factors, and potential for hospitalization. The affordability domain does not include indirect costs (e.g., transportation, time lost from work) or potential cost offsets as a result of use of a therapy. In conjunction with the NCCN guidelines, the Evidence Blocks are intended to
supply the oncologist and individual patient with information about value to support shared decision-making about care options.

**Table 1. Summary of Five Value Frameworks in the U.S.**

<table>
<thead>
<tr>
<th>Framework</th>
<th>Intended Purpose</th>
<th>Intended Primary Audience</th>
<th>Interventions Addressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC-AHA</td>
<td>Provide a more complete examination of cardiovascular care, helping to generate the best possible outcomes within the context of finite resources.</td>
<td>Clinicians, patients, payers</td>
<td>Cardiology treatments, primarily drugs</td>
</tr>
<tr>
<td>ASCO</td>
<td>Enable a physician and patient to assess the value of a particular cancer treatment regimen given the patient’s individual preferences and circumstances.</td>
<td>Clinicians, patients</td>
<td>Cancer drug/biologic regimens</td>
</tr>
<tr>
<td>DrugAbacus</td>
<td>Provide an interactive tool to help determine the price of a cancer drug based on its value compared with the price assigned by the pharmaceutical company.</td>
<td>Policymakers, payers, industry</td>
<td>Cancer drugs/biologics</td>
</tr>
<tr>
<td>ICER</td>
<td>Develop a conceptual framework to help inform users, primarily insurers, in their assessments of the value of medical services, including drugs, medical devices, and procedures.</td>
<td>Payers, policymakers, industry</td>
<td>Primarily drugs/biologics; has been extended to devices, procedures, and delivery system programs</td>
</tr>
<tr>
<td>NCCN</td>
<td>Provide the health care provider and the patient information to make informed choices when selecting systemic therapies based upon measures related to treatment, supporting data, and cost.</td>
<td>Clinicians, patients</td>
<td>Treatment regimens, primarily cancer drugs/biologics</td>
</tr>
</tbody>
</table>

**III. Background and Purpose of This Analysis**

With the emergence of several value assessment frameworks, Neumann and Cohen published a comparative overview of five US-based frameworks in 2015. The National Pharmaceutical Council (NPC) followed with a more detailed analysis of these five, titled *Current Landscape: Value Assessment Frameworks*. NPC’s analysis, as well as certain others’, cited concerns in one or more of the frameworks, including the use of untested methodologies, limited evidence base, lack of patient-centeredness, lack of a health system-wide perspective, and unclear or confusing output for users.

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Drawing from its analysis and seeking to address those concerns, NPC developed a set of guiding practices to ensure that value assessment tools are patient-centered and focused on supporting value in patient care and outcomes by meeting a set of good practices/standards. NPC’s *Guiding Practices for Patient-Centered Value Assessment* includes 28 specific elements comprising the following six key aspects of value assessments:  

- Assessment process
- Methodology
- Benefits
- Costs
- Evidence
- Dissemination and Utilization

The document also includes seven guiding practices for budget impact assessment (BIA), outlined separately, though not as a measure of value.

The five current value assessment frameworks examined by Neumann and Cohen and by NPC are still undergoing revision and refinement. As such, the guiding practices presented by NPC, as well as other potentially relevant methodological practices and standards, are available for framework developers to consider as they seek to improve their frameworks’ utility for a variety of stakeholders.

The Lewin Group was contracted by NPC to conduct an independent analysis of the extent to which the five major value assessment frameworks address or align with NPC’s guiding practices. The purpose of this analysis is two-fold:

1. Evaluate how the five major value assessment frameworks align with NPC’s *Guiding Practices for Patient-Centered Value Assessment* and compare and contrast these frameworks across the guiding practices.
2. Continue to guide the field in ensuring that value assessment frameworks meet a set of standards/good practices that helps to ensure that these tools support patient care and outcomes.

### IV. Methodology for This Analysis

In order to evaluate the frameworks against NPC’s guiding practices, Lewin began by reviewing and gathering information on each of the frameworks. Lewin built on the information available in NPC’s *Current Landscape: Value Assessment Frameworks* by seeking additional literature and information available in the public domain, including any other comparative reviews that have been conducted and any relevant grey literature.

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With the available information, two reviewers independently evaluated each framework against the NPC’s 28 specific guiding practices (GPs) to determine whether the relevant attribute of each framework fully meets, partially meets, or does not meet the corresponding GP (see Table 2). As the ICER framework was the only one of the five that includes a budget impact assessment (BIA), they also evaluated the ICER framework against NPC’s GPs for BIA.

Spreadsheets were constructed to categorically record each reviewer’s determination of whether or not a framework currently meets, partially meets, or does not meet a specific GP. The two reviewers also provided their rationales for their determinations. A senior staff member reviewed each evaluation and discussed discrepancies or inconsistencies with the reviewers. Following this discussion, the senior reviewer and two initial reviewers came to a consensus on the determinations. In some cases, there remained insufficient information to enable determining whether a framework met a GP. For some of the frameworks, it was determined that a GP was outside of the purpose or scope of the framework, in which case a determination of not applicable was assigned.

### Table 2. Evaluation Determination Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fully met</td>
<td>●</td>
<td>The framework meets all components of NPC’s guiding practice</td>
</tr>
<tr>
<td>Partially met</td>
<td>◆</td>
<td>The framework meets some component of NPC’s guiding practice, but there are other components that are unknown or not met (include details in Rationale column)</td>
</tr>
<tr>
<td>Not met</td>
<td>○</td>
<td>Available information suggests that the framework does not meet the guiding practice</td>
</tr>
<tr>
<td>Cannot be determined</td>
<td>◊</td>
<td>Applies to the following scenarios:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The framework does not provide information related to this Guiding Practice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A component of the framework or assessment methodology is still under development</td>
</tr>
<tr>
<td>Not applicable</td>
<td>NA</td>
<td>The framework is not structured in a way that applies to the guiding practice (e.g., when a framework does not apply a cost threshold)</td>
</tr>
</tbody>
</table>

After these initial determinations, the draft findings were shared with representatives from each of the five organizations that developed the value assessment frameworks via conference calls held with each organization. The representative developers were asked to provide input on the evaluation findings, including providing further explanation about the purpose or scope of their frameworks, providing missing information that Lewin could not find in the available documentation, and citing instances where they disagreed with the findings or supporting rationale. This input was provided via the calls and follow-up communications. Lewin also interviewed experts in the field who are knowledgeable about value assessment and represent various stakeholders to provide more input and context to the analysis. The input from framework developers and these experts was considered and incorporated into the analysis.

### V. Findings

The following sections present the findings from our evaluation regarding the extent to which each of the five frameworks addresses or aligns with the NPC GPs in the six key areas of value
assessment: assessment process, methodology, benefits, costs, evidence, and dissemination and utilization. A table for each area of value assessment presents the relevant GP and our determinations relative to each GP. A full table of the evaluation results is available in the Appendix. More specific descriptions of the NPC GPs are available at http://www.npcnow.org/guidingpractices.

Given that these value assessment frameworks have somewhat differing purposes and emphasize different perspectives or target audiences, initial comparisons reflect important differences and analytic challenges. Among these are different assumptions, methodologies, inputs, and outputs of each framework that yield different types of results. These, in turn, have led to stakeholder recommendations for transparency and other improvements. For example, although some of the frameworks are designed to incorporate user preferences, the overall score or recommended price produced may be inconsistent with user preferences. Even where a framework is not intended for use by individual patients, they may be affected ultimately by framework findings.

**VI. Assessment Process**

The first key area of NPC’s GPs relates to the application of the value assessment framework. The GPs in this area focus on the selection and announcement of assessment topics in a transparent manner, the involvement of stakeholders throughout the assessment process, sufficiency of staff and resources to conduct the assessment, and inclusion of a pathway for assessments to be updated based on new evidence and information. Table 3 lists the six NPC GPs that cover this key area, and the extent to which each framework aligns with them.

**Table 3. Assessment Process**

<table>
<thead>
<tr>
<th>Guiding Practice</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>Drug Abacus</th>
<th>ICER</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP1</td>
<td>⊘</td>
<td>⊘</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Proposed assessment topic, process and timelines should be announced in advance to enable stakeholder participation and feedback.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP2</td>
<td>⊘</td>
<td>⊘</td>
<td>⊐</td>
<td>●</td>
<td>⊐</td>
</tr>
<tr>
<td>Interested stakeholders should be involved in the assessment process to represent all perspectives.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP3</td>
<td>⊘</td>
<td>⊘</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>The scope of an assessment should be defined a priori and incorporate stakeholder input.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP4</td>
<td>⊘</td>
<td>⊐</td>
<td>○</td>
<td>⊐</td>
<td>⊐</td>
</tr>
<tr>
<td>Public comment periods should be included, with sufficient time to review materials and submit comments, and with transparency around how comments are addressed by the convening body.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Guiding Practice | ACC-AHA | ASCO | Drug Abacus | ICER | NCCN
--- | --- | --- | --- | --- | ---
GP5 Assessments should be regularly reviewed and updated to keep pace with and account for medical innovation. There should be a continuous open process for stakeholders to request a timely review of an assessment to account for new technology or other changes in the evidence base. | ⊘ | ⊘ | ⊘ | ● | ●
GP6 Sufficient time, staff and resources should be dedicated to support a thorough and robust assessment process. | ⊘ | ⊘ | ⊘ | ● | ●

Neither ACC-AHA nor ASCO have performed a formal assessment or otherwise progressed to the point where most of these six GPs could be evaluated. GP4 is indicated as being partially met by ASCO. After publishing examples demonstrating how its framework would calculate NHB scores along with accompanying information about the proposed framework, ASCO conducted a public comment period. Although the public comment was sought for the proposed approach rather than for a particular assessment, ASCO did use input from those public comments to make revisions in the framework.

The other three frameworks, DrugAbacus, ICER, and NCCN, have very different assessment formats. DrugAbacus is an online tool that allows the user to conduct a real-time assessment, resulting in different outputs depending on user preference inputs. ICER and NCCN publish assessments that are publicly available online.

### A. DrugAbacus

DrugAbacus partially met two and did not meet three of the GPs. Alignment with one of the GPs could not be determined.

- GP1 was not met. For DrugAbacus, the assessment topic, process, and timeline comprised the developers’ selection of drugs and the incorporation of relevant data for those respective drugs into the web-based tool. There was no advance notice that specific drugs were being added to the website.
- DrugAbacus partially met GP2. The developers accept feedback and other input from stakeholders. DrugAbacus seeks feedback particularly on methodology (e.g., other domains that may affect the value of a drug). Feedback can be provided via a contact page on the website. The addition of two domains in the recent update to the tool responded to such feedback.
- GP3 was not met because the scope of the assessment tool was not defined a priori and did not incorporate stakeholder feedback.
- Similarly, GP4 was not met because there was no comment period during the development of the tool.
• GP5 cannot be determined. It is unclear whether data underlying the website will be regularly reviewed and updated. The developers indicated during an interview that the DrugAbacus methodology will be updated when new concepts or domains are identified, but the details that would pertain to GP5 are unknown at this time.

• GP6 was partially met; DrugAbacus is supported by a research group and receives grant funding that has enabled its work to date.

B. ICER

ICER’s assessment process fully met four of the six GPs, partially met one, and did not meet another.

• ICER conducts a horizon scan and gathers payer input to identify potential assessments and announces a proposed assessment topic on its website and via an email distribution list, fully meeting GP1.

