Patient-Perspective Value Framework (PPVF)

Version 1.0

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GLOSSARY

Patient-Perspective Value Framework (PPVF): The PPVF provides a high-level methodology for how to assess the value of multiple healthcare options from the patient's perspective. It is made up of a set of patient-centered domains, technical criteria, and measures. It includes a methodology and specified types of data that can be applied in a variety of ways with additional analyses.

PPVF Application: A real-world use case of the PPVF. There are four initial categories of PPVF applications: 1) deploying the PPVF as a shared decision-making tool, 2) incorporating the PPVF into existing value frameworks, 3) using the PPVF to support public healthcare programs, and 4) using the PPVF to support researchers and life sciences companies in conducting strategic internal analyses (which could be condition-specific).

PPVF Domain: The PPVF includes five broad domains of patient value that represent core components of the patient's perspective on value. The five domains are:

1. **Patient Preferences** assesses a patient's personal goals and preferences. This domain functions as a lens through which the PPVF views the Patient-Centered Outcomes, Patient & Family Costs, and Quality & Applicability of Evidence associated with different healthcare options.

2. **Patient-Centered Outcomes** assesses the clinical, functional, and quality of life benefits and drawbacks of different healthcare options to the patient.

3. **Patient & Family Costs** assesses the medical, non-medical, and future out-of-pocket costs and other financial considerations and burdens associated with different healthcare options.

4. **Quality & Applicability of Evidence** assesses the strength and consistency of the evidence, as well as the degree to which the evidence applies to the individual patient. This domain functions as a lens through which we view the Patient-Centered Outcomes and Patient & Family Costs domains.

5. **Usability & Transparency** serves as a foundation for the PPVF and assesses the usability of the framework for its intended audience and transparency of the framework's approach. This domain determines how the weighted assessments of the other domains are communicated through a particular application.

PPVF Criteria: Narrower components of value that constitute a domain. As the PPVF is operationalized for a particular application, the criteria are used to assess each domain.

PPVF Measures: The specific factors used to assess the criteria within each domain

SECTION I. INTRODUCTION

Background

Skyrocketing healthcare costs have caused the most recent wave of healthcare transformation: the transition from the fee-for-service model to value-based care. That transition has caused a flurry of activity to determine how to measure value. For instance, 2015 was marked by a proliferation of new models for assessing the value of treatments – including those developed by the American Society of Clinical Oncology (ASCO), the Institute for Clinical and Economic Review (ICER), the National Comprehensive Cancer Network (NCCN), and Memorial Sloan Kettering. Most of these value assessment models were not created for patients, but rather for payers, researchers and policy-makers, and as such have relied primarily on traditional definitions of value that do not adequately incorporate the patient perspective. In fact, some of these organizations have acknowledged this limitation and have begun to address it through their own processes.

At the 2015 Partnering for Cures (P4C) conference, Avalere Health and *FasterCures* held a [workshop](#) to discuss value frameworks and the degree to which current value assessment models incorporate the patient perspective. There was a consensus among participants on the need for a value framework centered on the patient perspective.

As a result, Avalere and *FasterCures* partnered to formally launch the Patient-Perspective Value Framework (PPVF) Initiative, to develop a framework that truly incorporates patients' perspective on value. We embarked on the PPVF Initiative with the supposition that even though value can be defined differently by different stakeholders, all value assessments should robustly consider and measure what matters most to the ultimate consumers of healthcare: patients.

Objectives of the Initiative

The primary goal of the PPVF Initiative is to fill a gap in the market by developing and implementing a methodologically sound framework for conducting patient-centered value assessments. The framework can be used for various applications and by various audiences, including patients, clinicians, payers, and policymakers. Specifically, we have three objectives at this juncture:

1) Through collaboration and information-sharing, work to render traditional value assessment processes more patient-centered.
2) Serve as a call to action for researchers to begin to generate more robust data sources that consider and collect patient-centered metrics identified in the PPVF.

3) Directly impact decision making by patients, clinicians, payers, policymakers, and life sciences companies through the implementation of identified applications of the PPVF.

Structure of the Initiative

The PPVF Initiative has three phases, as outlined in **Figure 1**. Phase I focused on development of a framework for measuring value from the patient's perspective – this phase began in June 2016 and concludes in May 2017, with the publication of the PPVF Version 1.0. Phase II of the PPVF initiative will focus on refining, testing, and validating the PPVF in real-world settings over the course of 2017 and 2018. During Phase III – in 2018 and beyond – the PPVF initiative will focus on changing behavior and policy, as the PPVF gets integrated into a variety of applications, in which various decision makers – from patients and clinicians to policy makers and payers -- define and measure patient-centered value.

Figure 1: The PPVF Initiative

Phase I 2016 - 2017	Phase II 2017 - 2018	Phase III 2018 - Forward
Build PPVF Version 1.0	**Refine, Test & Validate**	**Implement**
• In Phase I, the PPVF Steering Committee built the Patient-Perspective Value Framework to fill a gap in the market and define value from the patient's perspective	• In Phase II, Avalere and *FasterCures* aim to refine, test, and validate the PPVF in real-world settings to ensure a tangible impact on how value is defined and measured	• Ultimately, we aim for the PPVF to be implemented and used by various decision-makers seeking to define and measure value from the patient's perspective

Phase I: Build the PPVF Version 1.0

Over several months of conversations with various constituencies, Avalere and *FasterCures* formed a multi-stakeholder Steering Committee comprised of 23 organizations, including patient groups, payers, life sciences companies, and other policy and research organizations. The Steering Committee met monthly from June 2016 through May 2017 to learn from each other, provide guidance, and collaborate to build

the PPVF Version 1.0. Avalere and *FasterCures* created and facilitated a process through which the Steering Committee could provide continuous feedback and input into each stage of the development of the framework. Avalere and *FasterCures* held monthly Steering Committee meetings and conference calls. Between monthly meetings with the full Steering Committee, Avalere, *FasterCures,* and individual PPVF Steering Committee members worked together to develop and collect feedback on various drafts of the PPVF.

Avalere and *FasterCures* also collected public comment and performed outreach directly with patients to: 1) receive feedback on the draft PPVF and 2) test the language used in the PPVF summary infographic for patient friendliness. Figure 2 summarizes this public comment and patient outreach process (see **Appendix A** for further detail).

Figure 2: Extensive Feedback on Draft PPVF

Feedback Mechanism	Participants	% Patients/ Caregivers/Patient Advocates
Public Call for Feedback	96	63%
Roundtable with Patient Advocates	12	100%
American Heart Association/American Stroke Association (AHA) Citizen Scientist Think Tank	4	100%
Michael J. Fox Foundation Survey	31	97%
Cancer Support Community Focus Group	8	100%
American Heart Association/ American Stroke Association Survey	119	94%
TOTAL	270	84%

Phase II: Refine, Test, and Validate

Phase II of the PPVF Initiative will run from 2017 through 2018 and will focus on refining, validating, and testing our methodology. Specific activities will be determined by the PPVF Steering Committee as a whole, but they will likely include continued efforts to collaborate with other framework developers, validate a quantitative scoring methodology, pilot applications, and revise the PPVF based on those pilots. As we develop applications, we will make a concerted effort to test applications with patients for usability and transparency.

Phase III. Implement

Phase III of the PPVF Initiative will begin in 2018 as the PPVF is operationalized in a variety of settings. Section V. of this report describes the applications of the PPVF, and examples of their implementation, in detail.

Roadmap of this Report

We have published concurrently a summary infographic that serves as a roadmap and executive summary for this methodology document. As shown on the centerfold of the infographic, there are three components of the PPVF: 1) the domains and criteria; 2) the measures, data sources, and methods; and 3) the applications. Section II summarizes these three components and Sections III, IV, and V describe each component in depth.

SECTION II. THE THREE PPVF COMPONENTS

The PPVF Version 1.0 is a condition-agnostic framework to guide the assessment of the value of different healthcare options (i.e., drugs, devices, diagnostics, and other interventions or, as the case may be, non-interventions) from the patient's perspective and in a patient-centered manner. The PPVF comprises three broad components, which are described in detail in Sections III, IV, and V, respectively:

1) Detailed patient-centered domains and technically specified criteria.
2) A set of measures, data sources, and associated methods for their evaluation.
3) Operational applications or use-cases.

Component 1: Domains and Criteria

The PPVF's five domains represent categories of considerations that are important to patients when making healthcare decisions. The five domains of the PPVF are: 1) Patient Preferences, 2) Patient-Centered Outcomes, 3) Patient & Family Costs, 4) Quality & Applicability of Evidence, and 5) Usability & Transparency. These domains serve different purposes within the PPVF and add different kinds of information to the framework, but are all critically important to patient decision making.

Each domain is made up of **a set of technically specified criteria** that explain the factors that must be considered when measuring a domain. For example, the Patient-Centered Outcomes domain includes the following criteria: *quality of life*, *complexity of regimen*, *efficacy & effectiveness*, and *safety: side effects/complications*.

Component 2: Measures, Data Sources, and Methods

Each criterion is assessed through a set of **data sources, measures, and methods.** For instance, *quality of life*, a criterion within the Patient-Centered Outcomes domain, will be measured by using available data sources to assess measures such as health-related quality of life, functional/cognitive status, palliation of symptoms, and symptom-free intervals. Wherever possible, PPVF assessments will use real-world evidence and patient-reported data in addition to clinical trial data.

The PPVF methodology is driven by the Patient Preferences domain. A PPVF assessment will measure patient preferences and then will use those preferences to weight measures, criteria, and domains.

Component 3: Applications

In order to fully operationalize the PPVF as a value assessment tool, we will need to apply it to a specific use-case that pertains to a condition and different healthcare

options. In Phase I of the Initiative we have not built out any specific applications. Instead, we outline the ways in which the PPVF could function in different situations.

We have identified four categories of initial PPVF applications**.** These categories include: 1) deploying the PPVF as a shared decision-making tool, 2) incorporating the PPVF into existing value frameworks, 3) using the PPVF to support public healthcare programs, and 4) using the PPVF to support strategic internal analyses (could be condition-specific). The methodology will be altered based on the particular use-case and condition under consideration. Section IV outlines some of the ways in which the methodology will be driven by the use-cases.

Figure 3 outlines an example use-case within each category of application. Applications of the PPVF will also inform revisions to the PPVF.

Figure 3: Applications and Example Use-Cases

Application Category	Example Use-Case
Shared Decision Making: The PPVF can be applied as a shared decision-making tool to support conversations between patients and clinicians.	Develop condition-specific electronic decision aid(s); Pilot and evaluate PPVF-driven decision aids for a particular condition in clinical settings.
Apply to Existing Frameworks: The PPVF can be applied to existing frameworks to better incorporate the patient perspective into value assessments.	Integrate PPVF into ICER, ASCO, or other frameworks to render them more patient-centered.
Support Public Healthcare Programs: The PPVF can be applied to support public healthcare programs through shared decision-making applications and others.	Standardize PPVF measures across patients with particular conditions, to more robustly assess clinicians' use of shared decision making and clinical decision support systems.
Strategic Internal Analyses: The PPVF can be applied to help researchers and life sciences companies evaluate the patient-centricity of their portfolios and promote the development of patient-centered products.	Develop a more patient-centered process for product development and internal assessments of the value of healthcare services.

SECTION III. DOMAINS AND CRITERIA

The Patient-Perspective Value Framework (PPVF) consists of five broad domains, which represent five key considerations that are important to patients when assessing the value of different healthcare options. Each of the five domains can be best described in terms of the question it answers, and includes a set of more detailed criteria, developed over the last year with guidance from the PPVF Steering Committee. Section IV dives into how the criteria and domains function to generate an overall value assessment of two or more healthcare options.

