Coalition *for* Patient Benefit

Patient Benefit: Measuring What Matters to Patients

A Proposal to Shift the U.S. Health Care System from "Clinical Benefit" Metrics to a More Patient-Centered Measurement of "Patient Benefit"

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SUBJECT MATTER EXPERTS

We are grateful to the subject matter experts listed below for their valuable insights and expertise, which significantly enhanced this whitepaper. While these experts and their organizations provided important input that helped shape our direction, the authors maintain sole responsibility for the paper's content. The views and analysis presented here should not be attributed to any of the contributing experts or their affiliated organizations.

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EXECUTIVE SUMMARY

The U.S. healthcare system's reliance on "clinical benefit" as a primary metric for evaluating healthcare interventions often fails to capture outcomes that matter most to patients and their communities. This white paper proposes shifting toward a more patient-centered framework of "patient benefit" to better align healthcare delivery with patient needs and goals.

Key Findings

Through extensive literature review and over 20 hours of interviews with stakeholders across clinical, academic, patient advocacy, and policy domains, this research identified several critical insights:

- Current clinical benefit measurements frequently overlook patient-prioritized outcomes and unmet needs, potentially leading to misaligned incentives in healthcare delivery
- While standardized quality measures exist, they often fail to translate meaningfully to patients' daily lives and goals
- Patient-Reported Outcome Measures (PROMs) offer valuable insights but must be integrated thoughtfully with clinical metrics
- Financial considerations, while important, should be analyzed separately from core patient benefit assessments

Proposed Definition

"Patient Benefit" represents improvement in health-related outcomes that are:

1. Prioritized by patients and their care partners
2. Specific and objectively measurable
3. Expected to improve a patient's wellbeing and/or ability to engage with their communities

A structured process for defining and measuring patient benefit includes:

1. Identifying target patient populations
2. Determining patient and caregiver prioritized outcomes through engagement and validated preference assessment methods
3. Establishing measurement approaches for prioritized outcomes

Challenges and Considerations

Key implementation challenges include:

- Methodological challenges in creating standardized measurements
- Systemic barriers within existing healthcare structures
- Equity considerations in ensuring fair representation across populations
- Need for balance between standardization and flexibility across different contexts

Applications

The patient benefit framework has potential applications across healthcare contexts, including:

- CMS drug price negotiations under the Inflation Reduction Act
- Value-based payment models
- Medical product development and clinical trials
- Coverage decisions and access determinations
- Quality measurement and improvement initiatives

Recommendations

Success in implementing this framework requires:

1. Integration of multiple stakeholder perspectives
2. Balance between standardization and flexibility across disease states
3. Careful attention to equity and access considerations
4. Robust implementation support and commitment to continuous improvement

This shift toward patient benefit measurement represents a critical opportunity to create a more patient-centered healthcare system that better serves the needs of patients, caregivers, and their communities while promoting more efficient and effective care delivery.

INTRODUCTION

In health care contexts, the phrase "clinical benefit" is used to evaluate the performance of our health care system (its products, items, services, treatments, therapies and approaches to improving health outcomes). It frequently focuses on criteria that can only be evaluated through scientific/medical assessment. Such an approach is limiting in that it can miss the unmet needs and outcomes that are meaningful to patients and their communities. Neglecting these critical insights can result in a health care system that fails to meet patient needs. It can create incentives that deprive patients of care that may be meaningful to them, stifle innovation, and generally create economic inefficiencies.

An alternative, more patient-centric approach, could help ensure what actual patients care about most is considered in care decisions, which in turn could dramatically improve the care quality from the patient perspective. As an alternative to use of "clinical benefit," focusing on a way to define "patient benefit" could be a critical area of health care policy development, with implications for improvements in care delivery, outcome measurement, and value assessment.

The following examination of *patient benefit* attempts to define process for determining patient benefit in different health policy contexts. Once patient benefit is established and understood in these systems, we can realign policy incentives to better meet the needs of patients, caregivers, and their communities. This analysis draws from literature and stakeholder interviews and was designed to inform future efforts to create policy solutions.