• GP 2 was also fully met. To involve stakeholders, the organization reaches out to manufacturers involved in the assessment topic to obtain input prior to releasing a scoping document for the proposed topic. ICER convenes three groups (the California Technology Assessment Forum, the Midwest Comparative Effectiveness Public Advisory Council, and the New England Comparative Effectiveness Public Advisory Council) that are independent, regional bodies of practicing physicians, methodological experts, and patient advocates that provide input on clinical practice and payer policy decisions.

• The scoping document is posted to ICER’s website prior to conducting the assessment to allow for public comment, which fully meets the recommendations in GP3.

• Although the public is given the opportunity to provide written comments and oral comments, the timeframes for doing so may not be sufficiently long, making GP4 only partially met. ICER indicated recently that it has extended the public comment periods. Once a topic is announced, there is a three-week “open input” period for written public comments that are used to inform the scoping document. Once the draft scoping document is posted, there is another three-week period for written public comments. Once the draft evidence report and draft voting questions are posted, there is a third public comment period, which lasts for four weeks. Each public meeting also includes time for oral public comments.

• GP5 was not met. ICER makes clear that its assessments are largely one-time efforts, and that it does not plan to review and update assessments at regular intervals.

• Regarding resources for supporting their assessments, ICER has a multidisciplinary team of approximately 20 staff members, externally commissions its economic models, and collaborates with universities and health care systems. Also, ICER engages outside clinical topic experts in multiple steps in its process (though not as voting committee members). These aspects fully align with GP6.
C. NCCN

NCCN’s guidelines with Evidence Blocks fully met three of the six GPs and partially met three.

- NCCN fully met GP1 in that its assessment process begins with announcement of the guideline being developed.

- NCCN partially met GP2. Relevant clinical subspecialties are represented on the NCCN guidelines panels. At least one patient and/or patient advocate is included as a full member of each guidelines panel, whenever possible, and votes on the guidelines and corresponding Evidence Blocks. NCCN does not issue drafts for public comment. According to NCCN, this recognizes that NCCN’s guidelines are used for coverage determination and that the turnaround times for vetting and responding to drafts would delay coverage of therapies and other interventions.

- NCCN partially met GP3. The scope of NCCN’s guidelines is established in advance of their updating. According to NCCN, because its guidelines address the continuum of care of a disease, it is difficult to reach out to all the different potentially relevant stakeholder groups. However, NCCN does accept input from external stakeholders regarding important aspects of the guidelines to address.

- GP4 was partially met. NCCN does not have a defined public comment period but accepts input on an ongoing basis. NCCN has a formal process for external individuals or entities to submit data and request changes, and NCCN responds to all inquiries. Requests are published on the NCCN website along with a summary of the panel’s review of the request, discussion, and rationale for the panel’s response and its formal vote.

- NCCN has an established process for reviewing and updating its guidelines. All active NCCN guidelines are reviewed and updated at least annually, fully meeting GP5. NCCN guidelines are also updated on an ongoing basis in response to clinically important new evidence. Stakeholders can also request a review at any time.

- GP6 was also fully met. NCCN Guidelines are developed and updated by 48 individual multidisciplinary panels, comprising more than 1,150 clinicians and oncology researchers from NCCN’s 27 member institutions. NCCN has designated in-house staff to support the guidelines program.

VII. Methodology

The second key area of NPC’s GPs addresses the methodology for conducting value assessments. These GPs emphasize having a broad focus on all aspects of the health care system, basing methods on established health economic methodology, making methods and models transparent, using realistic base case assumptions, and performing sensitivity analyses that take stakeholder input into account. Table 4 presents GPs 7-12 and the extent to which each framework aligned with these GPs.
Table 4. Methodology

<table>
<thead>
<tr>
<th>Guiding Practice</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>Drug Abacus</th>
<th>ICER</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP7 Value assessments should focus broadly on all aspects of the health care system, not just on medications.</td>
<td>☒</td>
<td>☒</td>
<td>☒</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>GP8 Methods should be based on established health economic methodologies, consistent with accepted standards.</td>
<td>☒</td>
<td>☒</td>
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<td>☐</td>
<td>☒</td>
</tr>
<tr>
<td>GP9 Methods, models, and assumptions should be transparent and assessment results should be reproducible.</td>
<td>☒</td>
<td>☐</td>
<td>☒</td>
<td>☒</td>
<td>☐</td>
</tr>
<tr>
<td>GP10 Base case assumptions must represent reality.</td>
<td>☒</td>
<td>☒</td>
<td>☒</td>
<td>☒</td>
<td>☐</td>
</tr>
<tr>
<td>GP11 Sensitivity analyses should be performed, taking into account input from external stakeholders. Where sensitivity analyses result in material changes to the interpretation of the result, a focused discussion should be included.</td>
<td>☒</td>
<td>☒</td>
<td>☒</td>
<td>☒</td>
<td>☒</td>
</tr>
<tr>
<td>GP12 Weights should be included to accommodate varying user preferences.</td>
<td>☒</td>
<td>☒</td>
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<td>☒</td>
</tr>
</tbody>
</table>

Fully met ☒ | Partially met ☐ | Not met ☐ | Cannot be determined ☒ | Not applicable NA

A. ACC-AHA

ACC-AHA did not meet two of the GPs under methodology. Given that the framework is still being developed, alignment with the remaining four GPs could not be determined.

- ACC-AHA did not meet GP7. ACC-AHA’s focus is on cardiovascular treatments, primarily drugs, so it does not focus broadly on all aspects of the health care system.

- Alignment with GPs 8-11 could not be determined. The methodology is still being developed. ACC-AHA indicates that it intends to use established and accepted methods and to be transparent. ACC-AHA intends to consider evidence from cost-effectiveness studies in order to assess value. It is not apparent whether there will be a base case used in assessments. The proposed methodology did not include mention of sensitivity analyses.

- ACC-AHA did not meet GP12. The framework does not include weights or related means to accommodate user preferences. However, ACC-AHA recognizes that clinicians and patients will be seeking how to use the value assessment in their decision-making process. Given the gaps in the value evidence base, ACC-AHA is not yet prescriptive about how best to incorporate the value assessment when using guideline recommendations at the point of care.
B. ASCO

ASCO fully met one GP, partially met another GP, and did not meet the remaining four GPs related to methodology.

- ASCO’s framework did not meet GP7 because it focuses on cancer drug regimens, not other types of interventions or other aspects of the health care system.
- Because the NHB score calculated in ASCO’s framework is based on methodology developed by ASCO rather than an established methodology, the framework did not meet GP8.
- ASCO fully met GP9 in that it makes its framework methodology and scoring system publicly available, including for treatments used in the advanced disease setting and those used in the adjuvant setting.
- ASCO partially met GP10 in that base case assumptions will depend on the nature of the clinical trial or trials being used to assess a treatment and whether or not these trials include representative patients and subgroups for which the treatments are intended. That is, any given trial’s enrollees (other aspects of the trial’s clinical scenario) may represent reality for a comparable patient population or subgroup in the community, but may not be representative of others for whom the treatment may ultimately be delivered.
- GP11 was not met. In the clinical scenario examples that ASCO has published, data from single trials were used, and a sensitivity analysis was not performed as per GP11. However, ASCO has indicated that, when actual NHB calculations are performed using the framework, they plan to draw from the published literature and not necessarily rely on single clinical trials. It is possible that more than one trial may be appropriate to use in a given clinical scenario, and a sensitivity analysis would be performed.
- The ASCO framework did not meet GP12 because it does not currently offer the user the ability to apply different weights to different factors based on their preferences as per GP12. However, ASCO has indicated that the software application that it plans to develop will have categories that are scored and weights that users will be able to adjust to reflect their preferences.

C. DrugAbacus

DrugAbacus fully met one GP, partially met another GP, and did not meet three GPs. Alignment with one GP in this set could not be determined.

- The DrugAbacus tool only evaluates cancer drugs, so GP7 was not met.
- The methodology for this tool was newly developed, so GP8 was also not met.
- GP9 was partially met. The DrugAbacus equation used to calculate an Abacus price of a drug, and an explanation of the eight domains that are currently part of the equation, are provided on the DrugAbacus website. However, the programmed values for each domain, which are based on the clinical trial data and/or market profile for each drug, are not provided.
• Base case assumptions are not made available and these depend on the selection of clinical trial used, so GP10 could not be determined.

• DrugAbacus does not perform sensitivity analyses, so GP11 was not met.

• As the DrugAbacus tool allows users to weight their preferences, GP12 was fully met.

D. ICER

ICER fully met one, partially met four, and did not meet one of the GPs.

• ICER partially met GP7. In September 2015, ICER introduced its value assessment framework, the results of which are now part of its evidence reports. As of September 2016, ICER has incorporated value assessments into eight of its completed topics and has five assessments that are in process. While ICER does not limit itself to the review and assessment of pharmacological interventions, since introducing the framework, most of the assessments have focused on pharmacological interventions. Of the eight completed value assessments, five focused on drugs, one focused on a drug and a device, and two focused on non-drug interventions. Of the five in-process value assessments, all are focused on drugs. ICER has conducted evidence reports on various health care topics since 2008, including devices, surgical procedures, and delivery system innovations in addition to drugs for various diseases.

• GP8 was partially met because of ICER’s use of new methodology in addition to established methods.

• GP9 was partially met. Although ICER’s methodology is described, more information would be needed to fully reproduce ICER assessment results.

• ICER partially met GP10. ICER consults a variety of stakeholders to help identify representative base case assumptions. ICER uses systematic reviews and meta-analyses to inform their model inputs. Before starting a model, ICER works with its model developers to discuss the most important inputs for the model and what inputs other relevant models and publications use. However, ICER’s assumptions about uptake rates of interventions do not necessarily reflect reality. According to ICER these are not estimates of actual uptake rates; they are intended to project scenarios in which an uptake rate would reach a level that may cause concern or alarm about budget impact for a user. Also, these rates are projecting “unmanaged” utilization, which is unlikely to reflect real conditions.

• ICER fully met GP11 in that it conducts sensitivity analyses around key assumptions.

• ICER did not meet the GP12 related to user weights because the value assessment is not adjustable to accommodate individual preferences. However, ICER generates prices for drugs that would achieve willingness-to-pay thresholds at each of $50,000, $100,000, and $150,000 per QALY gained, which users can consider in comparison to market prices. Similarly, ICER’s value graphs enable users to examine projected budget impacts based on those willingness-to-pay thresholds and a range of percent of eligible patient treated (e.g., uptake rates of 25%, 50%, and 75%).
E. NCCN

NCCN partially met three of the six GPs in the key area of methodology and did not meet the other three GPs.

- NCCN did not meet GP7 in that its guidelines with Evidence Blocks have focused on drug regimens. NCCN plans to extend the use of Evidence Blocks to radiology and surgery treatments.

- GP8 was not met. NCCN does not conduct formal economic analyses, but the Evidence Blocks include the domain of affordability of drugs. Panel members vote on the affordability of drug regimens based on an "educated estimate" of the total costs from a domain expert. Affordability is intended to account for the overall total cost of a therapy, including drug acquisition, administration, in-patient vs. out-patient care, supportive care, infusions, toxicity monitoring, antiemetics and growth factors, and potential for hospitalization.

- GP9 was partially met. The methods for NCCN’s guidelines with Evidence Blocks are publicly available. However, results are not reproducible since the Evidence Block scores represent the average of panel members' individual subjective scores. NCCN's methods involve expert's judgement, which is based on their experience with cancer patients in various real world settings.

- GP10 was partially met in that whether base case assumptions are realistic and accurate depends on the nature of the available evidence and whether it includes representative patients and subgroups for which the treatments are intended.