- **PATIENT PREFERENCES:** How do the patient's personal goals and preferences affect the value of different healthcare options?
    - Values
    - Needs
    - Goals & expectations
    - Financial trade-offs
- **PATIENT-CENTERED OUTCOMES:** What are the clinical, functional, and quality of life benefits/drawbacks of different healthcare options to the patient?
    - Quality of life
    - Complexity of regimen
    - Efficacy & effectiveness
    - Safety: side effects & complications
- **PATIENT & FAMILY COSTS:** What are the overall costs of different healthcare options to the patient and family?
    - Medical out-of-pocket (OOP) costs
    - Non-medical costs to the patient/family
    - Future costs of care
- **QUALITY & APPLICABILITY OF EVIDENCE:** What level of confidence does the patient have that a healthcare option will have specific effects for them?
    - Quality of evidence
    - Consistency of evidence
    - Differences in treatment effect
- **USABILITY & TRANSPARENCY:** Are the framework and its applications usable and transparent in construct, content, and format?
    - Transparent approach
    - Meaningful information
    - Accessible format
    - Usefulness

SECTION IV. MEASURES, DATA SOURCES, AND METHODS

Overall Process for Healthcare Option Comparison

The PPVF is a framework for value assessment. Section IV explains how each domain fits together to assess a healthcare option, and a methodology for assessing each of the domains and the criteria within them. For some applications, operationalizing the PPVF will require a quantitative scoring methodology relevant to that application or use case. In Phase II, we will operationalize a generic scoring methodology and then adapt it to the particular application.

Figure 4: How the Five PPVF Domains Function

Each domain contributes a different type of information on value to the patient and functions differently within the PPVF's methodology. **Figure 4** below depicts how the different domains function, interact, and impact one another.

Quality & Applicability of Evidence — Patient-Centered Outcomes — Patient & Family Costs — PATIENT PREFERENCES — USABILITY & TRANSPARENCY
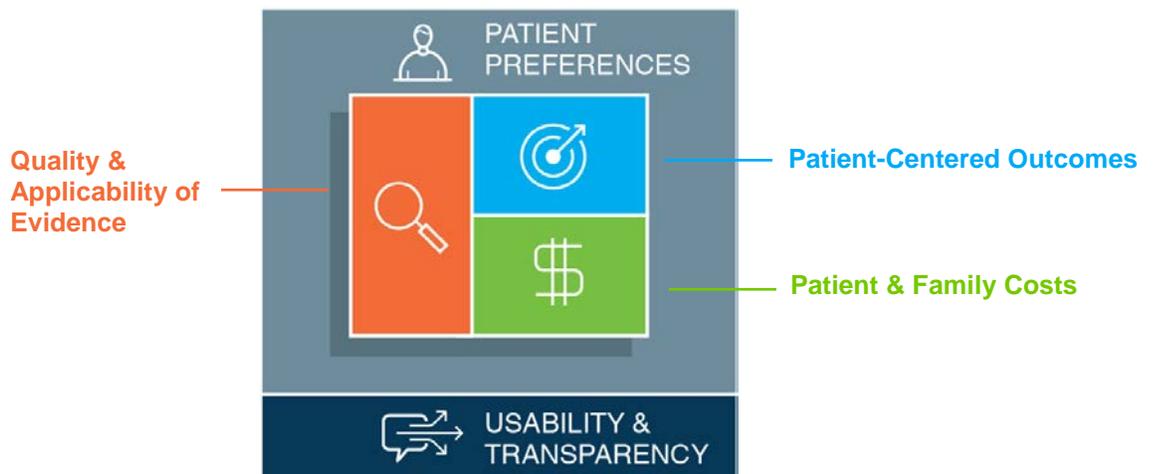
Given that individuals, and groups of individuals with a particular condition, have varying priorities, patient preferences are central to the PPVF's methodology for assessing the value of a healthcare option. In this framework, patient preferences are thought of as the specific values, needs, goals/expectations, and openness to financial trade-offs of an individual patient, or groups of patients with the same condition. Therefore, the graphic depicts how the Patient Preferences domain surrounds the three other objective domains of the framework: 1) Patent-Centered Outcomes, 2) Patient & Family Costs, and 3)

Quality & Applicability of Evidence. In practice, this domain shapes the assessment and weighting of the information within each domain as well as the domains themselves.

The Patient-Centered Outcomes and Patient & Family Costs domains contribute objective information to the framework on the benefits/drawbacks and overall costs associated with different healthcare options.

The Quality & Applicability of Evidence domain touches both the Patient-Centered Outcomes and Patient & Family Costs domains. This positioning depicts the notion that the quality of the evidence, as well as the degree to which the evidence indicates that a healthcare option will have a particular effect for an individual patient, is a key factor in how the PPVF considers both outcomes and costs.

Finally, the Usability & Transparency domain rests beneath the other four domains as a foundation for the PPVF. Some public comments noted that this domain should not be considered a formal PPVF domain because it is not used to assess the value of a healthcare option. However, we believe that this evaluative domain is central to the PPVF as it is intended to assess the value of the framework itself – it represents the PPVF's commitment to ensuring that the framework has a transparent approach and that the information displayed through each application is appropriate for, accessible by, and useful/meaningful to its intended audience. As indicated by its criteria, the Usability & Transparency domain contributes information about the audience, which determines the type and level of information displayed.

Clarifications to the PPVF's Methodology

Public comments called for some upfront clarifications regarding the PPVF's methodology. Three overarching concepts underpin the PPVF's methodology:

First, the PPVF is intended to be applicable to a range of healthcare options including drugs, devices, diagnostics, and other healthcare treatments/services. Therefore, the PPVF's measures are intended to be thorough, inclusive, and applicable across these options, but they will not necessarily all be relevant to the specific conditions and healthcare options being assessed for a given use case. Therefore, for each application, the first step will require selecting the measures that are most relevant to the patient's condition and healthcare options at hand.

Second, the PPVF can be used to assess and compare the value of two or more healthcare options, of which those options can include no treatment, watchful waiting and active surveillance, or palliative and end-of-life care. For example, the PPVF will allow for the comparison of the potential value of treating prostate cancer with surgery, radiation, or active surveillance/watchful waiting, by running the option of active surveillance/watchful waiting through the PPVF in the same way as the other potential healthcare options. Similarly, the PPVF can also consider palliative and end-of-life care for patients with terminal illnesses needing symptom management and other supportive

care services. Therefore, when applying the PPVF, we will ensure that a healthcare option is not devalued because it does not involve active treatment.

Third, the PPVF allows for the consideration of various sources of evidence beyond randomized controlled trials (RCTs), and the use of mixed-methods in areas where the data captured in RCTs are inadequate to measure value from the patient's perspective. The PPVF therefore allows for the consideration of observational data (e.g., from clinical registries or administrative/electronic medical record repositories), clinical practice guidelines, drug/device label information, plan design information, cost estimates (e.g., from FAIR Health) and other estimates from the literature. When applying the PPVF, the assessable evidence base will likely vary based on the condition/therapeutic area at hand. Although the Quality & Applicability of Evidence section outlines a preferred hierarchy of evidence assessment approaches, answers will be derived by triangulating multiple data sources and methods due the limitations of each one.

Patient Preferences

Patient preferences can be defined as patient statements about the relative desirability of particular healthcare options, treatment characteristics, and health states.[1] The incorporation of patient preferences into the process of assessing the value of a set of healthcare options is central to the PPVF.

How do the patient's personal goals and preferences influence their healthcare options?

The Patient Preferences domain assesses a patient's values, needs, goals, expectations, and openness to financial trade-offs and uses those assessed preferences as a weighting mechanism that impacts how the other measures, criteria, and domains of the PPVF contribute to the ultimate value assessment.

The methods through which patient preferences will be elicited in the PPVF will vary according to the application and the condition under consideration. For instance, different criteria will be inherently relevant if the PPVF is being applied to help breast cancer patients make decisions about healthcare options, compared to helping knee replacement patients make decisions regarding the type of joint replacement device they prefer. The flexible Patient Preferences domain can account for these inherent

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[1] Muhlbacher A. Patient-Focused Benefit-Risk Analysis to Inform Regulatory Decisions: The European Union Perspective. Value in Health. 2016. Available at: http://www.sciencedirect.com/science/article/pii/S1098301516304296.

preferences in addition to the particular preferences of individual patients in these situations.

In developing the methodology for the Patient Preferences domain described in this section, we performed a review of patient preferences literature and available data sources to inform a population-level methodology. We also reviewed available decision aid tools to inform an individual-level methodology. From this research, we identified which practices can be extrapolated and applied for the purposes of this framework and where gaps exist.[2,3]

Incorporating Population-Level Patient Preferences into the PPVF

The challenge in operationalizing patient preferences at the population level stems from the underlying question of who can realistically represent the patient voice, given that patient preferences are unique to the individual. However, a thorough review of the literature suggests that – within a specific disease state – there are patterns in patient preferences that may allow for some population-level assessment of patient preferences.[4,5,6,7,8,9,10] There is a lot more work needed in this space; however, below we outline several potential methodologies for ascertaining population- and subpopulation-level patient preferences, depending on the availability of the data and the particular application of the PPVF.

A commonly used method for eliciting preferences is the standard gamble in which a patient is presented with a choice between a specific healthcare outcome and a specific gamble (e.g., remaining at their current level of disability vs. a gamble between a chance for a cure or sudden death).[11] The time trade-off is another technique in which patients choose between two certain outcomes and then the patients are asked how many years in a healthy state would be equivalent to a certain number of years in a poorer state. Rating scale instruments can be employed in which the patient might be asked to define the best and worst states of health for both ends of the scale and then the patient rates

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[2] Ibid.

[3] Klein A, et al. Regulatory Decision Making in Canada—Exploring New Frontiers in Patient Involvement. Value in Health. 2016. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27712698.

[4] Anandadas CN, et al. Early prostate cancer--which treatment do men prefer and why? June 2011. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21083643.

[5] Hall JD, et al. Why patients choose prostatectomy or brachytherapy for localized prostate cancer: results of a descriptive survey. February 2003. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12597956

[6] Xu J, et al. Patient perspective on watchful waiting/active surveillance for localized prostate cancer. November-December 2012. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23136314.

[7] Mandelblatt J, et al. Patterns of breast carcinoma treatment in older women. August 2000. Available at: http://onlinelibrary.wiley.com/doi/10.1002/1097-0142(20000801)89:3%3C561::AID-CNCR11%3E3.0.CO:2-A/full?2-A/full.

[8] Smith ML, et al. Examining and predicting drug preferences of patients with metastatic breast cancer: using conjoint analysis to examine attributes of paclitaxel and capecitabine. Available at: http://link.springer.com/article/10.1007/s10549-014-2909-7.

[9] Ishitobi M, et al. Preferences for oral versus intravenous adjuvant chemotherapy among early breast cancer patients. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24293991

[10] Johnson P, et al. Discrete Choice Experiment to Estimate Breast Cancer Patients' Preferences and Willingness to Pay for Prophylactic Granulocyte Colony-Stimulating Factors. June 2014. Available at: http://www.valueinhealthjournal.com/article/S1098-3015(14)00010-2/fulltext#s0015.

[11] Taylor T, et al. Understanding the Choices that Patients Make. Journal of the American Board of Family Medicine. MedScape. 2000. Available at: http://www.medscape.com/viewarticle/405771_2.

their desirability for different health states on the scale that he or she defined.[12] Other techniques include the stated preference survey and discrete choice experiments (DCEs). The stated preference survey can provide a systematic approach to quantitatively assessing the preference for features of cancer screening tests such as cost, efficacy, and process.[13] DCEs are another technique that involves asking individuals to state their preference for different hypothetical scenarios, goods, or services.[14] Methodologically-sound, population-level approaches have also recently been identified through the Medical Device Innovation Consortium's work to catalog methods for incorporating patient preferences on benefits and risks into the regulatory assessment of medical technologies.[15]

The Food and Drug Administration (FDA) has begun to take strides to incorporate patient perspectives in approval determinations. For instance, in August 2016, the FDA released a guidance document outlining ways in which patient input, in particular perspectives on risk tolerance and benefit value, should be relevant in FDA decisions regarding medical device premarket approval and *de novo* classifications.[16] This example illustrates the progress in this space, and the ways in which regulatory processes will help drive the development of additional patient preferences data.