> "For too long, we've compartmentalized healthcare into silos – clinical outcomes here, patient-reported outcomes there. This fragmentation is not just inefficient; it's detrimental to patient care. We need a new definition of clinical benefit that encompasses both the measurable clinical impacts and the profound effects on a patient's quality of life."
>
> – Patient advocate

METHODS

To better define patient benefit for a policy environment, a literature review and qualitative analysis was conducted. Stakeholder perspectives on patient benefit definitions and implementation approaches across health care contexts were synthesized. Research consisted of two parts:

1. A search of peer-reviewed literature databases, including PubMed, Google Scholar, the New England Journal of Medicine, and JAMA, was conducted using key phrases such as "clinical benefit," "clinical benefit definition," and "patient clinical benefit." The term "clinical benefit" was found to yield the most relevant results. This approach aimed to identify sources that discuss the concept and definition of clinical benefit, focusing on its application in various policy contexts.
2. More than 20 hours of semi-structured interviews were conducted with 14 stakeholders representing three primary groups: clinical/academic experts, patient/advocacy organizations, and research/policy specialists. Conducted between July and September 2024, interview protocols addressed core domains

including benefit definition, measurement approaches, implementation considerations, and cross-population variation[a]. Interviews were structured to better understand the limitations of current policy and the concerns and needs of various stakeholder groups. Study limitations include variable response to standardized questions across stakeholder groups potentially affecting the comprehensiveness of certain analytical domains.

Qualitative analysis of the interview transcripts focused on identifying consensus areas, differences, research gaps, and implementation implications. A synthesis of these findings focused on informing the development and implementation of a standardized definition of patient benefit while maintaining equal consideration of all stakeholder perspectives represented in the source material.

The resulting summary document was then shared with the interviewees to solicit additional feedback and allow them to confirm the accuracy of the report. Most of their feedback was incorporated into a report that then served as a foundation for identifying key stakeholder insights discussed in subsequent sections of the white paper.

LITERATURE REVIEW FINDINGS

Health care and policy literature makes liberal use of the terms "patient benefit," "patient clinical benefit," and "clinical benefit," mostly without defining the terms. In some cases, researchers will create study-specific definitions of these terms. Other studies use definitions of specific clinical outcomes and characterize them as clinical benefit. For example, in studies evaluating cardiopulmonary bypass, one study assessed the clinical benefit of perioperative steroids in decreasing the risk of new onset atrial fibrillation in cardiopulmonary bypass patients.

A few notable examples of more wholistic approaches to measuring clinical benefit exist. The FDA-NIH Biomarker Working Group defines clinical benefit broadly, as "a positive clinically meaningful effect of an intervention, *i.e.*, a positive effect on how an individual feels, functions, or survives."[1] In oncology drug trials, researchers assessed/quantified clinical benefit by using the ESMO Magnitude of Clinical Benefit Scale and the ASCO Value Framework, both of which are tools to assess value of cancer therapies.[2] However, in studies focused on determining the clinical benefit of therapy trials for advanced soft tissue sarcoma, clinical benefit was evaluated by using the European Society of Medical Oncology Magnitude of Clinical Benefit Scale (MCBS). [3]

Are Quality Measures a Proxy for Patient Benefit?

Standardized quality measures, often used in health care systems and payment policies, are also commonly used to demonstrate clinical benefit. In fact, the Medicare program uses quality measures for a variety of policy purposes, including quality payment incentives for physicians. The Battelle Memorial Institute[b] serves as the

[a] See Appendix A
[b] The National Quality Forum was formerly recognized in this role.

federal, consensus-based entity responsible for reviewing and approving quality measures for the Medicare program.

The Agency for Healthcare Research and Quality (AHRQ) identifies three main types of health care quality measures[4]:

Types of Quality Measures

Structural Measures

- Give consumers a sense of a provider's capacity, systems, and processes to provide high-quality care.
- For example:
  - Whether the health care organization uses electronic medical records or medication order entry systems.
  - Proportion of board-certified physicians.
  - Ratio of providers to patients.

Process Measures

- Indicate what a provider does to maintain or improve health.
- Typically reflect generally accepted recommendations for clinical practice.
- For example:
  - Percentage of people receiving preventive services (e.g., mammograms or immunizations).
  - Percentage of people with diabetes who had their blood sugar tested and controlled.
- Can inform consumers about medical care they may expect to receive and can contribute toward improving health outcomes.
- The majority of health care quality measures used for public reporting are process measures.

Outcome Measures

- Reflect the impact of the health care service or intervention on the health status of patients.
- For example:
  - Percentage of patients who died as a result of surgery.
  - Rate of surgical complications or hospital-acquired infections.