- GP11 was not met, as NCCN does not perform sensitivity analyses.

- GP12 was partially met. NCCN does not include weights for patient preferences. However, the NCCN Evidence Blocks offer a visual representation of five domains, some or all of which could be of interest to individual patients that could potentially serve as a basis for discussing therapeutic options and patient preferences.

VIII. Benefits

The third key area of the NPC GPs addresses the benefits of the health care product or service being assessed. This set of three GPs focuses on using a broad array of factors that are important to patients and society, incorporating clinical benefits and harms in a way that recognizes heterogeneity, and use of a long-term time horizon. Table 5 presents GPs 13-15 related to benefits and whether each framework aligned with these GPs.
Table 5. Benefits

<table>
<thead>
<tr>
<th>Guiding Practice</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>Drug Abacus</th>
<th>ICER</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP13</td>
<td>⊘</td>
<td>⊘</td>
<td>⊘</td>
<td>⊘</td>
<td>⊘</td>
</tr>
<tr>
<td>GP14</td>
<td>⊘</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>GP15</td>
<td>⊘</td>
<td>○</td>
<td>⊘</td>
<td>⊘</td>
<td>●</td>
</tr>
</tbody>
</table>

Fully met ● | Partially met ○ | Not met ⊘ | Cannot be determined ⊘ | Not applicable NA

A. ACC-AHA

Alignment with all three GPs within the benefits domain could not be determined at this point in time given that ACC-AHA is still developing its tool. It appears that the measurement of value will account for the magnitude of benefit and cost-effectiveness to the extent that these data are available from high-quality health economic studies. ACC-AHA indicated that an area of uncertainty is how quality of life should be incorporated into value assessment. ACC-AHA also recognizes the need to address heterogeneity of treatment effect and the potential lack of data on how value may differ across subgroups.

B. ASCO

ASCO’s framework partially met two and did not meet one of the GPs in the area of benefits.

- The ASCO framework partially met GP13 in that it includes improvement in overall survival, progression-free survival, and response rate, and gives bonus points for palliation and treatment-free interval. However, at present, ASCO does not account for other outcomes and factors such as patient-centric metrics, indirect benefits, unmet need, burden of illness, credit for innovation, or development costs.

- GP14 was not met. ASCOs’ framework does not address heterogeneity of treatment effect in the scenario examples that ASCO used to test the framework; the examples given were all based on single trials that were not designed to be broadly representative. To the extent that future applications of the ASCO framework consider a broader evidence base when assessing a treatment, data on the differences in treatment effect may be available.

- ASCO partially met GP15. In the examples provided by ASCO, the time horizon depended on the endpoint assessed in the relevant clinical trial. ASCO has indicated that when long-term data are available and published for a treatment, these data will be incorporated into the tool and will influence the treatment’s NHB accordingly.
C. DrugAbacus

DrugAbacus fully met one GP, partially met one GP, and did not meet one GP.

- DrugAbacus includes measures of efficacy and safety (improvement in overall survival or surrogate), safety/risk (frequency and severity of side effects relative to the side effects that would otherwise be expected), unmet need, burden of illness, credit for innovation, and development costs. It does not include patient-centric metrics such as quality of life and indirect benefits such as productivity, so GP13 was partially met.

- GP14 was not met. Information on the clinical benefits and harms of the drugs included in the tool come from the clinical trials conducted to obtain FDA approval of the drugs. Many such trials are not designed or analyzed for subgroup analyses and are likely representative of average treatment response. To the extent such data were available for different subgroups, it is not apparent whether those data are reflected in the tool.

- DrugAbacus fully met GP15. DrugAbacus focused on and prioritized the endpoint of improvement in overall survival attributable to a drug from the clinical trial that led to FDA-approval for the first indication of the drug. DrugAbacus notes that in some cases, drugs are approved by the FDA without evidence of an overall survival gain, on the basis of an improvement in either progression-free survival or in response rates. For these drugs, DrugAbacus considered the margin of gain in progression free survival as a surrogate endpoint for gain in overall survival but assigned it a lower level of evidence rating. When other endpoints (e.g., response rates or single-arm trial endpoints) were all that were available, DrugAbacus converted them to estimates of overall survival benefit using available literature from studies of analogous treatments.

D. ICER

ICER fully met the three GPs related to the benefits of the health care product or service being assessed.

- ICER fully met GP13 in that their reports include a section on “other benefits and disadvantages” as well as a section on “contextual considerations,” which are discussed and considered qualitatively as part of the determination of care value by ICER’s advisory panels. The breadth of factors included by ICER for any given assessment may vary by clinical condition, intervention, and availability of relevant data.

- GP14 was considered fully met because ICER addresses findings from subgroup analyses in its evidence reports when relevant data are presented in the available evidence base (e.g., as in ICER reports for asthma and obeticholic acid).

- GP15 was also considered fully met. ICER’s determination of time horizons for value varies by clinical condition but generally long-term or lifetime time horizons are incorporated into the care value assessment when relevant data are presented in the available evidence base.
E. NCCN

NCCN’s guidelines with Evidence Blocks fully met one GP, partially met one GP and did not meet one GP in the value area of benefits.

- NCCN partially met GP13. NCCN’s Evidence Blocks focus on the efficacy of treatments, including improving survival, arresting disease progression, and reducing symptoms, but do not address such areas as QoL or loss in productivity.
- NCCN did not meet GP14. NCCN’s Evidence Blocks do not address heterogeneity of treatment effects. NCCN has indicated that, just as there are decision points in the guidelines that require clinicians to have discussions with their patients, the Evidence Blocks provide a basis for the discussion of factors that may affect a patient’s response to various treatment options.
- NCCN fully met GP15 in that the time horizon considered will vary with disease site and stage and the available evidence on overall survival, progression-free survival, response rates, etc.

IX. Costs

The fourth key aspect of the NPC GPs pertains to how cost is incorporated into value assessment. This section focuses on including all costs and cost offsets, using a time horizon that is long enough to incorporate benefits of treatment and costs of generics, representing costs that are most relevant to the user, and developing thresholds in a transparent manner. Table 6 presents GPs 16-19 and the extent to which each framework aligned with these GPs.

<table>
<thead>
<tr>
<th>Guiding Practice</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>Drug Abacus</th>
<th>ICER</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP16 All health care costs and cost offsets should be included.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>●</td>
<td>☐</td>
</tr>
<tr>
<td>GP17 The time horizon for costs should be long enough to incorporate the benefits of the treatment and the lower costs of medications when they become generic.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>●</td>
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</tr>
<tr>
<td>GP18 Costs should be representative of the net price most relevant to the user.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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</tr>
<tr>
<td>GP19 Thresholds should be developed in a transparent manner, may vary by population and disease, and should undergo a multi-stakeholder evaluation process.</td>
<td>☐</td>
<td>NA</td>
<td>NA</td>
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<td>NA</td>
</tr>
</tbody>
</table>

Fully met ● | Partially met ○ | Not met ○ | Cannot be determined ☐ | Not applicable NA
A. ACC-AHA

ACC-AHA partially met two GPs in the value area of costs. Alignment with two GPs could not be determined.

- ACC-AHA partially met GP16. The proposed methodology considers cost information from relevant health economic literature, including medical cost offsets.
- GP17 and GP18 could not be determined due to a lack of available information.
- GP19 was partially met. ACC-AHA defined high, intermediate, and low value according to the WHO-CHOICE project, which provides a framework for cost-effectiveness thresholds based in part on national GDP that can be applied globally to a wide range of health interventions. ACC-AHA has acknowledged that these thresholds may need modification as additional information becomes available or different national consensus standards for value-based thresholds are developed.

B. ASCO

The ASCO framework did not meet two of the GPs in the cost domain. Additionally, alignment with one of the GPs could not be determined, and one GP was not applicable to the ASCO framework.

- The ASCO framework did not meet GP16 because cost offsets and costs beyond drugs are not included. The framework only includes drug acquisition cost. ASCO plans to develop a user-friendly software tool to enable its value framework to be used by clinicians and patients to support patient-centered decision making. Once the tool is developed, ASCO anticipates that the drug cost element of its framework may prompt discussion of a patient’s copayment and any implications for therapeutic options.
- The framework’s alignment with GP17 could not be determined because the time horizon for costs will depend on how the individual assessments are conducted and the nature of available data. ASCO has indicated that this will only be determined by the particular condition and the available evidence used regarding overall survival, progression-free survival over time, and reduced need for medical interventions as a result of improved survival. This concern is juxtaposed against the specific ASCO intent to enable a patient to understand the expected short- or long-term benefits and toxicities of a therapy, and what they will have to pay for it out of pocket.
- GP18 was not met. ASCO has indicated that patient copayments will have to be determined at the point of service, perhaps with assistance from appropriately qualified staff, noting that the great diversity in health insurance plans and individual patient circumstances makes it impractical to approach this GP in a systematic way.
- ASCO does not set a threshold related to costs, so GP19 is considered not applicable to ASCO’s value assessment framework.

C. DrugAbacus

DrugAbacus did not meet three GPs in this set, and one GP was not applicable.
• Since DrugAbacus only includes drug costs (as paid by Medicare), as a comparator to the Abacus prices, and does not include cost offsets, GP16 was not met.

• GP17 was not met. Developers of DrugAbacus do not intend to incorporate cost offsets in the manner contemplated for GP17. They indicate that such an approach has drawbacks, including that it cannot be applied consistently across drugs because some clearly useful drugs may not lead to cost savings; most interventions that extend life increase lifetime spending because patients will require more health care; and it mistakenly assumes that savings themselves are correctly priced.12

• The tool only includes actual costs to Medicare, as a comparator. Therefore, GP18 was not met.

• GP19 is not applicable because DrugAbacus does not set a threshold.

D. ICER

ICER fully met two GPs, partially met one GP, and did not meet one GP in the cost domain.

• ICER fully met GP 16. Cost offsets are considered in a qualitative manner as part of the care value determination by ICER’s advisory panels. The BIA considers the difference in drug costs between a new drug and standard of care as well as the potential impact of the drug on hospitalization, doctor visits, tests, and other aspects as part of its weighted budget impact.

• GP17 was fully met. ICER’s determination of time horizons for value varies by clinical condition but generally long-term or lifetime time horizons are incorporated into the care value assessment, which includes determining cost-effectiveness, when relevant data are presented in the available evidence base.

• ICER’s framework did not meet GP18 because it uses Medicare fee schedules and drug list prices, which rarely correspond to the actual market price.

• GP19 was partially met. ICER has two types of thresholds: one set of thresholds is for the care value and one set is for potential budget impact. For care value, ICER provides three cost-per QALY gained ranges of cost-effectiveness that align to similar thresholds in the literature: <$100,000; $100,000-$150,000; and >$150,000 per QALY gained); these do not vary by population or disease. For BIAs, ICER presents potential affordability thresholds that are not variable by population or condition. ICER noted that the use of such thresholds is intended to provide an objective basis for allocation of limited resources. Both types of thresholds were based on transparent approaches. They were not subject to a multi-stakeholder evaluation process, although ICER has an open national process for comments and suggested revisions of its methodology in general.

E. NCCN

NCCN did not meet three of the GPs pertaining to costs. One GP was not applicable to NCCN.

GP16 was not met. As noted above, NCCN’s Evidence Block for affordability takes into account an “educated estimate” by a guideline panel of the overall total cost of a therapy, including drug acquisition, administration, in-patient vs. out-patient care, supportive care, infusions, toxicity monitoring, antiemetics and growth factors, and potential for hospitalization. The affordability measurement does not include indirect costs (e.g., transportation, time lost from work) or potential cost offsets as a result of use of the therapy.