The PPVF could also draw from data sources such as patient experience registries and data that health plans collect from their members, to ascertain population-level patient preferences for a particular condition. For example, the Cancer Support Community's (CSC) Cancer Experience Registry collects patient preference data to gain a greater understanding of the social and emotional needs of both the people impacted directly by cancer as well as their caregivers.[17] Recent research conducted by CSC, with 679 cancer survivors in the Cancer Experience Registry, highlighted the relative importance of factors such as length of life,

The Cancer Support Community is currently collecting patient preference data in its Cancer Experience Registry to gain a greater understanding of the social and emotional needs of both the people directly impacted by cancer as well as their caregivers.

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[12] Taylor T, et al. Understanding the Choices that Patients Make. Journal of the American Board of Family Medicine. MedScape. 2000. Available at: http://www.medscape.com/viewarticle/405771_2.

[13] Mansfield, Carol et.al. Stated Preference for Cancer Screening: A systematic Review of the Literature, 1990-2013. February 1 2016. Available at: https://www.cdc.gov/pcd/issues/2016/15_0433.htm

[14] Mangham L, et al. How to do (or not to do) … Designing a discrete choice experiment for application in a low-income country. Health Policy and Planning. 2008. Available at: http://heapol.oxfordjournals.org/content/24/2/151.full.

[15] Martin H, et al. A Framework for Incorporating Patient Preferences Regarding Benefits and Risks into Regulatory Assessment of Medical Technologies. February 2016. Available at: http://www.valueinhealthjournal.com/article/S1098-3015(16)00068-1/abstract?_returnURL=http%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1098301516000681%3Fshowall%3Dtrue.

[16] Patient Preference Information-Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling; Guidance for Industry, Food and Drug Administration Staff and Other Stakeholders; Availability. Food and Drug Administrations. August, 2016. Available at: https://www.federalregister.gov/documents/2016/08/24/2016-20221/patient-preference-information-voluntary-submission-review-in-premarket-approval-applications.

[17] Cancer Support Community. Cancer Experience Registry. Available at: https://www.cancerexperienceregistry.org/about

quality of life, impact on family, and financial cost of care for cancer patients (including non-metastatic breast, metastatic breast, prostate, ovarian, and other cancers).[18] This type of data and research could be central in informing patient preferences when applying the PPVF.

Mechanisms for Incorporating Individual Patient Preferences into the PPVF

When used as part of an individual-level application, for instance when patients and providers use the PPVF to engage in a shared decision-making conversation, we will customize Patient Preferences by asking the patient. To determine the best methodology for eliciting individual patient preferences for any given application, we reviewed existing tools and resources.

Existing decision aids can be grouped into two categories: 1) instruments designed for the pre-encounter visit, and 2) encounter tools (e.g., option grids). Pre-encounter decision aids can be used to help patients make more informed and thoughtful choices on healthcare options by providing patients with information on the options and outcomes relevant to the person's health status prior to meeting with the physician.[19] In comparison, encounter tools are designed for use at the time of a clinical encounter. For example, option grids are a form of encounter tool meant to create a collaborative conversation between a patient and a clinician by outlining comparison answers to a patient's frequently asked questions for different healthcare options.

Importantly, the literature indicates a need for further development and testing of these patient preference tools. For example, according to one study, we should focus on developing tools that are more tailored to a patient's preferred style of assessment, whether analytical decision aids in the form of computer software or more intuitive instruments such as weight scales.[20] Many organizations and researchers are working to address this gap by testing ways of systematically incorporating the criteria impacting patient preferences into new tools and decision aids that can help elicit patient preferences at decision points more readily and effectively.

Addressing Gaps in Patient Preferences Tools at the Individual and Population Level

The field of patient preferences research and decision aids is still in its infancy. Despite progress in this field of research, which is producing helpful proxies for measuring patient preferences at the population level, developing PPVF applications will often require partnering with relevant patient groups to conduct new research and fill gaps in the

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[18] Buzaglo J, et al. Cancer Patients' Priorities When Considering a Treatment Decision. Cancer Support Community. Available at: http://www.cancersupportcommunity.org/sites/default/files/uploads/our-research/presentations/Patient-value/2016_biennial_cer_value_poster_6.7.16final2.pdf.

[19] O'Connor A, et al. Decision Aids for Patients Considering Options Affecting Cancer Outcomes: Evidence of Efficacy and Policy Implications. Journal of the National Cancer Institute Monographs. 1999. Available at: http://jncimono.oxfordjournals.org/content/1999/25/67.full.

[20] Barratt A. Evidence Based Medicine and Shared Decision Making: the challenge of getting both evidence and preferences into health care. 2008. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18845414.

literature with regard to patient preferences for specific conditions and disease areas. As part of the PPVF Initiative, Avalere, *FasterCures,* and the PPVF Steering Committee are committed to partnering with patient groups, researchers, and others to do this research to not only inform PPVF applications, but also to contribute to the growing evidence base of patient preferences and patient-reported outcomes. Where there are gaps and limitations in available data that we are unable to fill, we will work with patient groups to outline recommendations for further research that can serve as a call to action for other researchers.

Specifically, we will look for opportunities to work with clinicians and patients to better understand the limitations and barriers to introducing preference and shared decision-making tools at the point of care, including impact on clinician workflow and patient priorities. Improving decision aids is a challenge, but the PPVF creates a significant opportunity to define value from the patient's perspective, and improved decision making tools will allow us to significantly impact patient and clinician decision making at the point of care.

How the Patient Preferences Domain Impacts the Other PPVF Domains

Once patient preferences have been elicited at either the individual or population level, this domain will serve as a weighting mechanism throughout the PPVF. This process will ensure that patient preferences are at the beginning, middle, and end of the entire value assessment process. The PPVF will use the Patient Preferences domain to weight and rank at three different levels within the PPVF: 1) within criteria, 2) among criteria, and 3) among domains.

Patient Preferences weighting within the Patient-Centered Outcomes domain.
Patient preferences can be used to weight and rank *within* the Patient-Centered Outcomes criteria; for example, within the *complexity of regimen* criterion, patients will have an option to indicate whether he or she more highly values a treatment option's route of administration, its site of care, and its length or dosing schedule. A patient will also have the option of weighting and/or ranking *among* the criteria in the Patient-Centered Outcomes domain, based on whether a patient has a preference over a treatment's impact on his or her overall quality of life, the complexity of a treatment's regimen, a treatment's efficacy and effectiveness, and a treatment's side effects/adverse events and complications.

Patient Preferences weighting within the Patient & Family Costs domain. Patient preferences will be used to weight and/or rank *within* the Patient & Family Costs criteria. For example, within the *non-medical costs and burdens to the patient & family* criterion, the patient will have an option to indicate whether he or she more highly values a healthcare option's effect on his or her wages, the associated cost of travel, or the costs of child and/or elder care, among other factors. A patient will also have the option of weighting and/or ranking *among* the criteria in the Patient & Family Costs domain, based on whether a patient more highly values a healthcare option's impact on his or her

medical OOP costs for the entire episode of care, their non-medical OOP costs, or the potential cost offsets and downstream OOP cost implications of the healthcare option.

Patient Preferences weighting among the PPVF domains. Finally, a patient will have the option of weighting and ranking each of the PPVF domains, based on his or her personal preferences among the clinical, functional, and quality of life benefits and drawbacks of a healthcare option (i.e., the Patient-Centered Outcomes domain), the overall costs they will incur for a healthcare option (i.e., the Patient & Family Costs domain), and the certainty that a healthcare option will have its purported effects for him or her (i.e., the Quality & Applicability of Evidence domain).

Patient-Centered Outcomes

Understanding the clinical benefits and risks of different therapy options is central to any value assessment. This domain aims to answer the question: "What are the clinical, functional, and quality of life benefits and drawbacks of different healthcare options to the patient?" The criteria outlined in this domain reflect some of the important factors that patients consider when making decisions among different healthcare options: quality of life, complexity of regimen, efficacy/effectiveness, and safety: side effects/complications.

What are the clinical, functional, and quality of life benefits and drawbacks of different healthcare options to the patient?

Research shows that these factors are important to patients when assessing different healthcare options. For example, in the areas of breast and prostate cancer, studies note how patients often make healthcare decisions based on factors such as the invasive nature of the surgery, duration of the therapy, or onerous treatment regimens.[21,22] Patients also care about how a treatment might impact their quality of life, including work, recreational activities, and interference with their sex life.[23,24] Other studies cite factors surrounding treatment-related side effects such as avoiding infection, vomiting, and incontinence.[25,26] Some studies also note that patients care about the

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[21] Gwede CK, et al. Treatment decision-making strategies and influences in patients with localized prostate carcinoma. August 2005. Available at: http://onlinelibrary.wiley.com/doi/10.1002/cncr.21330/full.

[22] Lifford K, et al. Understanding older women's decision making and coping in the context of breast cancer treatment. 2015. Available at: https://bmcmedinformdecismak.biomedcentral.com/articles/10.1186/s12911-015-0167-1.

[23] Anandadas CN, et al. Early prostate cancer--which treatment do men prefer and why? November 2017. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21083643.

[24] Teh YC, et al. Determinants of Choice of Surgery in Asian Patients with Early Breast Cancer in a Middle Income Country. Asian Pacific Journal of Cancer Prevention, Volume 15. 2014. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24815464.

[25] Johnson P, et al. Discrete Choice Experiment to Estimate Breast Cancer Patients' Preferences and Willingness to Pay for Prophylactic Granulocyte Colony-Stimulating Factors. June 2014. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24968998.

[26] Hall JD, et al. Why patients choose prostatectomy or brachytherapy for localized prostate cancer: results of a descriptive survey. February 2003. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12597956.

clinical outcomes and efficacy of a particular treatment, as well as the strength of the evidence.[27,28] For example, breast and prostate cancer patients often choose a particular healthcare option because it provides the "best cure" or "complete cancer removal" in order to avoid reoccurrence.[29,30]

Moreover, our outreach with patients and patient groups (outlined in Section I) confirmed that the criteria outlined in this domain are comprehensive and representative of the trade-offs and decisions that patients consider when assessing the value of different healthcare options. Please see Appendix A for further details on the results of the outreach conducted with patients/patient groups.

The Patient-Centered Outcomes domain renders the PPVF unique compared to other value frameworks, given that existing value frameworks largely fall short of consistently measuring outcomes that matter to patients.[31,32,33,34] Namely, existing frameworks tend to use measures that narrowly focus on clinical benefits, such as those typically used in RCTs (e.g., overall survival for breast cancer or HbA1c for diabetes), rather than including outcomes that consider the "whole patient" experience (e.g., functional/cognitive status, quality of life, and complexity of regimen). Most value frameworks also only consider data from head-to-head clinical trials, meaning that they do not allow for the comparison of treatments across or beyond individual trials, which limits the body of evidence considered to inform patient- and population-level decision making. Moreover, some existing value frameworks rely on the use of Quality Adjusted Life Years (QALYs) to assess the value of a therapy. Various stakeholders have criticized QALYs as a rigid measure that does not appropriately take into account the complex balance of quality of life and longevity that an individual patient may consider. The PPVF does not rely heavily on the use of QALYs, and instead draws from a variety of patient-centered outcomes deemed important to patients when considering different healthcare options. **Figure 5** summarizes the criteria, measures, and data sources for the Patient-Centered Outcomes domain.

Criteria and Measures

The PPVF aims to capture a broad scope of patient-centered outcomes of central importance to patients when determining value and making a choice among two or more

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[27] Holomboe E, et al. Treatment Decisions for Localized Prostate Cancer. October 2000. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1495597//.

[28] Liu G, et al. Patient preferences for oral versus intravenous palliative chemotherapy. January 2015. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8996131.

[29] Mandelblatt JS, et al. Patterns of breast carcinoma treatment in older women. August 2000. Available at: http://onlinelibrary.wiley.com/doi/10.1002/1097-0142(20000801)89:3%3C561::AID-CNCR11%3E3.0.CO;2-A/full.

[30] Anandadas CN, et al. Early prostate cancer--which treatment do men prefer and why? June 2011. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21083643.