AHRQ itself acknowledges at least one limitation in outcomes measures stating that, "while outcome measures may seem to represent the 'gold standard' in measuring quality… an outcome is the result of numerous factors, many beyond providers' control."[4] Risk-adjustment methods—mathematical models that correct for differing characteristics within a population, such as patient health status—can help account for these factors. However, the science of risk adjustment is still evolving. Experts acknowledge that better risk-adjustment methods are needed to minimize the reporting of misleading or even inaccurate information about health care quality.

Despite representing the ideal—the clinical goal of the medical intervention—another challenge of the outcome measure is how it translates to the patient's hopes and desires for the intervention. For example, a successful outcome for a cardiac surgery may be measured by a walk test: does the patient have the endurance to walk for a period on a treadmill at a certain incline. This may seem like an adequate measure of the heart's ability to withstand a degree of exertion, but what does that walk test represent in a patient's everyday life? The results of the walk test must be framed to the patient in terms of their respective goals for recovery (*e.g.*, ability to walk to the car to get to a doctor appointment, ability to cross a soccer field to attend a grandchild's match) and explained prior to intervention to manage patient and caregiver expectations for success. This example demonstrates that any type of quality measure, absent the context of its impact on the patient's daily life, and subject to the user's own assumptions, can be misinterpreted.

Patient-Reported Outcomes Measures

Because standardized quality metrics can be limited in their ability to be directly translated to patient goals and expectations, a body of research has focused on patient-reported outcomes and the need for Patient-Reported Outcome Measures (PROMs). PROMs have been developed alongside quality measures to determine whether an intervention results in a benefit to the patient and to determine how patients feel and function[5]. PROMs are thought to be the sturdiest measure of patient satisfaction since they incorporate outcome measuring tools such as minimal clinically important difference (MCID), patient-acceptable symptomatic state (PASS), and substantial clinical benefit (SCB)[6]. MCID, PASS, and SCB tools provide clinical significance to PROMs by reporting the proportion of individuals meeting measurable thresholds of satisfaction which in turn can translate to whether the intervention showed clinical benefit[7]. However, PROMs and other patient experience scales are not without controversy. Widely used PROMs such as Press Ganey Surveys, opioid pain scales, and Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS), have been known to increase the practice of "teaching to the test" or encouraging providers to focus on the things on which they will be evaluated, sometimes at the expense of patient care.

Additional Research Findings

These observations would suggest that true clinical benefit can only be established when the patient, as a partner in the research and/or treatment process, helps to define the terms against which their outcomes will be assessed. The following are examples of how different (U.S. and international) entities have attempted to include patient needs in their quality assessments[c]:

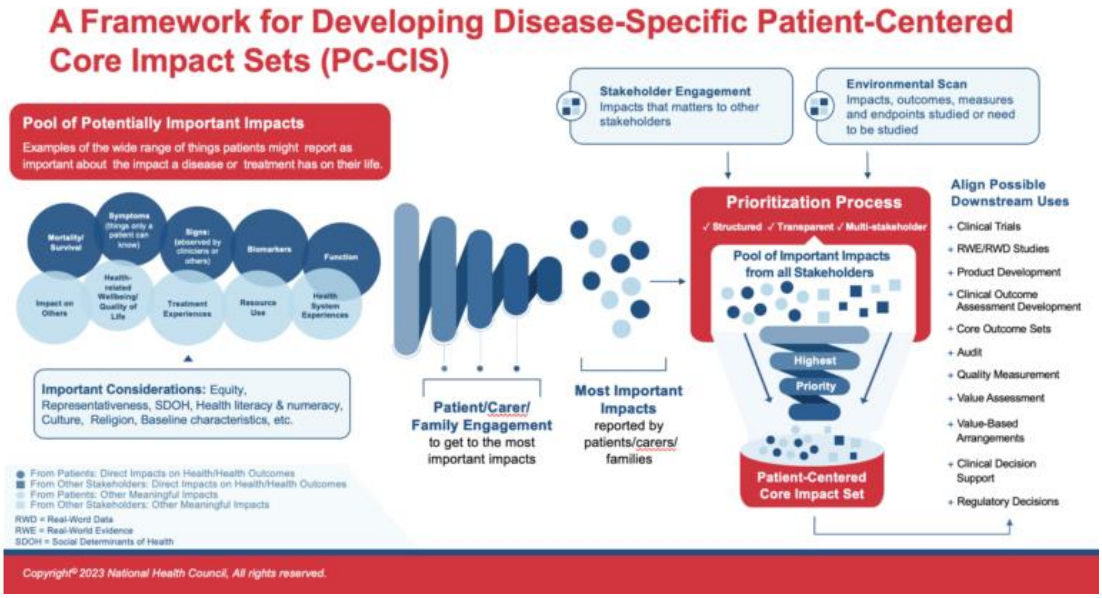
- The International Consortium for Health Outcomes Measurement (ICHOM) was created, to develop "core outcome sets" upon which all stakeholders could refer when defining value.
- A major principle of the Patient Centered Outcomes Research Institute (PCORI)'s requirements for funding research is its "Foundational Expectations for Partnerships in Research." These expectations include ensuring that patients are represented and engaged in every step of research.