Similarly, GP17 was not met because NCCN only considers total costs of a therapy and does not consider any potential cost offsets.

GP 18 was not met because NCCN does not address direct costs to patients, as these costs vary widely based on individual circumstances. NCCN notes that a low score for the affordability domain should prompt a discussion between the clinician and the patient about the anticipated direct costs to a patient of therapeutic options.

GP19 was not applicable because NCCN does not set a threshold.

X. Evidence

The next aspect of GPs pertains to the evidence used in a value assessment. This section focuses on identifying evidence in a systematic and transparent manner, giving stakeholders an opportunity to submit relevant evidence, using best available evidence, assessing quality of evidence using accepted methods, conducting formal analysis where evidence synthesis is warranted, and using subjective evidence minimally and transparently. Table 7 presents GPs 20-25 and the extent to which each framework aligned with these GPs.

<table>
<thead>
<tr>
<th>Guiding Practice</th>
<th>ACC-AHA</th>
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<th>Drug Abacus</th>
<th>ICER</th>
<th>NCCN</th>
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</thead>
<tbody>
<tr>
<td>GP20</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Evidence should be identified in a systematic, transparent and robust manner.</td>
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<tr>
<td>GP21</td>
<td>○</td>
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<tr>
<td>Stakeholders should be given the opportunity to submit relevant evidence, such as clinical trial and real-world evidence beyond the published literature.</td>
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<tr>
<td>GP22</td>
<td>●</td>
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<td>●</td>
<td>●</td>
<td>●</td>
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<tr>
<td>Best available evidence should be used for the assessment.</td>
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<tr>
<td>GP23</td>
<td>●</td>
<td>☐</td>
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<td>●</td>
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</tr>
<tr>
<td>Accepted methods should be used to assess quality of evidence, certainty of evidence and conflicting evidence.</td>
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<tr>
<td>GP24</td>
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<td>●</td>
<td>☐</td>
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<tr>
<td>Where evidence synthesis is warranted, formal analysis should be conducted, in accordance with accepted methodologies.</td>
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<td></td>
</tr>
<tr>
<td>GP25</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>Subjective evidence should be used minimally, if at all, and its inclusion should be clearly labeled.</td>
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</tbody>
</table>

Fully met ● | Partially met ○ | Not met ○ | Cannot be determined ☐ | Not applicable NA
A. ACC-AHA

ACC-AHA fully met five GPs and did not meet one GP in the evidence domain,

- ACC-AHA met GP20 in that its proposed methodology includes a search for health economic studies in addition to clinical effectiveness studies.
- ACC-AHA did not meet GP21, as there is no provision for ACC-AHA to accept stakeholder evidence.
- ACC-AHA met GP22. Development of the guidelines includes a systematic review of clinical effectiveness studies, which ACC-AHA intends to expand to include relevant health economic studies.
- ACC-AHA met GP23 and GP24. ACC-AHA already has a method for evaluating clinical effectiveness evidence for its clinical practice guidelines and plans to use a validated tool such as the Quality of Health Economic Studies (QHES) tool for evaluating the quality of health economic studies.
- GP25 was also met. ACA-AHA does not accept non-published evidence but may use subjective evidence (expert opinion). ACC-AHA makes it clear when subjective evidence is used.

B. ASCO

The ASCO value assessment framework fully met one of the GPs and did not meet three of the GPs pertaining to evidence. A determination could not be made for two of the GPs.

- As noted above, the clinical scenario examples that ASCO used to test its framework relied on single clinical trials. The identification of evidence, including whether stakeholders would be able to submit evidence, was not further described. Therefore neither GP20 nor GP 21 was met.
- GP 22, which focuses on the use of best evidence, was not met. ASCO has relied on single randomized clinical trials (RCTs) for its examples to date. ASCO has indicated that, when its software tool becomes available, it will be curated with the relevant RCTs for a given clinical indicator.
- Concerning GP23 and the need for accepted methods to assess evidence, ASCO has indicated that it anticipates establishing a level-of-evidence approach for the framework. For now, GP23 cannot be determined.
- Similarly, GP24 cannot be determined, as ASCO has indicated that it anticipates the need for accepted methods to synthesize and analyze the evidence from multiple trials.
- As the ASCO framework does not rely on subjective evidence, GP25 was fully met.

C. DrugAbacus

DrugAbacus partially met three GPs and did not meet three GPs in the key area of evidence.

- GP20 was partially met. DrugAbacus uses the evidence that supported FDA approval for each drug. The developers indicated that the tool draws from research conducted by
senior staff members on pricing of anti-cancer drugs and the database they developed. The DrugAbacus website refers to a paper published by Howard et al., although a full citation is not given.13

- The tool does not provide for stakeholders to submit evidence, and it is unclear whether newer or better evidence is included if it is available. As such, GP21 is not met.
- GP22 was partially met because DrugAbacus uses data from the FDA-approved first indication for included drugs, but it is not apparent whether newer or better evidence will be included once it becomes available.
- GP23 was not met because the quality of, certainty of, and conflicting evidence are not assessed.
- GP24 was not met, as no evidence synthesis is conducted.
- Although DrugAbacus relies primarily on clinical trial evidence, the developers indicated that some expert opinion is used. Since it is not transparent when and how expert opinion is applied, GP25 is considered partially met.

D. ICER

ICER fully met all of the GPs related to evidence.

- ICER fully met GP20. Evidence is identified in a systematic and transparent manner, and the evidence reviews are published with ICER reports.
- GP21 was fully met. ICER accepts manufacturer-submitted data and public data as well as other grey literature. (Evidence accepted from stakeholders is not necessarily incorporated into assessments.)
- GP22 was fully met in that ICER uses standard systematic review methods to identify best available evidence from peer-reviewed literature; it draws on grey literature only when it meets certain pre-specified criteria.
- GP23 and GP24 were fully met in that ICER uses accepted methods for assessing evidence quality, certainty, and conflicts as well as conducting systematic reviews and meta-analyses (including, e.g., ICER’s evidence rating matrix for level of evidence certainty and comparative net benefit, which closely resembles approaches used by well-recognized evidence appraisal programs).
- ICER also fully met GP25. ICER assessments rely largely on objective evidence; however, expert opinion and other subjective evidence are incorporated at specified stages of the value assessment by public deliberation panels. Also, ICER includes grey literature only when it meets certain criteria and provides a rational for the inclusion of it.

E. NCCN

NCCN fully met three GPs and partially met three GPs in the key area of evidence.

- GP20 was fully met. The Evidence Blocks for the quality and constancy of the evidence are based on the evidence review conducted to inform the development of the corresponding clinical practice guideline.

- GP21 was fully met. NCCN accepts externally submitted data and will consider non-published evidence from external sources.

- GP22 was fully met. NCCN uses a broad range of available evidence, including meta-analyses, RCTs, other clinical trials, and case reports. Its panel members contribute knowledge of the published data and draw from their clinical experience with patients in real-world settings.

- GP23 was partially met. Due in part to the frequency with which NCCN updates its guidelines, NCCN does not conduct or sponsor its own systematic reviews, and its examination of evidence quality does not appear to be as systematic as some other widely used evidence appraisal methods that examine the quality and related methodological attributes of individual studies and bodies of evidence. Nevertheless, the NCCN guidelines that are based on its methods are widely accepted for informing policies of federal and state agency payers, commercial payers, health care systems, and other users. The Evidence Blocks are a relatively new component of NCCN’s guidelines, and although the general methods and definitions of their domains are provided, there is less transparency about how the guideline content is translated into the scores for the Evidence Blocks, including for the quality and consistency of evidence. NCCN does provide comprehensive listings of all of its references, including from the published and grey literature.

- GP24 was partially met. NCCN does not conduct or sponsor formal evidence synthesis methods such as systematic reviews or meta-analyses. However, it does provide narrative reviews of the scientific and clinical rationale for its recommendations. This information provides the basis for the Evidence Blocks.

- GP25 was partially met. NCCN Evidence Block scores are based on an average of panel members’ individual scores for different domains. Panel members rely on both their knowledge of the published data and evidence cited in the NCCN guidelines and their clinical experience with the treatments in the real-world patient population. NCCN Evidence Block scores are accompanied by definitions that help to identify when subjective evidence or expert opinion are used, e.g., “case reports or clinical experience only” for an evidence quality block score of 2, and “anecdotal evidence only” for an evidence consistency block score of 1.

XI. Dissemination and Utilization

The final aspect of the NPC GPs pertains to the dissemination and utilization of value assessments. This section focuses on presenting assessment results in a way that enables users to interpret and apply them, clarifying the intended use and audience to avoid misuse, and issuing
press releases only for final assessments. Table 8 presents GP26-28 and the extent to which each framework aligned with these GPs.

### Table 8. Dissemination and Utilization

<table>
<thead>
<tr>
<th>Guiding Practice</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>Drug Abacus</th>
<th>ICER</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP26 Assessment results should be presented in a manner that is simple for the user to interpret and apply.</td>
<td>◇</td>
<td>◇</td>
<td>◇</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>GP27 Value assessment should clearly state the intended use and audience to avoid misuse.</td>
<td>●</td>
<td>●</td>
<td>◇</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>GP28 Press releases should only be issued for final assessments, include limitations of the assessment, and highlight areas where sensitivity analyses result in material changes to the interpretation of the results.</td>
<td>◇</td>
<td>◇</td>
<td>NA</td>
<td>○</td>
<td>●</td>
</tr>
</tbody>
</table>

Fully met ● | Partially met ◇ | Not met ○ | Cannot be determined ⊗ | Not applicable NA

### A. ACC-AHA

ACC-AHA fully met one GP in the area of utilization and dissemination. Alignment with two of the GPs could not be determined.

- Given that ACC-AHA is still developing its framework and has yet to conduct a formal assessment, the alignment with GPs on presentation of assessment results (GP26) and press releases (GP28) cannot be determined.

- GP27 was fully met. ACC-AHA indicates that, by incorporating its value assessments, the ACC-AHA clinical practice guidelines and performance measures will enhance the ability of clinicians, patients, and payers to consider how best to generate the best outcomes in the context of limited health care resources.

### B. ASCO

ASCO’s value assessment framework fully met one and partially met one of the GPs related to dissemination and utilization. Alignment with one of the GPs could not be determined.

- GP26 was partially met. Based on the examples of clinical scenarios to which ASCO has applied its framework and the corresponding worksheets provided in ASCO publications, the assessment results were clearly presented. However, interpretation of the NHB may be difficult for patients to understand and apply to their preferences or decisions without some guidance. Also, drug acquisition costs presented in the examples are of limited utility to patients. It is not yet known whether the software application tool will provide more patient support once patients have the ability to modify weights attributed to any of the elements in the NHB according to their personal preferences.

- The framework fully met GP27 in that the intended use and audience (physicians and patients) are transparent.
A determination could not be made for GP28, as only examples of assessments have been released thus far and the software application tool for the ASCO framework has not yet been developed. ASCO did release a notice prior to releasing version 2.0 of its framework.

C. DrugAbacus

DrugAbacus partially met two GPs; the third GP was not applicable to the tool.

- GP26 was partially met. Although DrugAbacus is an online tool with a generally intuitive graphical user interface, the ability of users to interpret and apply the results is likely to be highly variable, even for some policymakers and payers.