[31] ICER Value Assessment Framework. Available at: https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework/.

[32] ASCO Value Assessment Framework. Available at: http://ascopubs.org/doi/full/10.1200/JCO.2016.68.2518.

[33] NCCN Evidence Blocks. Available at: https://www.nccn.org/evidenceblocks/.

[34] DrugAbacus. Available at: http://www.drugabacus.org/.

healthcare options. Columns 1 and 2 of **Figure 5** summarize the criteria and measures that make up the Patient-Centered Outcomes domain.

The quality-of-life benefits of a treatment, such as: how a treatment will impact a patient's mobility, level of fatigue, or depression; functional and cognitive status, impacting work and recreational activities; and whether a treatment will palliate a patient's symptoms (e.g., pain). [35,36]

The complexity of a treatment's regimen, such as: the dosing/schedule (e.g., one tablet once daily vs. three times a day)[37,38,39], the site of a treatment (e.g., in the clinic/hospital vs. at home) and the associated logistics (e.g., transportation, living arrangements, caregiving roles *[note that these factors are addressed in the Patient & Family Costs domain]*)[40,41,42], the treatment's route of administration and invasiveness (e.g., IV, tablet, reconstructive surgery, and whether a device is implantable or wearable)[43,44,45], the treatment's length/duration (e.g., months of chemotherapy, length of time spent with IV in arm)[46,47], and the level of device maintenance/quality check necessary. This criterion also assesses a healthcare option's interaction with any current treatments that a patient might currently be pursuing, compared to another healthcare option being considered. For example, whether a new healthcare option being considered will necessitate careful monitoring, a current medication change, and/or other medication therapy management actions. This is particularly important for those complex patients who have multiple co-morbidities.

[35] Teh YC, et al. Determinants of choice of surgery in Asian patients with early breast cancer in a middle income country. 2014. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24815464.

[36] Anandadas CN, et al. Early prostate cancer--which treatment do men prefer and why? June 2011. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21083643.

[37] A Lloyd, et al. Eliciting patient preferences for hormonal therapy options in the treatment of metastatic prostate cancer. July 2007. Available at: http://www.nature.com/pcan/journal/v11/n2/full/4500992a.html.

[38] Johnson P, et al. Discrete Choice Experiment to Estimate Breast Cancer Patients' Preferences and Willingness to Pay for Prophylactic Granulocyte Colony-Stimulating Factors. January 2014. Available at: http://www.valueinhealthjournal.com/article/S1098-3015(14)00010-2/fulltext#s0015.

[39] Lifford K, et al. Understanding older women's decision making and coping in the context of breast cancer treatment. January 2015. Available at: https://bmcmedinformdecismak.biomedcentral.com/articles/10.1186/s12911-015-0167-1

[40] Fallowfield L, et al. The preferences and experiences of different bisphosphonate treatments in women with breast cancer. July 2011. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20878871.

[41] Schonberg M, et al. Factors Noted to Affect Women Aged 80 and Older's Breast Cancer Treatment Decisions. March 2014. Available at: http://europepmc.org/articles/pmc4117244.

[42] Lifford K, et al. Understanding older women's decision making and coping in the context of breast cancer treatment. January 2015. Available at: https://bmcmedinformdecismak.biomedcentral.com/articles/10.1186/s12911-015-0167-1.

[43] Makoto I, et al. Preferences for oral versus intravenous adjuvant chemotherapy among early breast cancer patients. November 2013. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3839808/.

[44] Gwede C, et al. Treatment decision-making strategies and influences in patients with localized prostate carcinoma. August 2005. Available at: http://onlinelibrary.wiley.com/doi/10.1002/cncr.21330/full.

[45] Sidana A, et al. Treatment decision-making for localized prostate cancer: what younger men choose and why. April 2011. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21520163.

[46] Holmboe E, Concato J. Treatment Decisions for Localized Prostate Cancer. October 2000. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1495597/.

[47] Makoto I, et al. Preferences for oral versus intravenous adjuvant chemotherapy among early breast cancer patients. November 2013. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3839808/.

The treatment's efficacy and effectiveness, such as: whether a treatment shows improved clinical outcomes for a specific condition (e.g., overall survival for breast cancer, HbA1c for diabetes), and/or its impact on disease progression.[48,49,50,51]

While we believe that this criterion is, in many ways, inextricably linked to quality of life, we have made the decision to include two separate criteria in the Patient-Centered Outcomes domain. By considering these two criteria separately, we will ensure adequate capture of all the outcomes related to healthcare options. Under the PPVF methodology, clinical endpoints such as HbA1c for diabetes will be captured under the *efficacy/effectiveness* criterion, and measures of level of cognitive function, for instance, will be captured under the *quality of life* criterion. The outcomes considered under the *quality of life* criterion are critical outcomes that should be considered on equal footing as more traditional clinical outcomes, and the PPVF allows for equal weighting of the two criteria. The PPVF Steering Committee recommends that researchers designing future studies broaden their assessment of efficacy and effectiveness beyond narrow clinical endpoints to assess the impact on the "whole patient" by also measuring quality-of-life metrics.

The safety of a healthcare option – **the risks of side effects, adverse events, and complications associated with a treatment***,* such as: sexual dysfunction, bowel problems, exposure to radiation, joint and muscle pain, etc.[52,53,54,55] Patients also value the associated frequency, severity, and duration of the side effects/adverse events/complications, and understanding the proportion of patients who discontinue/drop out of the treatment due to the side effects, adverse events, and/or complications.[56,57]

Data Sources

The PPVF differentiates itself from most existing frameworks by allowing for the consideration of various sources of data, including observational data (e.g., patient-reported outcomes [PROs] collected from clinical registries), in addition to evidence

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[48] Johnson P, et al. Discrete Choice Experiment to Estimate Breast Cancer Patients' Preferences and Willingness to Pay for Prophylactic Granulocyte Colony-Stimulating Factors. January 2014. Available at: http://www.valueinhealthjournal.com/article/S1098-3015(14)00010-2/fulltext#s0015.

[49] Liu G, et al. Patient preferences for oral versus intravenous palliative chemotherapy. January 1997. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8996131.

[50] Xu J, et al. Patient perspective on watchful waiting/active surveillance for localized prostate cancer. November-December 2012. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23136314.

[51] Mazur D, et al. How Patients' Preferences for Risk Information Influence Treatment Choice in a Case of High Risk and High Therapeutic Uncertainty. October 1999. Available at: http://mdm.sagepub.com/content/19/4/394.abstract.

[52] Hall J, et al. Why patients choose prostatectomy or brachytherapy for localized prostate cancer: results of a descriptive survey. February 2003. Available at: https://www.ncbi.nlm.nih.gov/pubmed/12597956.

[53] Steginga SK, et al. Making decisions about treatment for localized prostate cancer. February 2002. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11856106.

[54] DiBonaventura M, et al. Patient Preferences and Treatment Adherence Among Women Diagnosed with Metastatic Breast Cancer. October 2014. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4268769/.

[55] Ishitobi M, et al. Preferences for oral versus intravenous adjuvant chemotherapy among early breast cancer patients. 2013. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3839808/.

[56] Schonberg M, et al. Factors Noted to Affect Women Aged 80 and Older's Breast Cancer Treatment Decisions. May 2014. Available at: http://europepmc.org/articles/pmc4117244.

[57] Teh Y, et al. Determinants of Choice of Surgery in Asian Patients with Early Breast Cancer in A Middle Income Country. 2014. Available at: https://umexpert.um.edu.my/file/publication/00012434_106087.pdf.

reported from clinical trials. The inclusion of observational data in the PPVF provides an opportunity to consider a broader array of patient-centered outcomes that may not be reported in traditional clinical trials.

When applying the PPVF, we will prioritize the use of accepted study methods such as meta-analyses for comparing interventions across a particular measure. This study design will dominate others in terms of quality-of-evidence rankings. We may also need to consider both placebo-controlled trials and active controlled studies in order to provide information from studies that most closely aligns with patient-centered outcomes and patient preferences. However, it is likely that the quality and completeness of the evidence base will vary across therapeutic areas. Therefore, in many cases, the most meaningful assessment of patient-centric outcomes may require triangulating multiple data sources (e.g., including real-world evidence) and methods.

When applied, the PPVF will allow for (and specifically emphasize) the inclusion of sub-population data that may be most relevant to the patient, beyond just a study's overall population data. This will serve to provide patients with a greater level of confidence in determining whether a healthcare option will have its purported clinical benefit or result in potential harm for them. Where subpopulation data are available for a given outcome, patients will also have the option of weighting the importance of these data with clinical guidance from the physician. The focus on introducing and assessing subpopulation data from the evidence base, where available, is a key distinguishing feature of the PPVF and a component of the Quality & Applicability of Evidence domain.

Moreover, when applied, the PPVF will also incorporate a mechanism for patients and clinicians to consider data for a given PCO measure that may be reported for one healthcare option, but may not be reported for the other healthcare option(s) under assessment. This will ensure that certain healthcare options are not overlooked or not considered due to a lack of comparable data across options.

Understanding the current status of the evidence base within each therapeutic area under consideration will allow for assessment of the maturity and timeliness of existing evidence, and help us identify remaining evidentiary gaps. When applying this framework in practice, it will be crucial that we catalog areas where evidentiary gaps exist in order to encourage and target future patient-centered research/evidence generation and the development of patient-centered data sources. Ultimately, the PPVF could therefore act as a mechanism for identifying and, ideally, spurring efforts to address gaps in the evidence base for specific patient-centered outcomes.

Column 3 in **Figure 5** below outlines the ideal data sources that the PPVF will rely on for assessing each criterion. However, should those data not be available, relevant proxies and alternative data sources will be used for the specific condition and application at hand.

Figure 5: Criteria, Measures, and Ideal Data Sources that Constitute the Patient-Centered Outcomes Domain

CRITERIA	MEASURES	IDEAL DATA SOURCES
Quality of Life (both generic and disease-specific instruments)	• Health-related quality of life (e.g., instruments that capture Patient Reported Outcomes [PROs] such as vitality, depression, fatigue) • Functional/cognitive status (e.g., instruments that capture PROs evaluating mental/physical/social functioning) • Palliation of symptoms *(Note: also captures the duration/magnitude of palliation, e.g., through a continuous scale)* • Symptom-free intervals (e.g., pain)	• Reported in randomized control trial (RCT) and observational/registry data
Complexity of Regimen	• Dosing/treatment schedule • Treatment length (including need for rehabilitation) • Typical site of care/pharmacy channel • Route of administration & invasiveness of procedure/device	• Drug/device label information • Reported in RCT and observational/registry data • Monograph/clinical dossier information • Clinical practice guidelines

Efficacy/Effectiveness
(long- and short-term)
	• Significant improvement in:
	
	   o Primary end point (e.g., HbA1c for diabetes, impact on disease progression)
	   o Secondary end point
	   o Tertiary end point
		• Reported in RCT and observational/registry data
		• Drug/device label information

Safety: Side Effects/Complications	• Frequency, severity, and duration • Discontinuation (drop out) rates due to side effects/adverse events/complications	• Reported in RCT and observational/registry data • Drug/device label information • Surveillance data collected through Risk Evaluation and Mitigation Strategies data (i.e., post-marketing safety studies for drugs)

Assessment Methodology

Figure 6 describes the high-level process for assessing the Patient-Centered Outcomes domain using the criteria, measures, and data sources mentioned in **Figure 5**.

The Patient-Centered Outcomes domain integrates and operationalizes certain criteria from the Quality & Applicability of Evidence (QAE) domain, which will be described in more detail later in this document. Specifically, two criteria within the QAE domain – quality of evidence and differences in treatment effect (determined by relevant subpopulation data when available) – will be operationalized as part of the assessment and weighting of the PCO domain. However, a third important criterion of QAE – consistency of evidence – will be operationalized separately and is addressed in more detail later in this document.