- A report from the 2022 Innovation and Value Initiative Methods (now the Center for Innovation & Value Research) Summit acknowledges it is important to go beyond the health gains to measure value and look at the broader societal perspective (impact on caregivers and family members, health equity, and implications of future innovations)[8]. Another study

[c] *This list may not be comprehensive. Inclusion on this list should not be interpreted as endorsement by the authors or supporting organizations*

observed that the inputs of patients and their caregivers are crucial to inform the selection, measurement, and interpretation of outcomes in clinical trials[6].

- The National Health Council has developed a robust approach to developing disease-specific patient-centered core impact sets (PC-CIS)[9]. By far one of the most comprehensive approaches available to date, it informs this project through its comprehensive methods of identifying and prioritizing outcomes through standardized, transparent, and multi-stakeholder techniques. Similarly, the International Consortium for Health Outcomes Measurement (ICHOM) dedicated in part to developing "core outcome sets" upon which all stakeholders could refer when defining value.



- Researchers from Duke University School of Medicine Department of Health Measurement discussed clinically meaningful benefit in the scope of noticeable change versus valuable change. Their study defined noticeable change as a change perceptible to the person or their caregiver. This can be conveyed by verbal communication, of the presence or absence of a symptom, or expression of feelings. Change can be considered valuable if it is worthwhile to the patient or caregiver, which is context dependent. The study proposed to swap the word "meaningful" in clinically "meaningful" benefit as it is too ambiguous and replace it with either "noticeable" or "valuable." The concept of "clinically noticeable benefit" or "clinically valuable benefit" would be a better way to define clinical benefit because it provides clarity to what the measure is. Researchers concluded that when that clarity is achieved, then the input of patients and caregivers in clinical trial objectives, design, analysis, and interpretation can be better incorporated[6].

- In January 2024, a patient advocacy organization, Cancer Support Community (CSC), hosted "A summit on amplifying voices of patients, caregivers, and people with disabilities in Inflation Reduction Act drug price negotiations.[10]" The summit, which was funded, in part, by pharmaceutical companies, explored the topic of "clinical benefit" or "patient benefit" and IRA drug price negotiations. Panelists and participants established that "what is important to patients should be included in a drug's value. CMS should use data about what patients value when defining a drug's 'clinical benefit.' CMS should also create an ongoing process to include voices of patients and providers in valuing drugs." The session also leveraged and inspired further research into "possible unintended consequences of the IRA and a framework of patient

engagement with CMS to mitigate concerns surrounding the implementation of the Medicare Drug Price Negotiation Program," and concluded that, "this framework, centering on a 2-way dialogue of patient and caregiver experience data and feedback, should be used by CMS to create a transparent, patient-centered, and successful implementation of the Medicare Drug Price Negotiation Program under the IRA.[8]"

- The European Medical Device Regulation (EU MDR) provides a definition of "clinical benefit" that acknowledges the opportunity to recognize patient-centric metrics: "the positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s), related to diagnosis, or a positive impact on patient management or public health.[11]"