- GP27 was partially met. The website indicates that DrugAbacus is a “draft of a tool that could be used to determine appropriate prices for cancer drugs based on what experts tend to list as possible components of a drug’s value,” and lists ways in which the tool should not be used. However, it does not explicitly state the intended audience, referring only to “users.” During an interview, the developer described DrugAbacus as primarily a research tool meant to explore and test different domains or factors that could affect a drug’s value. The developer indicated that the targeted primary audience would tend to be more knowledgeable regarding these domains/factors, such as policymakers and industry. The terms & conditions accompanying DrugAbacus note that it should not be used as a substitute for medical advice or care or as a substitute for pharmacoeconomic or clinical efficacy assessment, and that users should not rely on it for decisions about pricing, insurance coverage, forecasting, or benefits or harms of drugs.

- GP28 was not applicable because DrugAbacus is designed for online user-conducted value assessments, the results of which vary by user, and there is not a formal assessment process that would use press releases to announce results.

D. ICER

ICER fully met two GPs and did not meet one GP related to dissemination and utilization.

- GPs 26 and 27 were met. ICER publishes assessment results on a user-friendly website and clearly states the intended uses and audiences.

- GP28 was not met, although this is by design. ICER issues press releases when draft assessments are posted for public comment and when final assessments are completed. ICER has indicated that calling public attention to its draft assessments is intended to encourage stakeholder input and feedback toward a better-informed final assessment. In its reports, ICER does note certain limitations affecting its findings, such as limitations in the available evidence for comparing the net health benefits of alternative interventions.

E. NCCN

NCCN fully met two GPs and partially met one GP related to dissemination and utilization.

- GP26 was partially met. Although the visual representation of the Evidence Blocks is straightforward, the accompanying criteria in the user guide may be vague for some users. Also, there are no criteria for the affordability Evidence Block (e.g., dollar ranges).
According to NCCN, as with the other Evidence Blocks, the affordability Evidence Block is intended to prompt conversations between clinicians and patients, recognizing that affordability for each patient may differ (e.g., subject to insurance coverage).

- GP27 was fully met. NCCN states that its intended audience is all users of NCCN guidelines, including clinicians and patients, as well as other stakeholders involved in the treatment decision-making process.

- GP28 is fully met. NCCN does not issue draft press releases for its guidelines and accompanying Evidence Blocks, but it issues press releases for the final products.

XII. Budget Impact Assessment

In addition to the 28 GPs on value assessments, NPC has provided seven GPs for budget impact assessments (BIAs). NPC notes that BIA is a measure of resource use, not a measure of value. This section is focused on: examining all aspects of the health care system, separating BIAs from value assessments, including timeframes long enough to incorporate benefits of the innovation and lower costs of generic medications, using realistic estimates regarding uptake rates, incorporating sensitivity analyses to acknowledge uncertainty in the inputs, avoiding artificial affordability caps, and including relevant stakeholders to address budget impact concerns.

Table 9. Budget Impact Assessment

<table>
<thead>
<tr>
<th>Budget Impact Assessment Guiding Practice</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIA1 Budget impact assessments should examine all aspects of the health care system, not just medications.</td>
<td>●</td>
</tr>
<tr>
<td>BIA2 Budget impact assessments should be separate from value assessments.</td>
<td>●</td>
</tr>
<tr>
<td>BIA3 Budget impact assessments should include time frames that are long enough to incorporate the benefits of the innovation and the lower costs of medications when they become generic.</td>
<td>●</td>
</tr>
<tr>
<td>BIA4 Budget impact assessments should include realistic estimates regarding the uptake rate. Stakeholders may have done extensive assessments of potential uptake and should be given the opportunity to submit their results. A sensitivity analysis of different uptake rates should be conducted.</td>
<td>○</td>
</tr>
<tr>
<td>BIA5 Budget impact assessments should acknowledge the considerable uncertainty in the inputs by incorporating sensitivity analyses and reporting ranges around estimates.</td>
<td>●</td>
</tr>
<tr>
<td>BIA6 A BIA is simply an assessment of budget impact, and should not be judged against artificial affordability caps.</td>
<td>○</td>
</tr>
<tr>
<td>BIA7 Assessments of ways to address budget impact concerns should include all relevant stakeholders and consider all approaches.</td>
<td>○</td>
</tr>
</tbody>
</table>

ICER is the only framework of the five examined in our analysis that currently includes BIA. In the BIA domain, ICER fully met two GPs, partially met three, and did not meet two.

- BIA1 was fully met. According to ICER, the BIA compares net change in total health care costs over a five-year timeframe of the new drug compared to the current standard
drug being used to treat the condition. ICER has stated that net change in total health care costs includes not only the difference in drug costs but also the potential impact of the use of the drug on hospitalizations, doctor visits, tests, and other aspects as part of its weighted budget impact. For example, in its assessment of treatments for opioid addiction, ICER included cost savings from decreased emergency department visits.

- **BIA2** was partially met. The long-term care value determination and the short-term BIA are two components of ICER’s value assessment that are determined separately, and users can consider them as such. In assessing the potential short-term budget impact of a new treatment, ICER assigns one of four potential uptake patterns based on condition/market, ranging from a low of 10% over five years to the high uptake rate of 75% over five years, all in an unmanaged environment. ICER does not intend these uptake rates to be estimates or projections of anticipated actual uptake rates. ICER also determines value-based price benchmarks, which draw on the care value and short-term budget impact. Although ICER states that the value-based price benchmarks are not a formal part of its value assessment framework and are not intended to be viewed as caps, they are presented in ICER’s reports and have the potential to be misinterpreted by users if users are not able to discern and understand the care value and budget impact assumptions and determination on which these benchmarks are based. ICER is aware that the term “provisional health system value,” which ICER uses in relation to these benchmarks, may also not be the most clear terminology and is soliciting feedback on this term and other terminology ICER has used, as part of ICER’s recent national call for feedback on improvements to the framework.

- **BIA3** was partially met. ICER does not consider budget impact beyond five years, reasoning that payers and some other stakeholders place greater (or even all) weight or emphasis on shorter-term budget impact. For some diseases or conditions, five years may suffice for accruing virtually all of the benefits and costs associated with medications.

- **BIA4** was not met. ICER uses a wide range of uptake rates. ICER states that it does not seek to project realistic estimates of uptake rates; rather, it identifies potential uptake rates at which interventions with certain prices would generate budget impacts that may be of significant concern to particular users. According to ICER, it is developing a revised approach to BIA for its 2017 update of the framework, which it is considering and vetting with a multi-stakeholder group that would address concerns about the need for more realistic estimates for uptake rates.

- **BIA5** was fully met. Although not labeled as sensitivity analyses, ICER provides an integrated value graph that allows users to examine how varying their assumptions about the main inputs of price, acceptable levels of cost effectiveness, and uptake rates would affect estimated budget impact.

- **BIA6** was not met because ICER uses an affordability cap (based in part on a function of gross domestic product).

- **BIA7** was partially met. Although each manufacturer involved in the review of a treatment being assessed by ICER is offered time to speak during the oral public comment period of the public meeting, they are part of the policy roundtable discussion only if ICER formally invites them to participate in the discussion by ICER. The policy
roundtable discussion is the part of the public meeting during which issues, including budget impact concerns, are discussed. ICER indicated that it is considering how to accommodate the manufacturer perspective in the roundtable discussion when the review involves multiple manufacturers.

XIII. Summary of Findings

Table 10 presents the evaluation of each framework by each key area of value and presents the determinations for each organization across the 28 GPs.

### Table 10. Overall Alignment with GPs

<table>
<thead>
<tr>
<th>Guiding Practice</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>Drug Abacus</th>
<th>ICER</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assessment Process</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP1 Proposed assessment topic, process and timelines should be announced in advance to enable stakeholder participation and feedback.</td>
<td>◊</td>
<td>◊</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>GP2 Interested stakeholders should be involved in the assessment process to represent all perspectives.</td>
<td>◊</td>
<td>◊</td>
<td>○</td>
<td>●</td>
<td>◐</td>
</tr>
<tr>
<td>GP3 The scope of an assessment should be defined a priori and incorporate stakeholder input.</td>
<td>◊</td>
<td>◊</td>
<td>○</td>
<td>●</td>
<td>◐</td>
</tr>
<tr>
<td>GP4 Public comment periods should be included, with sufficient time to review materials and submit comments, and with transparency around how comments are addressed by the convening body.</td>
<td>◊</td>
<td>◐</td>
<td>○</td>
<td>◐</td>
<td>◐</td>
</tr>
<tr>
<td>GP5 Assessments should be regularly reviewed and updated to keep pace with and account for medical innovation. There should be a continuous open process for stakeholders to request a timely review of an assessment to account for new technology or other changes in the evidence base.</td>
<td>◊</td>
<td>◊</td>
<td>○</td>
<td>◐</td>
<td>●</td>
</tr>
<tr>
<td>GP6 Sufficient time, staff and resources should be dedicated to support a thorough and robust assessment process.</td>
<td>◊</td>
<td>◊</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td><strong>Methodology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP7 Value assessments should focus broadly on all aspects of the health care system, not just on medications.</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>◐</td>
<td>○</td>
</tr>
<tr>
<td>GP8 Methods should be based on established health economic methodologies, consistent with accepted standards.</td>
<td>◊</td>
<td>◐</td>
<td>○</td>
<td>◐</td>
<td>○</td>
</tr>
<tr>
<td>GP9 Methods, models, and assumptions should be transparent and assessment results should be reproducible.</td>
<td>◊</td>
<td>●</td>
<td>◐</td>
<td>◐</td>
<td>◐</td>
</tr>
</tbody>
</table>
### Comparison of Value Assessment Frameworks Using the NPC Guiding Practices

<table>
<thead>
<tr>
<th>Guiding Practice</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>Drug Abacus</th>
<th>ICER</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP10</td>
<td>⊗</td>
<td>◐</td>
<td>⊗</td>
<td>⊗</td>
<td>⊗</td>
</tr>
<tr>
<td>Sensitivity analyses should be performed, taking into account input from external stakeholders. Where sensitivity analyses result in material changes to the interpretation of the result, a focused discussion should be included.</td>
<td>⊗</td>
<td>◐</td>
<td>⊗</td>
<td>●</td>
<td>⊗</td>
</tr>
<tr>
<td>GP11</td>
<td>◐</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>Weights should be included to accommodate varying user preferences.</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>○</td>
<td>⊗</td>
</tr>
<tr>
<td>Benefits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP13</td>
<td>⊗</td>
<td>◐</td>
<td>⊗</td>
<td>●</td>
<td>⊗</td>
</tr>
<tr>
<td>The measurement of value should include a broad array of factors that are important to patients and society.</td>
<td>⊗</td>
<td>◐</td>
<td>⊗</td>
<td>●</td>
<td>⊗</td>
</tr>
<tr>
<td>GP14</td>
<td>⊗</td>
<td>◐</td>
<td>○</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>Clinical benefits and harms should be incorporated in a manner that recognizes the heterogeneity of treatment effect rather than the average response.</td>
<td>⊗</td>
<td>◐</td>
<td>○</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>GP15</td>
<td>⊗</td>
<td>◐</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>The time horizon for value should be long-term, ideally lifetime.</td>
<td>⊗</td>
<td>◐</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP16</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>All health care costs and cost offsets should be included.</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>GP17</td>
<td>⊗</td>
<td>◐</td>
<td>○</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>The time horizon for costs should be long enough to incorporate the benefits of the treatment and the lower costs of medications when they become generic.</td>
<td>⊗</td>
<td>◐</td>
<td>○</td>
<td>●</td>
<td>○</td>
</tr>
<tr>
<td>GP18</td>
<td>⊗</td>
<td>◐</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Costs should be representative of the net price most relevant to the user.</td>
<td>⊗</td>
<td>◐</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>GP19</td>
<td>●</td>
<td>NA</td>
<td>NA</td>
<td>⊗</td>
<td>NA</td>
</tr>
<tr>
<td>Thresholds should be developed in a transparent manner, may vary by population and disease, and should undergo a multi-stakeholder evaluation process.</td>
<td>●</td>
<td>NA</td>
<td>NA</td>
<td>●</td>
<td>NA</td>
</tr>
<tr>
<td>Evidence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP20</td>
<td>●</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Evidence should be identified in a systematic, transparent and robust manner.</td>
<td>●</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>GP21</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Stakeholders should be given the opportunity to submit relevant evidence, such as clinical trial and real-world evidence beyond the published literature.</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>GP22</td>
<td>●</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Best available evidence should be used for the assessment.</td>
<td>●</td>
<td>○</td>
<td>○</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>
Accepted methods should be used to assess quality of evidence, certainty of evidence and conflicting evidence.