As outlined in **Figure 6**, the process for assessing the PCO domain includes six broad steps. The first two relate to organizing and assembling the data and the last four relate to evaluating and scoring the data. When organizing and assembling the data, the first step is to determine whether complete data exist for all relevant measures across the healthcare options being compared (referred to here as "comparators"). Complete data are defined as comparable data available for relevant outcomes, across comparators. If complete data do not exist for relevant measures across comparators, these will be categorized as "non-comparable", but will be made available to the framework's end user with appropriate caveats to contextualize the "non-comparable" evidence. Consequently, these data may be utilized to inform the decision-making process, even though they are not comparable across healthcare options. If complete data do exist for relevant measures across comparators, they will be organized by population-level data vs. sub-population-level data for each comparator. Sub-population data refer to segments of the overall study population that have been analyzed in a similar manner to the overall analysis. Sub-population segments are built on sociodemographic or clinical

characteristics such as age, race/ethnicity, gender, comorbidity, and disease stage. These sub-population data: 1) will be used to determine the extent to which the evidence is relevant to a specific patient/patient population, and 2) can be weighted more/less favorably than overall study population data, according to patient preferences.

Once the data are organized and assembled, the end user will begin to evaluate and score the evidence. In Phase II of the PPVF Initiative, we will focus on developing a PPVF scoring methodology, which will be used to conduct the following four steps: 1) grade the evidence for each measure, 2) assess the incremental improvement for each measure of the PCO domain with complete data, 3) apply weights to each measure and criteria in the PCO domain according to patient preferences, 4) score and synthesize the PPVF measures and criteria for the PCO domain, for each comparator.

Figure 6: Process for Assessing the Patient-Centered Outcomes Domain
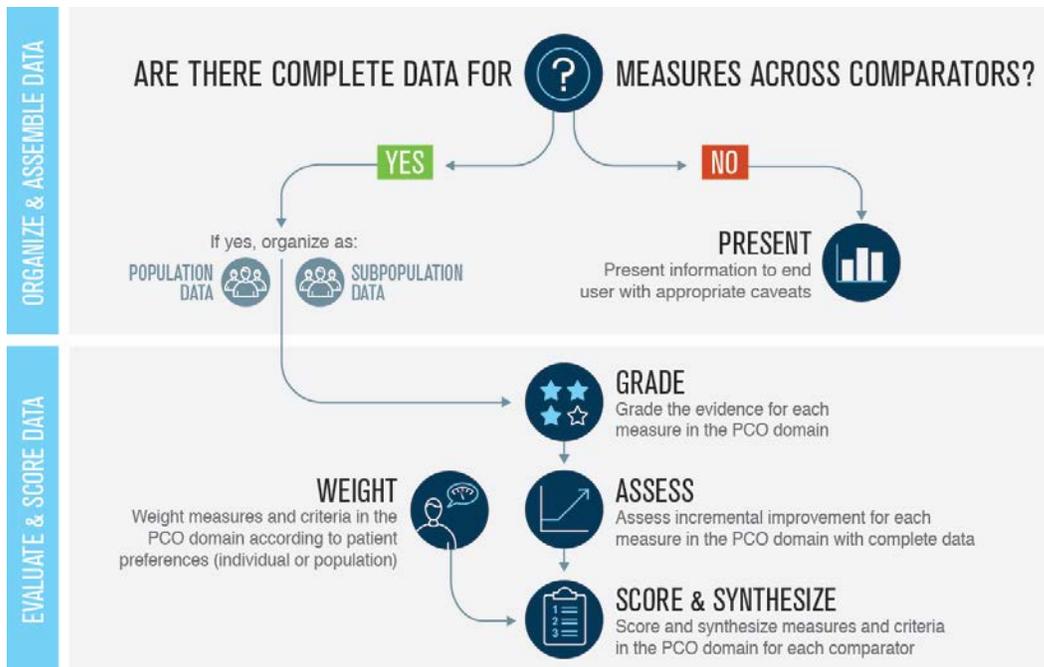
Patient & Family Costs

Financial considerations and burdens are a critical component of any healthcare value determination. Whereas traditional value assessment methodologies primarily focus on the cost to the healthcare system, the PPVF primarily focuses on costs to the patient and family. The PPVF's Patient & Family Costs (PFC) domain considers not only medical out-of-pocket (OOP) costs but also non-medical costs to the patient and family and the future costs of different healthcare options.

What are the overall costs of different healthcare options to the patient and family?

Patient & Family Costs: Criteria and Measures

Figure 7 describes the criteria and measures that make up the PFC domain, along with the data sources we will use – in an ideal scenario – to measure them.

Figure 7: Criteria, Measures, and Ideal Data Sources that Constitute the Patient & Family Cost Domain

CRITERIA	MEASURES	IDEAL DATA SOURCES
Medical OOP Costs	• Out-of-pocket (OOP) costs to patient (includes direct costs of treatment as well as costs of physical, mental, or occupational therapy required)	• Patient-specific plan design information, including cost-sharing requirements (for individual-level applications) • Literature-based estimates of expected healthcare resource use; published list prices for products, services, or interventions; payment benchmarks such as the Medicare Fee Schedule; and national averages for particular sets of services based on payment databases (e.g., FAIR Health) (for population-level applications) • Estimates of patient assistance program support and availability
	• Supportive care agents	• Patient-specific plan design information,

CRITERIA	MEASURES	IDEAL DATA SOURCES
		including cost-sharing requirements (for individual-level applications) • Estimates from literature (for population-level applications)
	• Device maintenance	• Estimates from literature • Incorporates patient-specific plan design information (for individual-level applications)
Non-medical Costs to the Patient and Family	• Cost of travel	• Regional transportation costs to treatment or supportive care (for individual-level applications) • Transportation cost averages for medical visits based on distances and mode of travel from national survey data (e.g., National Household Travel survey) (population-level applications)
	• Cost of child/elder care	• Regional (for individual-level applications) or national (for population-level applications) market rates for child and elder care • Patient-reported child/elder care needs (for individual-level applications) • National averages regarding child/elder care needs (for population-level application) • Literature that estimates cost implications of treatment on ability to fulfill child and elder care responsibilities
	• Cost of supportive care (e.g., assistance with activities of daily living)	• Estimates from literature on expected assistance needed • National averages for particular sets of services based on payment databases (e.g., FAIR

CRITERIA	MEASURES	IDEAL DATA SOURCES
		Health) (for population-level applications)
	• Required lifestyle/behavioral change (e.g., smoking cessation, exercise, diet)	• Expert clinical recommendations of lifestyle or behavior changes needed • Estimates from the literature on the time and monetary cost of associated with those lifestyle or behavior changes
	• Patient & family work productivity/ lost wages	• Estimates regarding expected time horizons for treatment and supportive care from physicians (for individual-level applications) or literature (for population-level applications) • Estimates from literature • Patient/family members' income (for individual-level applications) • Representative income brackets (e.g., Bureau of Labor Statistics data) (population-level applications)
	• Patient & family education/skill building (e.g., learning how to self-administer medications, such as injections, or operate equipment, such as nebulizers and oxygen tanks)	• Estimates from literature and device/drug labels on level of support required to maintain a certain treatment regimen • Expert clinical recommendations regarding the level of skill required or recommended for the delivery of a particular healthcare option
	• Required hours of caregiving	• Estimates regarding average hours of caregiving required
	• Complexity of patient support (can include assessing whether a family member/caregiver would need to assist the patient with	• Estimates from the literature of the cost of skilled professionals to meet

CRITERIA	MEASURES	IDEAL DATA SOURCES
	activities of daily living or with medical/nursing tasks)	patient needs, where applicable • Estimates from the literature on the hours required for un-skilled caregivers to be trained in meeting patient needs
	• Administrative burden (captures care coordination issues, insurance coverage hassles, and other administrative burdens)	• Estimates from the literature, including burden of prior authorizations that might be expected or prescribing requirements that would require additional costs to access medication • Use plan-specific information where available (individual-level applications)
Future Costs of Care	• Subsequent healthcare utilization	• Estimates from the literature, including observational data or modeling of offsets that accumulate over time based on effectiveness of treatment
	• Changes in the cost of therapies	• Estimates based on modeling

Limitations: Data Availability

There are a number of limitations based on the availability and completeness of data sources in given applications. For instance, for individual-level applications, the ideal data source is plan-specific benefit design information that will allow the framework's application to accurately predict the cost of different healthcare options. However, in many cases this information may not be known or feasibly acquired. Another common limitation that we anticipate is the availability of patient-specific information to inform the calculation of travel costs for different healthcare options. In the absence of patient-specific inputs, we will use averages similar to the approach for population-level applications, as outlined below.

Similarly, population-level cost estimates for each of the measures in **Figure 7** do not exist for every condition and healthcare option. In situations where access to ideal data sources is limited, the methodology will be adapted to develop reasonable estimates to inform the framework. The assessment methodology described below accounts for this limitation.

Key Considerations in Assessing the Patient & Family Cost Domain

The methodology by which we will assess each of these measures and criteria will be adapted based on circumstances related to the interventions and applications.

As an example, we will incorporate patient-specific plan design information to measure the first criterion – *medical out-of-pocket (OOP) costs* – for applications of the framework at an individual level (e.g., a shared decision-making tool to be used by an individual patient with his or her clinician)*. On the other hand, for population-level applications of the framework (e.g., incorporating the PPVF into another value framework), we will not have access to any patient-specific plan information. Consequently, we will reference data from studies published in the literature that report cost estimates of direct medical OOP costs, and in some instances health plan cost data for a particular population could be incorporated.

The methodology for assessing this domain will also be adapted based on whether the particular application relates to an acute or chronic condition. For an acute condition, we will measure each criterion for an episode of care reflective of that acute condition, whereas for a chronic condition, we will measure costs over a defined time horizon that is appropriate for the particular condition (e.g., months, years). This is, of course, a complex distinction as there are some conditions, including ulcerative colitis or Crohn's disease that may have acute episodes or "flare-ups" during which a patient may need to make treatment decisions. The methodology will be adjusted accordingly in these cases.

Finally, as described above and as with other domains, there are limitations associated with available data. We anticipate both an ideal case – where we have access to all the data we need to measure a particular criterion – and alternative situations in which our data sources are incomplete, incompatible, and costs (particularly OOP costs) may be difficult to access. Below we go into detail about the different ideal data sources and how we will assess this domain in the event that those data sources are incomplete or unavailable.

Assessment Methodology

The Quality & Applicability of Evidence domain impacts the PFC domain. In particular, the *quality of evidence* criterion will affect the weight applied to each of the criteria and measures in the PFC domain.

Medical out-of-pocket costs
- *Individual-level applications.* For each healthcare option, estimates for direct medical OOP costs to the patient over the entire episode of care will be developed based on the patient's actual or estimated plan benefit design/cost-sharing. In most cases, we will assess a composite of up to three measures – OOP costs for the actual treatment, OOP costs for supportive care, and any OOP costs associated with device maintenance (if applicable).

- *Population-level applications.* For each healthcare option, we will assess literature on expected healthcare resource use to gain an understanding of the products and healthcare services that must be "monetized." Reported costs or alternative list prices for healthcare options will be utilized to assess differences in costs of products (e.g., drugs, devices), and payment benchmarks such as the Medicare Fee Schedule and national averages of OOP costs based on payment databases (e.g., FAIR Health) to assess differences in the costs of services (e.g., specialist visits, inpatient admissions). Finally, we will apply reasonable estimates of OOP cost across the various services to arrive at a population-level OOP estimate across comparators.

Non-medical costs to the patient and family
- *Individual-level applications:* For each healthcare option, total lost wages for the patient and family will be calculated using expected time horizons needed for treatment and supportive care (based on estimates provided by the physician), along with a patient or family member's income (e.g., salary, hourly wages). The cost of travel will be derived from patient self-reporting or calculated using regional estimates of costs of air, train, bus, or automobile travel/parking to treatment or supportive care. The cost of child or elder care will be derived from patient self-reporting or calculated based on the regional market rates. Where access to patient-specific information to inform travel and child or elder care costs is not available, an alternative approach similar to that outlined for population-level applications can be used. Other measures like required hours of caregiving, complexity of patient support, and administrative burden will be calculated using estimates from the literature.
- *Population-level applications:* For each healthcare option, total lost wages will be calculated using expected time resources needed for treatment and supportive care (estimate provided by literature), along with pre-determined income brackets that are representative of the U.S. population. The cost of travel will be calculated using national averages for costs of air, train, bus, and automobile travel/parking based on the typical site of care for different healthcare options and average for patient travel distance to those types of sites based on National Household Travel Surveys for medical care. Total cost of elder and child care will be estimated based on national averages of the amount of care needed, the cost of this care, and assumptions from the literature regarding the impact of different healthcare options on a patient's ability to fulfill child and elder care duties. Other measures like required hours of caregiving, complexity of patient support, and administrative burden will be calculated using estimates from the literature.