Where evidence synthesis is warranted, formal analysis should be conducted, in accordance with accepted methodologies.

Subjective evidence should be used minimally, if at all, and its inclusion should be clearly labeled.

Assessment results should be presented in a manner that is simple for the user to interpret and apply.

Value assessment should clearly state the intended use and audience to avoid misuse.

Press releases should only be issued for final assessments, include limitations of the assessment, and highlight areas where sensitivity analyses result in material changes to the interpretation of the results.

### A. ACC-AHA

ACC-AHA appears to be in an early phase of development in comparison to the other value assessment frameworks addressed in this analysis. Given its stage of development, alignment with the NPC GPs could not be determined for 17 of the 28 GPs. A recent update on the ACC-AHA efforts to incorporate value assessment into its guidelines indicates that the next ACC-AHA guideline will include value as part of its recommendations, based on a review of published economic assessments relating to the key questions of the guidelines.¹⁴

ACC-AHA fully met 6 of the 28 GPs, 5 of which were in the evidence domain. ACC-AHA has an established methodology for evidence review for its guidelines and has described how it will expand this methodology to include review of cost-effectiveness studies and other health economic studies to determine a level of value that can be included with each of its graded recommendations.

ACC-AHA did not meet 3 of the 28 GPs, 2 of which were in the area of methodology. ACC-AHA’s value assessments will focus on cardiovascular treatments, primarily drugs, and will not have weights for user preferences.

---

B. ASCO

ASCO fully met 3, partially met 5, and did not meet 10 of the 28 GPs. One GP was not applicable. The ASCO framework fully met 1 out of 6 GPs in the methodology domain, 1 out of 6 GPs in the evidence domain, and 1 out of 3 GPs in dissemination and utilization. The framework was most aligned with the benefits domain, partially meeting 2 out of the 3 GPs in this domain. The framework did not align with 10 of the 28 GPs, including at least half of the GPs in the areas of methodology and evidence. Four of 6 GPs in the methodology domain and 3 of 6 GPs in the evidence domain were not met.

Alignment with 9 of the GPs could not be determined. This is largely due to the relatively early stage of development of the ASCO framework.

Once ASCO has further updated and improved version 2.0 of the framework and has developed its planned software tool for aiding oncologists and their patients in their decision-making process, the framework (and tool) likely will align with more of the GPs. For example, to date, the clinical scenarios that ASCO tested in its framework relied on single trials; however, ASCO intends to consider a broader evidence base once it starts to formally conduct its assessments. The current framework does not allow for the consideration of patient preferences, but it is anticipated that the software tool being developed will have weights to reflect patient preferences for the different factors that are part of the assessment. Unless it broadens its concept of costs, ASCO will still not be aligned with GP16, which calls for the inclusion of all health care costs and cost offsets. As described above, the framework includes only drug acquisition cost, and the planned software tool will be used to account for a patient’s copayment at the point of service.

C. DrugAbacus

DrugAbacus fully met 2, partially met 9, and did not meet 13 of the 28 GPs. In addition, 2 GPs were not applicable, and alignment with 2 GPs could not be determined. DrugAbacus fully met 1 GP in the methodology domain and 1 GP in the benefits domain. DrugAbacus partially met at least half of the GPs in the evidence and dissemination and utilization domains. Most GPs were not fully met; at least half of the GPs were not met in the categories of assessment process, methodology, costs, and evidence.

As noted above, although DrugAbacus is often compared to value assessment frameworks, its developers emphasized that it is primarily a research tool to examine the effects of different concepts of value combined with users’ preferences on the price of drugs. Unlike the other frameworks in this analysis, DrugAbacus does not appear to proactively solicit feedback and have formal processes in place for accepting and addressing feedback on the tool. There is only an online form on the DrugAbacus website that can be used to inquire about or comment on the tool. However, the developers are open to feedback on the tool and have added domains to the tool as a result of feedback they received. They do not have plans to update the tool with additional drugs unless new concepts are identified that they want to examine using the tool.

Based on a review of the tool and information received from its developers, there are some GPs with which the tool could be readily aligned without affecting its primary purpose. For example, the developers could be more transparent about the underlying data of the tool by providing a citation to the study by Howard et al. A search of the literature resulted in identification of the
study, which provides information on the evidence found and reviewed for each included drug in DrugAbacus. Also, the 2016 update to the tool was not announced. A more recent examination of the tool finds two new domains on the DrugAbacus page, which the DrugAbacus developers subsequently confirmed were added recently in response to stakeholder feedback.

D. ICER

ICER fully met 18, partially met 6, and did not meet 4 of the 28 GPs. There were no GPs considered not applicable to the ICER value assessment framework.

- In terms of value domains, ICER aligned the most with GPs related to the assessment process (fully meeting 4 out of 6 GPs), evidence (fully meeting 6 out of 6 GPs), and dissemination and utilization (fully meeting 2 out of 3 GPs). ICER partially met at least half of the GPs in domains of methodology (3 out of 6 GPs) and benefits (3 out of 3 GPs). ICER did not meet 1 GP in each of the following domains: assessment, methodology, cost, and dissemination and utilization.

ICER is the only framework in this analysis that includes a BIA. ICER fully met 2, partially met 3, and did not meet 2 of the BIA GPs.

ICER is also one of the framework developers that actively seeks stakeholder input and feedback to inform ongoing efforts to improve its framework; this involves its processes for public comment on treatments being assessed and its national call for suggestions for improving the framework. The national call that ICER issued in 2016 notes areas for potential revision, including: methods to integrate patient and clinician perspectives on the value of interventions, incremental cost-effectiveness ratios (appropriate thresholds, best practice in capturing health outcomes through the QALY or other measures), methods to estimate market uptake and potential short-term budget impact of new interventions, and methods for setting a threshold for potential short-term budget impact to serve as a useful “alarm bell” for policymakers to consider whether affordability may need to be addressed. These areas appear to coincide with many of the aspects of the ICER framework for which various stakeholders have expressed concerns.

E. NCCN

NCCN fully met 9, partially met 11, and did not meet 7 of the 28 GPs; 1 GP was not applicable. NCCN aligned most with GPs in the assessment process, evidence, and dissemination and utilization domains, fully meeting at least half of the GPs in each of those domains. NCCN did not meet 3 GPs in the methodology domain, 3 GPs in the costs area, and 1 GP in the benefits domain. One GP in the costs domain was not applicable.

NCCN has established its Evidence Blocks methodology. NCCN’s guidelines and Evidence Blocks also take into consideration a broader evidence base than the other frameworks. However, NCCN’s guidelines with Evidence Blocks have focused only on drug regimens, and do not include a sensitivity analysis or formal economic analysis. While NCCN does examine the available evidence, the Evidence Block scores are based on panel members’ individual scores based on their own review and knowledge of the available evidence and their expert opinion. According to NCCN’s developers, because it continually updates its guidelines, NCCN accepts feedback and input at any point in time via its website and has a formal process in place for addressing the comments it receives.
XIV. Discussion

The value assessment frameworks examined here, including their respective purposes and target users, were more or less underway prior to publication of the NPC GPs. As such, these frameworks were not designed to align with the NPC GPs. Even so, various sets of guidelines and best practices have long been available in such closely related areas as systematic reviews, evidence appraisalal, health economic methods, and health technology assessment, some of which are also reflected in the NPC GPs.

Of course, meeting the various GPs does not suffice for confirming a high-performing value framework, as these checklist items do not convey how, or how well, a GP is fulfilled. More extensive, longitudinal analyses would be required to capture the context and nuances of the performance of each framework across a series of topics. The current analysis focused on the general methodology of each framework; it may be that a framework organization’s execution of these GPs varies across its topics. A separate NPC-sponsored analysis that compares four of the frameworks’ assessments of treatments of multiple myeloma illustrates how the frameworks can vary in their alignment with the GPs when applied to a particular topic.

Developers of all of these frameworks characterize them as works-in-progress, evolving, and responsive to external feedback. Even so, the ICER framework, NCCN Evidence Blocks, and DrugAbacuses are operational and their findings are publicly available and cited by decision-makers. As these and other value assessment frameworks are further developed and refined, their developers should consider incorporating some or all aspects of NPC GPs as appropriate.

A. Overall Ratings

A comparison of the frameworks based on this analysis finds certain basic similarities across two or more frameworks (e.g., intended purposes and audiences, clinical areas), yet many substantial differences. Tables 11 and 12 present a comparison of key features and domains across the five frameworks. Although ICER fully met more GPs than the other frameworks, this is due in part to its more advanced stage of development relative to the other frameworks. In addition, ICER has drawn much of its approach from practices that are well established in much of the HTA community and related evidence-based technology evaluation programs. NCCN had the second-highest number of fully met GPs. NCCN developed its Evidence Blocks upon its longer history of oncology clinical practice guidelines. The Evidence Blocks themselves have been applied to at least 20 assessments of cancer treatments to date.

A detailed comparison of the frameworks’ processes, methods, and other attributes relative to the NPC GPs helps to highlight opportunities for improvement across these and other frameworks in support of value-based health care. The following are ten such opportunities that merit immediate attention.

1. Intended Audiences

Although all assess clinical and economic components of value of health care interventions and have covered certain same or similar topics, these frameworks were designed for different purposes and target audiences. For the most part, they are directed to two main audience categories: 1) providers and patients and 2) policymakers and payers or industry. ACC-AHA,
ASCO, and NCCN all focus on providing value assessments that can be used to help inform clinician and patient decision-making, although their methods and outputs differ. ACC-AHA indicates that the use of its level of value assessments in its practice guidelines and performance measures will also reach payers. ICER addresses value assessment on a broader scale of interest to policymakers, payers, and industry. While DrugAbacus is also available for use by policymakers, payers, and industry, it is intended to be more of a research tool for probing the effects of a specified set of variables on the value of drugs.

Value frameworks should make abundantly clear who are their primary target audiences or users, as well as how they address the interests of those users. For example, the designation of a framework’s intended target users is likely to influence stakeholder engagement, the types of evidence used for patient outcomes, the time horizons for analysis, selection of relevant costs, presentation of results, anticipated impacts, and other factors that will influence assessment findings. Further, notwithstanding a framework’s primary target audiences, its value-based results are likely to affect other stakeholders, including patients, and should employ user input, data sources, analytic methods, and means to incorporate user preferences accordingly.

2. Transparency

Limitations in transparency and reproducibility, such as in evidence sources, methods, and management of stakeholder feedback, can diminish the credibility and utility of value frameworks and prevent them from meeting the needs of multiple users. For DrugAbacus, the topic selection, data used to populate its tool, and the manner in which it uses expert opinion have not been clearly identified. Also, recent important updates to the tool were not announced. While it is clearly explained, how NCCN translates its guideline content into Evidence Block scores appears to be largely subjective.

Due in part to its generally more relative maturity, systematic process, important roles of stakeholder panels, and improving documentation, ICER’s overall transparency is generally favorable. Although ICER’s extensive provisions for soliciting comments are transparent, there is less clarity regarding how and to what extent it addresses these comments in its assessments. Some stakeholders have expressed that ICER’s economic modeling is insufficiently transparent and have been unable to replicate the model results. According to ICER’s recent documentation, its modeling analysis plans are intended to provide sufficient information for experienced researchers to be able to replicate the economic model and analyses, including to extend such analyses. ICER also states that, in order to protect the intellectual property rights of ICER’s external collaborators, the actual executable models and associated computer code will not be provided as part of the deliverable to ICER. Toward ensuring the credibility of these models, ICER and its collaborators could consider arranging for outside experts to examine or test these models in a way that would not compromise their intellectual property.

These and other value frameworks have distinct opportunities to improve their transparency, and in doing so, their reproducibility and utility to users. In the communities that conduct HTAs, pharmacoeconomics, systematic reviews, outcomes research, and related research and assessments, there are robust, evolved examples of process and methods documentation that contribute to transparency and enable reproducibility. Among these are: the U.S. Preventive Services Task Force Procedure Manual (December 2015), the Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0, 2011), the AHRQ Methods Guide for...
Effectiveness and Comparative Effectiveness Reviews (2014), and the National Institute for Health and Care Excellence Guide to the Methods of Technology Appraisal 2013.

3. **Stakeholder Input and Feedback**

Clear, timely, and responsive provisions for stakeholder input and feedback are recognized globally as standard attributes of publicly accountable HTA programs and related efforts involving health and economic evaluations. The five frameworks vary widely in their provisions for stakeholder input. ICER has formal processes and timeframes in place for stakeholder input and public comment. Among these frameworks, ICER appears to be the most proactive in soliciting input. Since releasing the initial version of its framework, ICER has made updates in response to input and feedback and has solicited feedback for its next version, to be released in 2017. NCCN also has formal processes in place for accepting and addressing input and feedback. However, due largely to the frequency with which NCCN updates its guidelines (and accompanying Evidence Blocks) and its intent to make these available to the public as promptly as possible, it does not provide draft guidelines for public comment. ACC-AHA has not performed a value assessment or otherwise progressed to the point where its ability to accept stakeholder input could be evaluated. ASCO has not performed a formal value assessment, it did respond to abundant feedback on the initial pilot version of its framework applied to four clinical conditions, making updates and releasing a second version of the framework in June 2016. Also, ASCO has an online form on its website that can be used to provide input and feedback. As noted above, DrugAbacus responded to feedback in its most recent iteration of the tool by adding two value domains and indication-based pricing for several drugs.

Beyond making provisions for stakeholder input, as reflected in NPC GPs 1, 3, 4, and 5, it is necessary to demonstrate responsiveness to such input. While it may not be necessary to itemize the disposition of each stakeholder comment (as is done in some government programs), value frameworks’ credibility will be influenced by their record of responsiveness to input from across stakeholder groups.

4. **Patient Involvement**

Although all of the frameworks cite some interest in commitment to patient interests, they vary widely in the extent to which they seek or reflect patient involvement. Inadequate patient involvement can undermine the validity, credibility, and utility of value findings. Although the patient perspective is not the primary one for some of the frameworks, patients are ultimately affected by value-based decisions of other stakeholders. The frameworks that already identify patients as an intended primary audience as well as the frameworks that do not can improve their utility by incorporating relevant NPC GPs. For these frameworks as well as others in place or under development, the NPC GPs that deserve greatest attention for ensuring strong patient orientations include those pertaining to: interested stakeholder involvement in the assessment process (GP2), adequate comment periods and transparency regarding how comments are addressed (GP4), incorporating patient-relevant factors into value measurement (GP13), incorporating clinical benefits and harms that recognize heterogeneity of treatment effects (GP14), presenting cost information most relevant to the user (GP18), opportunity for stakeholders to submit relevant evidence (GP21), presentation of assessment results in manner that readily enables user interpretation and application (GP26), and clearly stating the intended use and audience to avoid misuse (GP27).
Of particular note regarding incorporating patient-relevant factors is the imperative of gaining, in the initial scoping of a value assessment, patient input on the particular patient populations and subgroups, interventions, comparators, outcomes, and costs of interest. Doing so should recognize that patient communities, even among those with a particular disease or condition, are highly diverse. Separate efforts are underway to help ensure that patient-relevant factors and patient-centeredness are incorporated into value assessments, such as the National Health Council (NHC) Patient-Centered Rubric. According to NHC, the rubric is to serve as a tool that the patient community, providers, health systems, and payers can use to evaluate the patient-centeredness of value models. The rubric is also intended to guide value model developers in ensuring patient engagement throughout their processes.  

5. Expert Involvement

The quality and credibility of the value assessments depends in part on the types and extent of expert involvement. To the extent that these frameworks use more advanced methods to evaluate clinical, epidemiological, and economic evidence, conduct extensive economic modeling, and intend to serve more diverse target users—including various types of clinicians, patients, and industry—they should revisit their mix of expertise and the ways in which experts are involved in their processes. The processes used by these frameworks draw on expertise in different ways, ranging from a small set of in-house experts for DrugAbacus to national clinical expert panels of NCCN to combinations of staff and external multistakeholder panels of ICER.

NCCN guidelines and Evidence Blocks are developed by 48 panels, primarily comprising clinicians and oncology researchers, including those with expertise pertaining to each guideline panel, along with at least one patient or patient advocate per panel and support from a small internal staff. ICER convenes three independent regional voting advisory groups comprising practicing physicians, methodological experts, and patient advocates that provide input on clinical practice and payer policy decisions. Although these groups generally do not include topic-specific clinical experts, ICER does engage topic-specific clinical experts in developing the draft scope of its reports, as expert report consultants, and/or to supply clinical information support to the voting advisory groups (though not as group members themselves) and policy roundtables. ICER’s internal multidisciplinary team is complemented by academic-based teams that conduct much of ICER’s economic modeling.

6. Types of Interventions

Among the frameworks that have been used to assess treatments, there is a majority focus on drugs and biologics. Given their organizational missions, ACC-AHA will focus on cardiovascular interventions, while ASCO and NCCN are focused specifically on cancer treatments, mainly cancer drugs and biologics. DrugAbacus is intended to focus only on drugs, and the tool currently includes only cancer drugs. Although ICER intended scope is not limited to one type of treatment, it has also recently focused on drug treatments for a variety of conditions. Certainly, some of this focus reflects that drugs and biologics are often stand-alone interventions, their market status is clearly and publicly delineated by regulatory action based on

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readily identifiable evidence of generally high rigor, and their entry prices are increasingly regarded as high and attract public attention. However, an array of value assessments lacking in devices, diagnostics, surgical procedures, multimodal interventions such as drug-diagnostic combinations, and programmatic interventions could bias the basis of informed decision-making for all stakeholders. ICER’s recent topics of diabetes prevention programs and palliative care represent examples of multimodal and programmatic interventions deserving more attention. Demand for the assessment of other types of interventions is also likely to increase from payers and health systems that are at financial risk for generating value.

7. Evidence Sources and Quality

The disparity in evidence sources across the frameworks exemplifies a broader challenge to the relevance and utility of evidence-based analyses. Evidence selection, including clinical, epidemiologic, economic, and other, can influence value assessment findings in ways that are substantial and difficult to discern by target users and the broader public. Across the five frameworks, the primary evidence sources for an assessment range from reliance on single RCTs to bodies of evidence comprising RCTs, other clinical trials, observational studies, conference abstracts, regulatory review content, and network meta-analyses. The cost data used for particular drugs alone (aside from other costs that are included variably across the frameworks) also varies across the frameworks, including Medicare fee schedules, drug list prices, and expert panel members’ more subjective judgments about drug costs. Framework protocols should carefully consider, and be fully transparent regarding, their methods, sources, and criteria for selection of evidence. Further, the limitations and other attributes of the evidence sources, e.g., gaps in the data, inclusion and exclusion criteria, and how those limitations affect assessment findings should be addressed.

Further, frameworks should rate the quality of the evidence used in their assessments in a transparent manner using standard, accepted methods. ICER uses standard evidence rating methods of the U.S. Preventive Services Task Force and the Grading of Recommendations Assessment and Evaluation (GRADE) Working Group, incorporated into an ICER evidence rating matrix. The guidelines into which the ACC-AHA value assessments are to be incorporated use standard evidence rating methods. NCCN uses its own evolved version of categories of evidence and consensus for its guidelines. ASCO and DrugAbacus do not appear to rate the quality of the trials used in their frameworks.

Frameworks should anticipate and account for updates to the available evidence base pertaining to their assessments. Concerns about the timing of value assessments that have been conducted for newer treatments are related to the limited evidence base at the time they were conducted. While ICER has expressed the need to generate findings as soon as possible in order to assist its users in coverage and reimbursement decisions, it does not currently plan to update assessments that it has conducted to date. ICER could benefit its users by conducting updates as new clinical evidence or economic data appear that might have a material impact on its findings regarding effectiveness, safety, value, or budget impact. NCCN differs from ICER in this respect in that it has a process in place for updating its guidelines and accompanying Evidence Blocks annually or more frequently as important new evidence warrants.
8. Costs and Other Economic Aspects

The great variation among the five value frameworks with respect to the NPC GPs pertaining to economic analyses highlights the importance not only of transparency of the assumptions, evidence, and methods used but recognition of their impact on the findings of value assessments and how these findings will be applied. These include, certainly, such matters as identification of economic perspective, scope of inclusion of types of costs and cost offsets, presenting costs relevant to particular users, time horizon of analysis, setting and applying cost-effectiveness thresholds, and multiple aspects pertaining to the role of budget impact analysis. Although it is not possible to address all of these here, the one pertaining to cost-effectiveness thresholds exemplifies the need for value framework developers and other stakeholders in value-based health care to contribute to more explicit practices or guidance on the basis for and appropriate role for these thresholds.

Two of the five value frameworks use cost-effectiveness thresholds, the ranges of which closely overlap. AHA-ACC’s five levels of value also include three ranges: <$50,000; $50,000 to <$150,000; and >$150,000 per QALY gained. ICER uses three ranges of care value: <$100,000; $100,000-$150,000; and >$150,000 per QALY gained. ACC-AHA bases its ranges on the cost-effectiveness framework of the WHO-CHOICE project, which is derived in part from per capita national GDPs. ACC-AHA has acknowledged that these levels may be modified as additional information becomes available or different national consensus standards for value-based thresholds are developed. Similarly, ICER ties its ranges to societal willingness to pay based on WHO per capita GP as well as to aspects of individual willingness to pay and opportunity cost to health systems.

Although such thresholds may have less practical relevance in health care systems that are not subject to fixed budgets, and therefore less apparent constraints of opportunity costs, they continue to be used at least as informal reference points for value and informing health care policies and decisions. To the extent that value frameworks in the U.S. employ particular cost-effectiveness thresholds, particularly consistent ones as do ACC-AHA and ICER, these thresholds will likely persist as rough benchmarks and be incorporated into policies and decisions where feasible. For those and other reasons, stakeholders in value must address a broad set of issues pertaining to cost-effectiveness thresholds. These pertain to, for example, who should set thresholds; stakeholder engagement in setting them; the socioeconomic basis for deriving thresholds; the principles and assumptions underlying thresholds; the manner and extent to which thresholds will be incorporated into health care policies; their relevance and validity for certain population groups, diseases, and interventions (rare diseases, end-of-life care, etc.); and many matters regarding the selection and quality of the health and economic data and the modeling and other methods used to determine cost effectiveness subject to these thresholds.