Future costs of care. Based on the peer-reviewed literature, estimates will be calculated based on the changes to healthcare utilization and downstream offsets and effects as a result of different healthcare options over an identified time horizon.

- *Individual-level applications.* Estimated future healthcare utilization will be determined and apportioned based on the patient's plan benefit design (or anticipated standardized design) to calculate expected reductions or increases in utilization and OOP costs over an identified time horizon to determine estimated future costs.
- *Population-level applications.* We will apply estimated future utilization to national payment benchmarks such as the Medicare Fee Schedule and average cost-sharing information using national estimates for OOP costs related to component of care to determine estimated future costs.

Figure 8 outlines a methodology for how the different criteria that make up the PFC domain can be synthesized into a single assessment. While we envision some applications and situations in which this assessment will yield a single score or monetary value, there will be many situations in which such a single output is not possible or desirable. Situations like this include:

- When available data sources do not allow for full assessment of each measurement.
- For applications that do not require a single score output, such as certain shared decision-making applications or other qualitative value assessments.

The below methodology describes an ideal case in which a single score output is desired and the available data exist.

Figure 8: Patient & Family Costs Domain Assessment Methodology

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Assess the *Medical OOP Costs* of Treatment/Episode of Care

- Compare the medical OOP costs of all relevant products and/or services associated with each health care option.

Assess the relevant *Non-Medical Costs to the Patient & Family* for Treatment/Episode of Care

a) Compare the following non-medical costs associated with each health care option, if relevant:

- o   Cost of travel (including consideration of treatment schedule)
- o   Cost of child/elder care
- o   Cost of supportive care (when care is delivered by a family member rather than a paid caregiver, this measure may be merged with *patient & family work productivity/lost wages*)
- o   Required lifestyle/behavioral change
- o   Patient & family work productivity/lost wages
- o   Patient & family education/skill building

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	o Required hours of caregiving o Complexity of patient support o Administrative burden
Weight Measures Within *Non-Medical Costs to Patient & Family* Criterion b) *Individual*: The patient has the opportunity to directly customize the weights of the measures of this criterion. c) *Population*: The preference weights will be garnered from the literature if available, and will be set as equal in the absence of peer-reviewed evidence.	
Assess the *Future Medical Costs* associated with each health care options d) Compare the costs of health care utilization that extend beyond the immediate episode of care associated with each health care option.	
Weight the PFC Criteria e) *Individual*: The patient has the opportunity to directly customize the weights of the three criteria. f) *Population*: The preference weights will be garnered from the literature if available, and will be set as equal in the absence of peer-reviewed evidence.	

Measuring System-wide Costs

The PPVF Version 1.0 focuses primarily on costs to the patient and family and does not currently include a measure of system-wide costs. However, we envision that future versions of the PPVF will address applications to inform policymakers and others about system-wide costs. The incorporation of patient and family costs will allow those future system-wide cost assessments to provide a more comprehensive assessment by including issues such as non-medical costs and future costs.

We received feedback from a number of commenters that we will need to measure medical, non-medical, and future costs more broadly, as the PPVF is used to develop applications to other value frameworks, to support public healthcare programs, and in the form of public analyses of particular conditions.. In addition, we understand that there are situations in which system-wide costss are not only important to value assessments, but also to patients who may have a preference for a treatment that has a lower cost to the system.

Quality & Applicability of Evidence

The Quality & Applicability of Evidence domain is intended to assess the quality and consistency of the available evidence, and the degree to which it is applicable to a specific patient or patient population. The overall aim of this domain is to answer the question: "What level of confidence does a patient have that a given healthcare option will have specific effects for them?"

What level of confidence does a patient have that a given healthcare option will have specific effects for them?

This domain assesses three key criteria: the *quality of the evidence*, a measure of the strength of each study's design; the *consistency of evidence* across studies, a measure of the variability of study results; and the *differences in treatment effect* for different types of patients. The *consistency of evidence* criterion is a measure used in traditional evidence assessment processes to gauge the degree to which the body of evidence represents credible and robust information regarding outcomes of interventions. It is an important consideration in determining how and what evidence should be considered in the value assessment process. The *differences in treatment effect* criterion identifies available subpopulation data to provide information on the differences in treatment effect for different types of patients.

The Quality & Applicability of Evidence (QAE) domain further differentiates the PPVF from traditional definitions of value by how it interacts with the other domains. In **Figure 4**, the Quality & Applicability of Evidence domain is positioned inside the Patient Preferences domain and alongside the Patient-Centered Outcomes (PCO) and Patient & Family Costs (PFC) domains. This is to indicate that different patients have different preferences with regard to evidence as described in the Patient Preferences section above. The positioning alongside the PCO and PFC domains indicates that the evidence also impacts a patient's perspective on the outcomes of different healthcare options and the cost of those healthcare options.

Criteria, Measures, and Methods to Assessing Quality & Applicability of Evidence

Figure 9 describes the criteria, measures, and the associated methods that make up the Quality & Applicability of Evidence domain.

Figure 9: Criteria, Measures, and Methods that Constitute the Quality & Applicability of Evidence Domain

CRITERIA	MEASURES	METHOD
Quality of Evidence	• Adherence to generally accepted methods.	• Consider established evidentiary grading scales

		(trial-based and observational data-based).
Consistency of Evidence	• Variability of study results – measures the degree to which different studies illustrate the same results.	• Consider consistency in magnitude of effect that is reported across evidence base.

Differences in Treatment Effect	• Measure of heterogeneity across different subpopulations:
	  o Demographics
	  o Comorbidities
	  o Disease stage
		• Consider reported variance in outcome measure based on specific subpopulations.

How the Quality & Applicability of Evidence Domain Interacts with Other Domains

As displayed in **Figure 4**, Quality & Applicability of Evidence provides a lens through which the patient views both PCO and PFC domains, and is impacted by Patient Preferences. The evidence collected through the assessment process underpins the data used to compare interventions, based on the measures found in the PCO and PFC domains. This evidence must be evaluated for its level of quality (based on the strength of evidence according to the various types of study designs and data sources that are used) and consistency (the degree to which there is certainty of the results across studies).

Within the PCO domain, two elements of the QAE domain are integrated into the framework and operationalized by applying a *quality of evidence* assessment to the individual studies that report the measures being evaluated. Quality assessments will be based on evidence scoring tools that are commonly used to gauge the strength of the evidence based on the particular design that is employed (e.g., using hierarchical ranking of study designs), and will provide a weighting for each outcome based on the methodological rigor employed to produce results for the outcome.

This same approach to integrating these elements of *quality of evidence* will also be applied to the PFC domain to the degree that individual studies are available and can be assessed for the measures described in the domain.

As described earlier, the *differences in treatment effect* criterion captures an important concept that is operationalized within this framework. This is achieved by identifying study results that report out at the subpopulation level and provide the opportunity to assess the alignment between the patient with the particular subpopulation and the resulting outcomes. When applied at the individual level, patients will have the opportunity to consider the comparisons across interventions for those subpopulations that are most meaningful to them, thereby creating an inherent weighting toward the resulting comparisons for those particular outcomes.

When applied, the PPVF will use the *consistency of evidence* criterion to describe how often similar findings are reported across studies. This criterion will be operationalized using an assessment of the results and by determining the degree of variance across these studies. Given that this criterion is also a way to operationalize the certainty with which a patient would expect to see results for the outcomes of interest across the comparison of interventions, this provides an opportunity for weighting the *consistency of evidence* criterion against the other domains to align with patient preferences.

Patients vary in how they will engage with this information. Some will want more and some will want less. In many cases, patient and caregiver desire for information will vary at different points in their care journey, and the applications ultimately should allow for that level of moment-in-care flexibility. Therefore, it is important to have options for addressing this level of distinction. It is also helpful for applications to include default options that allow patients to bypass those decisions when data are limited, of limited relevance, or more detailed than is comfortable for those patients.

Application-Specific Methodology Considerations

The methodology by which each of these measures and criteria will be assessed will likely change based on certain circumstances: 1) whether the PPVF is being applied at the population vs. individual level, and 2) the availability and completeness of data.

Whether the PPVF is being applied at the population or individual level significantly impacts the third criterion, *differences in treatment effect*, but not the first criterion, *quality of evidence.* In a population-level application, the PPVF will not be able to consider the individual characteristics of any given patient. Therefore, in order to convey information about the differences in treatment effect for different subpopulations, the PPVF will identify subpopulation data that is comparable for the different healthcare options under consideration. How this information is ultimately conveyed to the audience will depend on the specifics of the population-level application, or on the intended use of the healthcare option assessment.

In an individual-level application, the PPVF will collect information about the patient's characteristics, including race, income level, age, gender, comorbidity, disease stage, and others. Based on that information, the PPVF will allow for the identification of appropriate subpopulation data that are identified through the evidence assessment process. In circumstances where more than one subpopulation is appropriate for the patient, the PPVF will create a mechanism for the patient to indicate a preference as to which subpopulation data are more relevant to them. In a shared decision-making application, this preference exercise will be part of a patient's conversation with a clinician that incorporates the patient's goals and preferences as well as the physician's clinical evaluation about which characteristics, in this case, generate the most relevant data for the patient.

Data availability and completeness affects each domain. The ideal case is one in which we have access to a range of comparable data sources and robust RCT data that indicate differences in treatment effect across subpopulations and are confirmed by real-world evidence. We will often not have access to this level of data and therefore will need to shift the methodology for assessing the Quality & Applicability of Evidence based on what data sources are available.

Assessing Healthcare Options

After the Patient-Centered Outcomes, Patient & Family Costs, and Quality & Applicability of Evidence domains have been individually assessed, users of the framework will:

1) Use patient preferences to weight between these domains.
2) Assess the comparative value of the two or more healthcare options under consideration.

STEP 1: Weighting Among Domains

Before completing the final assessment of the healthcare options being considered, users of the PPVF must weight among the Patient-Centered Outcomes, Patient & Family Costs, and Quality & Applicability of Evidence domains for each healthcare option under consideration. The weighting method will differ based on various factors of the application, including whether it is applied at the population-level or individual level.

In a population-level application, population-wide data collected on patient preferences or desirability of trade-offs for one domain over others will be utilized. In the absence of these data, all three domains will be weighted equally.

In an individual-level application, in the context of shared decision making, patients will be asked to rank the above three domains in order of importance and magnitude, based on their personal preferences. If the assessment of the literature reveals a clear preference among most patients for one domain over another, those will become the default. Patients will have the opportunity to apply points or scoring to customize that default and illustrate that more points will equate to higher preference and importance to them.

STEP 2: Calculating the Comparative Value of Different Healthcare Options

Once the domains have been weighted according to patient preferences, the preference-weighted domain-specific assessment scores will be summed to arrive at the "overall value assessment score" for each of the healthcare options (i.e., drugs, devices, diagnostics, interventions) being considered. These "overall value assessment scores"

can then be compared across the healthcare options being considered to identify patient centered value for each option.

Usability & Transparency

The final domain of the PPVF is Usability & Transparency. While all the domains contribute different types of information and function differently within the PPVF, Usability & Transparency stands apart as the foundation of the framework. Despite its different function, we have included it as one of the five domains of patient value to ensure that its importance will not be diminished at any point in the framework.

Is the framework and its applications usable and transparent in construct, content, and format?

This domain represents the PPVF's commitment to ensuring that the framework has a transparent approach and that the information displayed through each application is appropriate for, accessible by, and useful and meaningful to its intended audience. For example, a shared decision-making application of the PPVF, intended to facilitate a conversation between a patient and a clinician, might display qualitative information about each criterion, rather than a single score output. It represents our commitment to publishing a detailed methodology and seeking continuous public input, as well as our commitment to continuous self-evaluation as we develop future versions of the framework and individual applications.

Usability & Transparency: Criteria and Methods Considerations

Figure 10 displays the criteria and methods considerations that make up this domain. This domain is an evaluative domain. Measures associated with each method consideration will be determined based on the audience and the application.

Figure 10: Criteria and Methods Considerations that Constitute the Usability & Transparency Domain

CRITERIA	METHODS CONSIDERATIONS
Transparent Approach	• Clear methods and parameters • Clear interpretation of results • Clear justification of evidence • Inclusive of all options

	• Transparency of individuals involved
Meaningful Information	• Stays true to patient perspective
Accessible Format	• Education levels and health literacy • Various ages • Accessible to persons with disabilities
Usefulness	• Rate of utilization • Satisfaction • Patient engagement

Assessing the Usability & Transparency Domain

The Usability & Transparency domain serves two main purposes. First, it considers the **audience** and the **application** to determine how the information is communicated. Second, it evaluates the framework and the application for usability and transparency.

> *Who are the audiences for the PPVF's applications?*
>
> • Patients/Caregivers
> • Providers
> • Payers
> • Life science companies
> • Policymakers
> • General public (varying levels of literacy/health literacy)
> • Researchers
> • Other framework developers

- **Audience**. The applications of the PPVF will have a wide range of audiences, which will impact how the criteria within the Usability & Transparency domain are assessed.

- **Application**. The PPVF has a range of potential applications. The particular application at hand will impact the framework throughout the methodologies associated with the other domains outlined above, but will play a particular role here as this domain determines how the information regarding different healthcare options is conveyed.

For example, a shared decision-making tool will have an audience of patients and providers. Therefore, the framework's approach needs to be transparent, true to the patient perspective, and accessible and useful to both the patient and the provider. In this case, considering the audience and the application, we would determine via surveys and

patient focus groups what information is most useful to the type of patient and provider being served by the application, and then design a tool that displays that information. It may be that for this application the most useful way is to perform a healthcare option assessment based on the data available – including patient preferences as obtained from the individual patient, clinical data about the outcomes of different healthcare options, cost data based on the individual's insurance benefit, and other factors such as location of treatment center and availability of family caregivers, as well as an assessment of evidence to determine the likelihood of a given treatment effect occurring for that individual patient – and display the recommended healthcare option followed by information about other healthcare options in the order of a patient's preference.

After displaying the information in this way, we will then evaluate the applications usability and transparency using a mixed method approach that includes interviews, observations, and surveys of users.
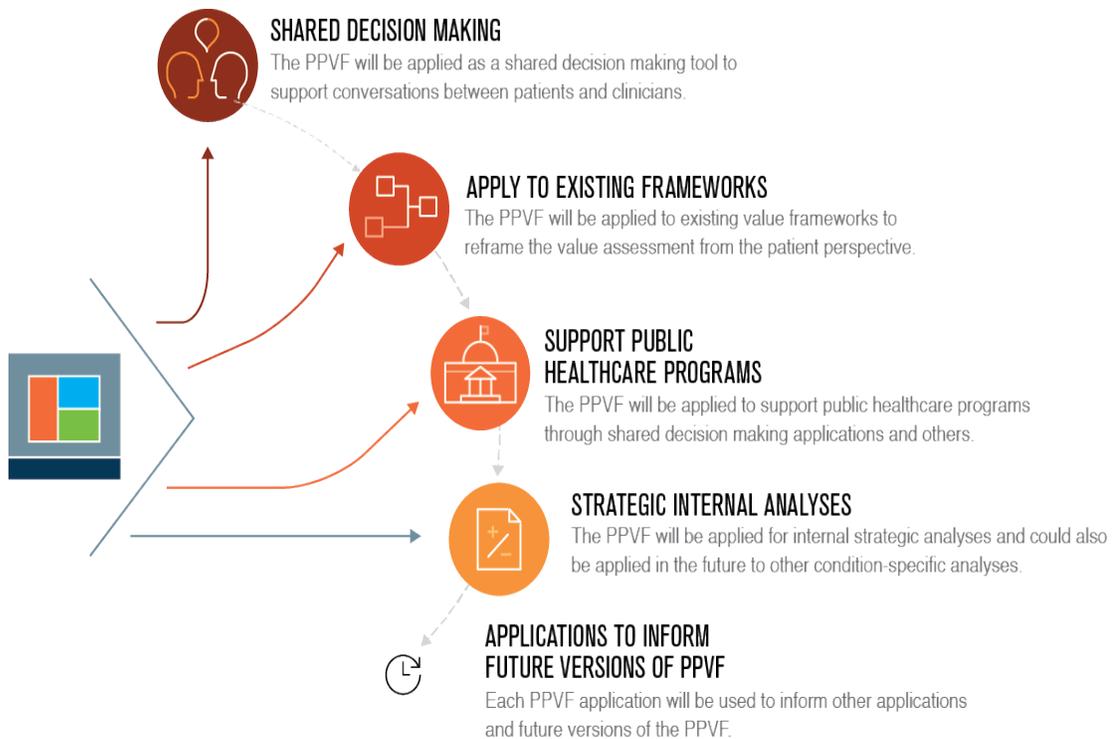
SECTION V. ROADMAP TO APPLICATIONS

We have designed the PPVF to be flexible so that it can be operationalized across a variety of individual- and population-level applications. **Figure 11** outlines four initial categories of applications of the PPVF. Section V describes each category of application and give an example of how it will be operationalized in Phase II and Phase III.

Operationalizing some applications will require a quantitative scoring methodology relevant to that application or use-case. As a part of Phase II, we are working to operationalize a generic scoring methodology which will be adapted based on the particular application.

Figure 11: Future Applications of the PPVF

SHARED DECISION MAKING
The PPVF will be applied as a shared decision making tool to support conversations between patients and clinicians.

APPLY TO EXISTING FRAMEWORKS
The PPVF will be applied to existing value frameworks to reframe the value assessment from the patient perspective.

SUPPORT PUBLIC HEALTHCARE PROGRAMS
The PPVF will be applied to support public healthcare programs through shared decision making applications and others.

STRATEGIC INTERNAL ANALYSES
The PPVF will be applied for internal strategic analyses and could also be applied in the future to other condition-specific analyses.

APPLICATIONS TO INFORM FUTURE VERSIONS OF PPVF
Each PPVF application will be used to inform other applications and future versions of the PPVF.

Shared Decision Making

A PPVF-based shared decision-making tool will be used to support conversations between patients and clinicians. Decision aid tools vary in scope, format, and complexity. Some are on paper, some are a list of questions meant to

be completed at home, and some are electronic and integrated into electronic health record systems.

Example Application

Step 1: Identify partners, pilot sites, and conditions. In order to support this application, we will first identify partners, including clinicians to provide content expertise, health systems to provide pilot sites, payers to provide data, and technology partners to operationalize the decision aid. Based on the resources of our partners, we will coalesce around one or two conditions across which to pilot the decision aid. Once a condition has been selected, we will identify clinical sites to pilot the decision aid. Pilot sites may include diverse care settings like safety net clinics, primary care practices, large health systems, and post-acute care providers.

Step 2: Design the decision aid. In collaboration with our identified partners, we will leverage the PPVF domains, criteria, and methods to develop 1-2 condition-specific decision aids. This will involve a significant review of literature to determine the measures on which sufficient evidence exists and may involve additional research directly with patients to determine baseline patient preferences of patients in the population of focus. We will also test the decision aid for usability.

Step 3. Pilot the decision aid. We will develop and provide training modules to each pilot site on how to administer the PPVF decision aid to patients. With input and guidance from clinician partners, we will develop clinician-facing training modules to accompany each decision aid. Pilot sites will pilot the decision aids for three months

Step 4. Evaluate the decision aid. We will use a mixed-method approach to evaluate the decision aid, including observations, interviews, and surveys. During the pilot testing period, we will use an ethnographic design approach to evaluate the challenges and successes of using the PPVF decision aid for improving share decision making and integrating it into the patient life flow and clinician workflow. Specifically, we will conduct observations and interviews with patients, caregivers, and clinicians who used the decision aid. In addition, we will conduct pre- and post-surveys with patients and clinicians at the pilot sites to evaluate their experience using the PPVF-based decision aid. We will measure decision quality, decisional conflict, patient experience, patient knowledge, trust in the clinician, clinician workflow burden, and patient "life flow" burden.

Addressing Limitations: Shared Decision Making

The PPVF methodology allows for three levels of weighting and ranking. Users can rank domains, criteria within domains, and measures within criteria. We recognize that this could present a potential administrative or time burden to the patient and the clinician in the context of a shared decision-making application. However, we feel that the benefits of creating a framework that is flexible enough for a patient to drill down as far as possible on all aspects of decision making, based on his or her level of comfort and understanding, outweighed such concerns at this juncture. We plan for PPVF decision

aids to use default weighting for those patients who do not wish to engage at that level of decision making. As we develop specific shared decision-making applications, we will pay special attention to overcoming the limitations associated with patient and clinician burden.

Apply to Existing Value Frameworks

The goal of applications in this category is to render existing value frameworks more patient-centered. The PPVF Steering Committee has actively engaged with existing framework developers (e.g., ASCO, ICER, NCCN, DrugAbacus) throughout Phase I. For instance, in February 2017, leaders from all four of these framework development organizations presented at a PPVF Steering Committee meeting on their own next steps and how the PPVF is relevant and useful to their work. Several applications fall into this category, whether they be active collaboration with these frameworks or external PPVF-driven analysis.

Example Application

Step 1: Partner and condition identification. We will identify a partner among existing value framework developers. As mentioned, we have been working closely with a number of the framework developers over the last year and have initiated collaboration discussions with some of them. We will then collaboratively identify one or two specific conditions on which to focus for this project.

Step 2. Comparative assessment of the evidence. We will review the evidence base for the PPVF measures associated with that condition, including a review of patient preferences literature. If necessary, we will conduct original research directly with patients. We will then compare the identified list of measures with those used in the partner value assessment, highlighting differences in the evidence considered.

Step 3. Comparative assessment of the methodology. Using the evidence identified in Step 2, we will apply the PPVF methodology to the healthcare options considered by the alternate framework. We will then compare both the final result as well the methodological steps that drove that result to those of the partner value assessment.

Step 4. Recommend adjustments. Based on the work done to compare the evidence, methodology, and result of each of the partner framework and the PPVF, we will make recommendations as to how the partner framework could incorporate additional PPVF measures and criteria and become more patient centered.

Step 5. Partner to implement adjustments. We will then work with the partner framework to implement and publish PPVF-based adjustments to their framework.

Application to Public Healthcare Programs

The PPVF could be applied to public healthcare programs to help inform the execution and measurement of projects focused on patient preferences, shared decision making, beneficiary engagement, and others. The goals of this type of application are to have a direct impact on how value is considered in the public domain and to ensure that patients have a voice in that conversation. This standardized set of patient preferences in the example could be used to inform a range of activities, including value determination for payment, shared decision making, patient-focused drug development activities, and others.

Example Application

Step 1: Select conditions. We will work with partners to identify conditions that will have broad impact and where we have resources to support this work. We will likely choose either one type of cancer or a cross-section of cancers as well as a chronic condition such as heart disease or arthritis.

Step 2: Exploratory research. We will first conduct qualitative, exploratory research to build upon the preliminary patient preferences research conducted while developing PPVF Version 1.0 (described in **Appendix A**). We envision using two online discussion boards with 12-15 patients each. These discussion boards will allow us to engage in conversation with patients and gain a better understanding of their preferences, motivating factors, and decision-making considerations. We will use this step to confirm that existing PPVF measures cover all factors of concern for those populations of patients and to surface themes, concepts, topics, and/or trends in patient preferences that warrant capture in the next stage of this project.