9. User Preference Entry

Whether to help inform clinical decision making or pricing or payment policies, value assessment is influenced by user perspective and context. Given widespread acceptance that

value depends on stakeholder perspectives, and that there is intra- as well as inter-stakeholder variation in preferences for components of value, value assessment frameworks should enable entry of user preferences where feasible. Given the potential impact of the findings of value frameworks, they should provide for entry of preferences by their primary target users as well as by others who may be affected by their findings.

These frameworks vary widely in their provisions for user input, although their developers generally indicate an interest in enabling such input. DrugAbacus is the only one that currently allows for interactive weighting of user preferences. Given the domains and outputs of DrugAbacus, its users are more likely to be policymakers than patients or clinicians. The ACC-AHA framework does not provide for weighting of patient preferences. ASCO is developing an interactive software tool for that will yield a NHB score but will also enable users to weight their preferences at the point of care. While ASCO currently includes drug acquisition costs, it intends for providers and patients to discuss the patient copayments when using the planned software tool at the point of care. NCCN’s Evidence Blocks do not provide for weights or other means to account for individual patient preferences; however, the Evidence Blocks are intended to serve as a way of facilitating a discussion between a provider and patient that may address patients’ individual preferences. As noted above, the ICER value framework does not enable user entry for its care value or budget impact analyses; however, ICER presents price benchmarks as a function of ranges of willingness to pay (cost-effectiveness thresholds) and potential uptake rates.

10. Potential Misinterpretation and Misuse

Misinterpretation and ambiguity or confusion can arise within and across value frameworks. Among the reasons for the lack of comparability of the findings of the frameworks are the differences in how they integrate or synthesize their source evidence and other inputs. This ranges from a side-by-side presentation of the inputs, with no combination or synthesis, to various qualitative and quantitative syntheses.

Certainly, there is utility in having multiple frameworks address the same or similar topics from different stakeholder perspectives or using alternative methodologies. However, to the extent that the frameworks yield contrasting results on the same or similar topics, they can confuse users. Stakeholders that are unable, or do not choose, to discern the intended uses and underlying assumptions of these frameworks may misinterpret or misapply their results. Depending on their particular needs or biases, some users may grasp certain findings while ignoring others, or not devote attention to the basis for these selected findings. While framework developers cannot be responsible for all biased or uninformed uses of their assessments, they should make concerted efforts to ensure that the basis of their work is transparent and, to the extent practical, endeavor to minimize misinterpretation or misuse of their findings.

The cost and affordability domains of the ASCO framework and the NCCN Evidence Blocks, respectively, are defined in those tools, which are intended to support clinician and patient decision-making. However, neither of those cost-related domains is able to convey estimated actual costs to patients of a particular cancer regimen. Although ICER states that its value-based price benchmarks are not a formal part of its value assessment framework and are not intended to be viewed as caps, their presentation in ICER’s reports have the potential to be misinterpreted by users who do not discern and understand the underlying care value and budget impact assumptions and how those benchmarks are derived. ICER has indicated that it is aware that the term
“provisional health system value,” used in relation to these benchmarks, may not be sufficiently clear. ICER has solicited feedback on this term and other terminology as part of its recent national call for feedback to improve that framework. In general, the framework developers have expressed interest in improving clarity and diminishing misinterpretation and misuse.

B. Value Assessment Here to Stay

The current prominence of these value frameworks follows several decades of progression in such fields as health technology assessment, pharmacoeconomics, outcomes research, comparative effectiveness research, patient-centered outcomes research, and others. All have responded to national and global demands for evidence and analyses of health and economic impacts of health care interventions. These demands continue to increase, along with greater emphasis on patient-centeredness, transparency, methodological rigor, and involvement of stakeholders. The five frameworks examined here represent accumulations of approaches and methods designed to serve their target audiences. Further, they are demonstrating a willingness to evolve, even as additional value assessment approaches are emerging. Whether known as “value assessment” or otherwise, these functions will persist, and it is in all stakeholders’ interests to ensure that they continue to improve.

As noted above, the strengths and limitations of the frameworks, their experiences to date, and ongoing feedback from their target audiences and other stakeholders suggest directions for improvement across the field:

- Involve patients from the start
- Anticipate implications beyond primary target audiences
- Continue to increase transparency and enable reproducibility
- Enable and be accountable for stakeholder input and responsiveness
- Identify and acquire the appropriate evidence for each assessment
- Determine roles and standards for cost-effectiveness thresholds
- Determine roles and standards for budget impact analysis
- Enable user preference entry
- Provide for timely reassessment
- Progress toward unified rigorous, methods

Recognizing the different primary target audiences of these frameworks and the broad benefit in reflecting different stakeholder perspectives on value, all of these frameworks will benefit from alignment with—and efforts to advance—standards for stakeholder engagement, methodological rigor, transparency, reproducibility, and accountability.

Also here to stay is the imperative to evolve and raise standards for value frameworks as these and other frameworks accumulate field experience and their developers and stakeholders push to improve the state of the art. Indeed, the NPC GPs themselves, as well as related guidelines and best practices, should evolve to reflect methodological advances, changing user demands, and
greater accountability to ensure that value frameworks support shared clinical decision-making, improved outcomes, efficient resource allocation, and related health care policies.
### Table 11. Comparison of Key Features of Frameworks

<table>
<thead>
<tr>
<th>Framework/Tool</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>DrugAbacus</th>
<th>NCCN</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Intended Audience(s)</strong></td>
<td>Clinicians, patients, payers</td>
<td>Clinicians, patients</td>
<td>Policymakers, payers, industry</td>
<td>Clinicians, patients</td>
<td>Payers, policymakers, industry</td>
</tr>
<tr>
<td><strong>Primary Treatment Focus</strong></td>
<td>Cardiovascular treatments, primarily drugs</td>
<td>Cancer drug/biologic regimens</td>
<td>Cancer drugs/biologics</td>
<td>Treatment regimens, primarily cancer drugs/biologics</td>
<td>Primarily drugs/biologics; has been extended to devices, procedures, and delivery system programs</td>
</tr>
<tr>
<td><strong>Format</strong></td>
<td>Will be integrated into ACC-AHA guidelines</td>
<td>Will be integrated into user-friendly software tool for use at point of service</td>
<td>Results presented in online tool following input of user preferences</td>
<td>Integrated in NCCN guidelines</td>
<td>Evidence report and meeting summary</td>
</tr>
<tr>
<td><strong>Primary Output(s)</strong></td>
<td>Five value levels: high value, intermediate value, low value – possibly augmented where appropriate with uncertain value – and value not assessed</td>
<td>Net Health Benefit (NHB) comprised of clinical score, toxicity score, and bonus points for symptom palliation, treatment-free survival, QoL, improved survival in tail-of-curve</td>
<td>Abacus price/month based on efficacy, tolerability, novelty, R&amp;D costs, rarity, population burden, unmet need, and prognosis, as well as user preferences</td>
<td>Evidence Blocks for efficacy, safety, quality of evidence, consistency of evidence, affordability on scales of 1-5</td>
<td>Long-term care value, Short-term budget impact, Value-based price benchmarks</td>
</tr>
<tr>
<td><strong>Evidence/ Data Sources</strong></td>
<td>Published clinical trials and health economic studies</td>
<td>Pivotal clinical trial used to support FDA approval</td>
<td>Pivotal clinical trial(s) from FDA approval of first indication</td>
<td>Meta-analyses, RCTs, non-RCTs, case reports, clinical experience</td>
<td>Clinical trials, information from manufacturers</td>
</tr>
</tbody>
</table>
## Comparison of Value Assessment Frameworks Using the NPC Guiding Practices

<table>
<thead>
<tr>
<th>Framework/Tool</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>DrugAbacus</th>
<th>NCCN</th>
<th>ICER</th>
</tr>
</thead>
</table>
| **Evidence Synthesis/Rating** | • Systematic evidence reviews for clinical and health economic studies  
• Use of ACC-AHA level of evidence categories for clinical outcome studies; use of QHES health economic studies  
• N/A | • N/A | • N/A | • Evidence Blocks for quality and consistency of evidence  
• Level-of-evidence grade  
• Online interactive tool  
• Updated tool July 2016  
• Feedback accepted | • Incorporate into NCCN guidelines on different topics  
• Feedback accepted | • Comparative clinical effectiveness review  
• Cost-effectiveness analysis  
• Assessed topics presented in reports  
• Updated framework based on feedback (Version 1.5) July 2016  
• Planned update 2017 (Version 2.0)  
• Feedback solicited |
| **Stage of Development** | • Only initial methodology paper published  
• Has not been applied to any treatments  
• Updated version based on feedback (Version 2.0) May 2016  
• Interactive software tool planned for use at point of service  
• Feedback solicited | • Only applied to clinical scenarios in two published methods papers  
• Updated tool July 2016  
• Feedback accepted | | | |
### Table 12. Comparison of Key Domains/Factors across Frameworks

<table>
<thead>
<tr>
<th>Framework/Tool</th>
<th>ACC-AHA</th>
<th>ASCO</th>
<th>DrugAbacus</th>
<th>NCCN</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td>• Clinical benefits (not specific) – likely to vary by condition and treatment</td>
<td>• OS</td>
<td>• OS</td>
<td>• Survival</td>
<td>• Varies by condition, patient groups’ input, available evidence</td>
</tr>
<tr>
<td></td>
<td>• PFS</td>
<td>• PFS</td>
<td>• PFS</td>
<td>• Curative potential</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Response rates</td>
<td>• Response rates</td>
<td>• Disease control</td>
<td>• Disease control</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Palliation</td>
<td>• Palliation</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other Benefits</strong></td>
<td>• No information</td>
<td>• Treatment-free survival</td>
<td>• N/A</td>
<td>• N/A</td>
<td>• Benefits not captured in comparative clinical effectiveness review (e.g., patient adherence due to new method of administration)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Palliation</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>• Tail of the curve survival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Quality of life</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Toxicity/Safety</strong></td>
<td>• Considers harms – likely to vary by condition and treatment</td>
<td>• Toxicities (any grade)</td>
<td>• Toxicities (grade 3 or 4)</td>
<td>• Toxicities (any grade)</td>
<td>• Not explicitly stated, appears to be considered under efficacy</td>
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<td></td>
<td></td>
<td>• Other side effects</td>
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<tr>
<td><strong>Contextual Considerations</strong></td>
<td>• No information</td>
<td>• N/A</td>
<td>• Novelty of drug</td>
<td>• N/A</td>
<td>• Ethical, legal, or other issues affecting relative priority of illness and intervention (e.g., disease with high severity and no existing treatments)</td>
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<td>• R&amp;D costs</td>
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<td>• Rarity of disease</td>
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<td></td>
<td>• Population health burden</td>
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<td></td>
<td>• Unmet need</td>
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<td></td>
<td></td>
<td>• Prognosis (severity of disease)</td>
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<tr>
<td><strong>Societal Affordability</strong></td>
<td>• N/A</td>
<td>• N/A</td>
<td>• N/A</td>
<td>• N/A</td>
<td>• Affordability thresholds for budget impact analysis</td>
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