Step 3: Quantitative validation. Building off the Step 2 exploratory research, we will develop a tailored survey for each condition. The primary objective of these surveys is to gauge the relative importance of the PPVF measures, criteria, and domains to patients with a certain condition. This will allow us to rank the PPVF measures against each other and identify the core components that are of high importance to patients. We anticipate that samples will include at least 200 patients each.

Strategic Internal Analyses

The PPVF can be leveraged to drive patient-centeredness in product development as well. For instance, we envision partnering with researchers and life sciences companies to evaluate the patient-centeredness of current and future products.

Step 1: Select therapeutic area and product(s) of focus. For this type of project, it will be important to target a specific therapeutic area because of the variety in preferences among patients with different conditions.

Step 2: Evidence assessment and gap analysis. Once the therapeutic area and product(s) have been selected, we will conduct an assessment of all the available evidence for the PPVF measures and criteria. We will begin with a review of condition-specific patient preferences literature, including studies analyzing patient experience registries. If significant gaps in the available patient preference evidence are found, we will consider conducting additional original research directly with patients.

For the PPVF criteria and measures in the Patient-Centered Outcomes, Patient & Family Cost, and Quality & Applicability of Evidence domains, we will analyze relevant study protocols, existing trial data, and available data shared by partners. We will identify data relating to the measures and criteria and indicate where gaps in those data exist.

Step 3: Qualitative mapping to inform evidence-generation strategy. Based on the available evidence gathered in Step 2, we will qualitatively map the product(s) against the PPVF. This will allow us to identify areas in which patient-centered evidence exists and areas in which it does not. We will use this qualitative mapping strategy to generate recommendations regarding how our partner should amend its evidence-generation strategy to better focus on patient-centered measures; as well as understand the relative patient-centered value of different healthcare services.

Conclusion

These above four mentioned applications of the PPVF were identified by Avalere, *FasterCures* and the Steering Committee throughout the development of the framework. As we learn from the experience of implementing and piloting these applications, we will continue to identify other opportunities to apply the PPVF and impact how value is defined in real-world settings. We expect that further applications of the PPVF will be recognized as we move toward value-based care and a value-oriented payment environment, and measuring value from the patient's perspective will hold increasing importance.
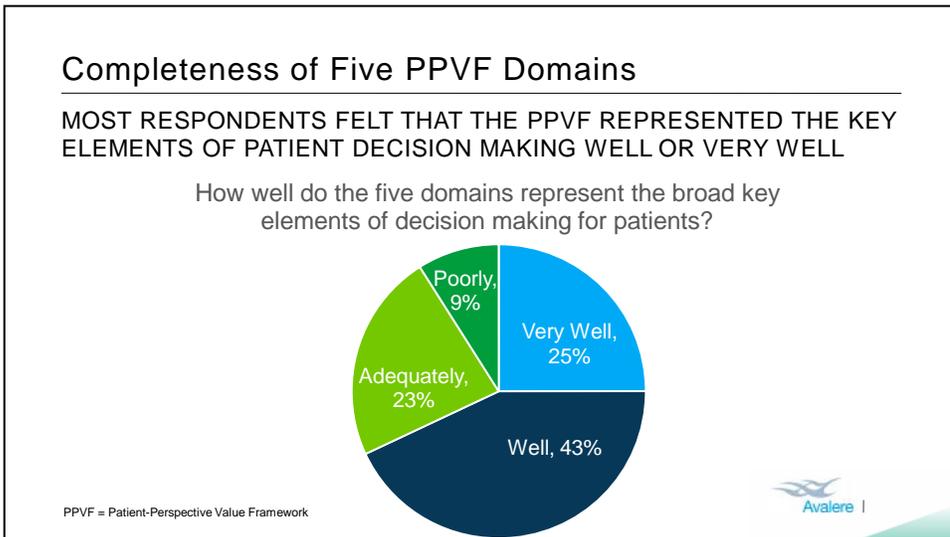
APPENDIX A.

As summarized in Section I. Introduction, we collected input on the draft PPVF from the public through a 45-day public comment period and performed outreach directly to patients and patient advocates. The below slides summarize the high-level findings from these activities that helped inform our updates to the draft PPVF.
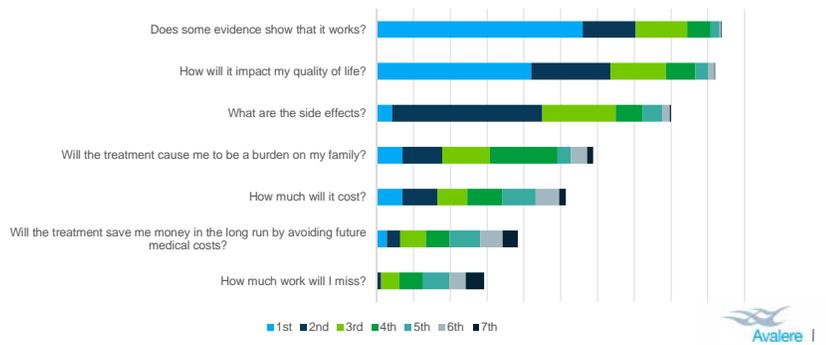
Findings from Public Input
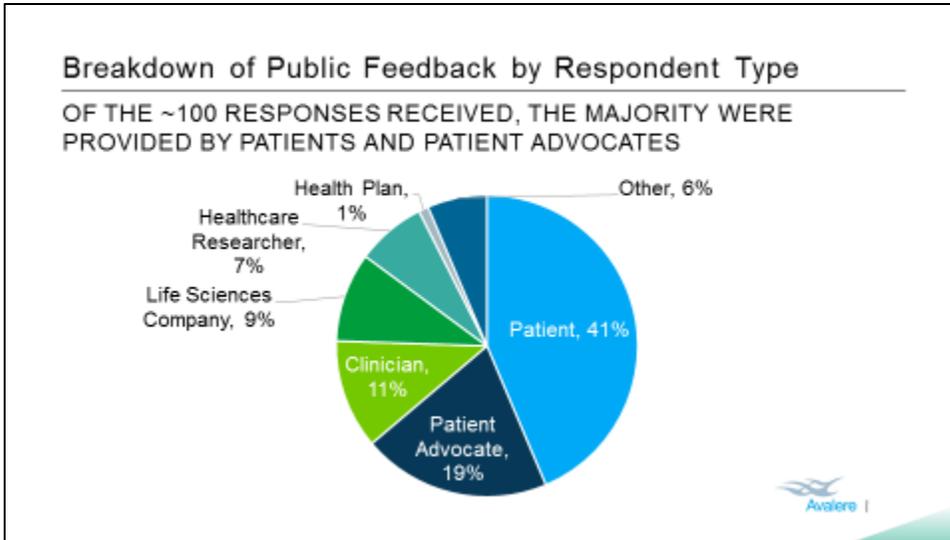
Most Respondents Valued Efficacy/Effectiveness and Quality of Life Most Highly

When you think about a health care decision that you have to make,
what are your most important considerations? (Rank 1 - 7)

Does some evidence show that it works?
How will it impact my quality of life?
What are the side effects?
Will the treatment cause me to be a burden on my family?
How much will it cost?
Will the treatment save me money in the long run by avoiding future medical costs?
How much work will I miss?

■1st ■2nd ■3rd ■4th ■5th ■6th ■7th

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Findings from Outreach with Patient and Patient Advocates
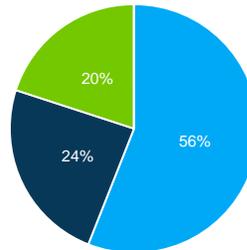

Michael J. Fox Foundation Survey: Participants and Key Findings

WHO PARTICIPATED?*

- 84%
- 12%
- 4%
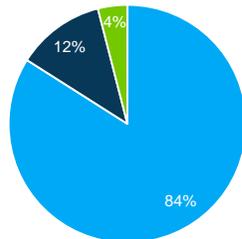
■ Patient
■ Family/Caregiver
■ Other: Community Outreach

REPRESENTATIVENESS OF PPVF DOMAINS?

- 56%
- 24%
- 20%

■ Very Well   ■ Well
■ Adequately   ■ Poorly
■ Very Poorly

*On average, respondents were diagnosed with PD 8 years ago

Avalere |

44

Michael J. Fox Foundation Survey: Key Findings

- Quality of life metrics differed based on disease stage and own definition
- Patient preferences:
  - Patients easily comprehended and actively made decisions about tradeoffs
  - Differed based on the type of treatment under consideration
  - Short-term vs. long-term side effects
- Real world evidence and patient reported data
- Opinions of family members and physicians
- Physician trust and quality
- Ability to access other treatments in the future

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Cancer Support Community Focus Group: Characteristics

8 participants	Mean / # of Participants	Percent
Age (years)	Mean: 58	(Range: 40-67)
Female	7	87%
Non-Hispanic White	5	62%
Black	3	38%
Income <$40,000	4	50%
Associate's degree or higher	5	62%
Employed full or part-time	1	12%
Retired	3	38%
Disability	3	38%
Rural	1	12%
Suburban	2	25%
Urban	4	50%

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Cancer Support Community Focus Group: Key Findings (2 of 2)

- Efficacy vs. Quality of Life
- Short-term side effects vs. long-term side effects
- Does it work for "patients like me"
- Burden on family
- Different care options were associated with the different doctors who presented them

Avalere |

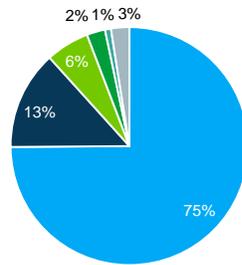## Roundtable with Patient Advocates Hosted by FasterCures: Key Findings

- Patient & Family Financial Considerations: what's covered?
- Quality & Applicability of Evidence domain needs to remain dynamic
- Calculating a timeline for a payer's return on investment
- Physician time is a critical barrier to shared decision making conversations
- An opportunity to coordinate data collection

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American Heart Association/American Stroke Association Survey: Participants and Key Findings

WHO PARTICIPATED?[*]

2% 1% 3%
6%
13%
75%

*On average, respondents were diagnosed with heart disease or stroke 5.7 years ago

- Patient
- Family/Caregiver
- Patient Advocate
- Clinician
- Healthcare Researcher
- Other

REPRESENTATIVENESS OF PPVF DOMAINS?

4%
5%
28%
31%
32%
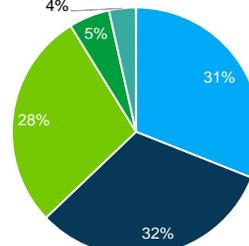
- Very Well
- Adequately
- Very Poorly
- Well
- Poorly

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American Heart Association/American Stroke Association Survey: Key Findings

- Strength of evidence, quality of life, and side effects were most important
  - Between 79% and 88% percent of respondents ranked each of these to be the most or among the most important consideration
- Cost was less important: 50% of respondents said cost was the most or among the most important consideration
- The vast majority of patients strongly considered whether the treatment would cause them to be a burden to their family. Only 5% of respondents indicated that this was not something they consider
- Decision aids will be most helpful at home to discuss with family, during discussions with providers, and at later points in the care journey.

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About Avalere

Avalere is a vibrant community of innovative thinkers dedicated to solving the challenges of the healthcare system. We deliver a comprehensive perspective, compelling substance, and creative solutions to help you make better business decisions. As an Inovalon company, we prize insights and strategies driven by robust data to achieve meaningful results. For more information, please contact info@avalere.com. You can also visit us at **avalere**.com.

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About *FasterCures*

FasterCures, a DC-based center of the Milken Institute, is driven by a singular goal – to save lives by speeding up and improving the medical research system. We focus on cutting through the roadblocks that slow medical progress by spurring cross-sector collaboration, cultivating a culture of innovation, and engaging patients as partners. *FasterCures* brings together all stakeholders across the medical enterprise to ensure inclusion of multiple perspectives in vital cross-disciplinary problem-solving, with the ultimate goal of turning scientific advances into meaningful medical solutions for patients. Through our programs, we identify what's working and what isn't across the research ecosystem and share that knowledge so that every sector – and every patient – can benefit.

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