STAKEHOLDER FEEDBACK

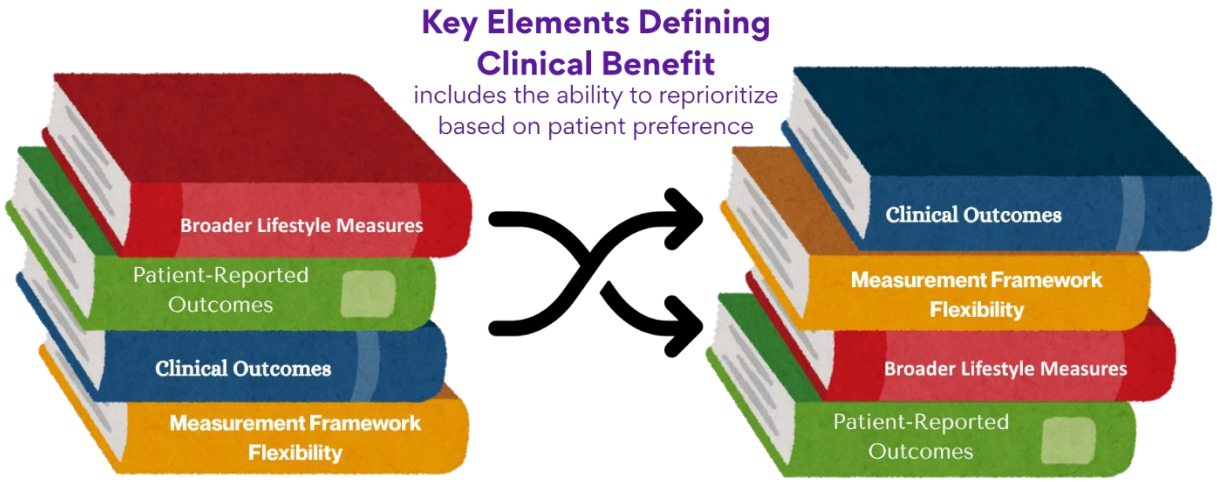
Key Elements and Criteria for Patient Benefit

With this understanding of how the literature evaluates clinical benefit, stakeholder interviews were conducted to better understand what should constitute a new "patient benefit" definition. Interviewed stakeholders broadly agreed that a comprehensive definition of patient benefit must incorporate both clinical measures and patient-reported outcome measures[12]. Clinical outcomes form a foundational component, encompassing traditional medical metrics, disease-specific indicators, and standardized assessment tools. Patient-reported outcomes evaluate changes in patient experience including symptom improvement, functional ability changes, quality of life impacts, and treatment satisfaction. Even beyond patient-reported outcomes, however, patient advocacy organization stakeholders particularly stressed impact measures, focusing on effects on daily activities, work productivity, and social participation. Their emphasis highlights the importance of making room in the health care system to acknowledge patients' experiences and address otherwise unmet, or even unacknowledged, needs.

> "Patient clinical benefit should be defined by patients themselves, focusing on outcomes that matter to them. This goes beyond just medical outcomes to include impacts on quality of life, ability to work, caregiving responsibilities, and treatment accessibility. Patient preferences and experiences should drive the definition of clinical benefit, not just be factored in at the end. However, the definition may need to be nuanced based on different contexts, such as hospitals, payers, or clinical guideline developers."
>
> – Physician society

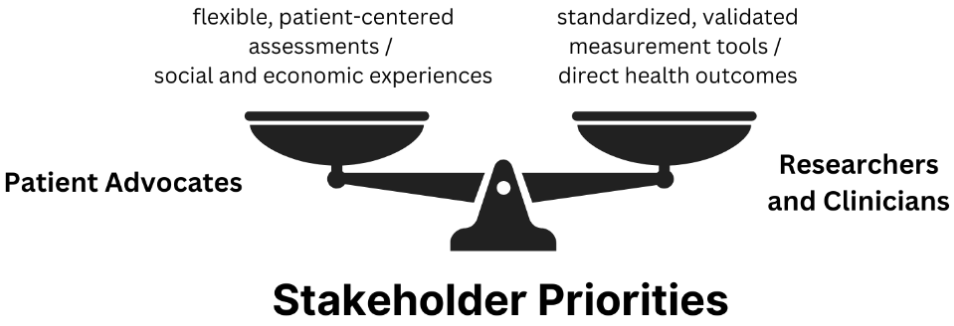
The analysis revealed framework flexibility as a critical consideration, with stakeholders supporting frameworks that preserve core principles while accommodating condition-specific variation. Population considerations emerged as significant, with emphasis on accounting for demographic and socioeconomic factors in framework development.

> "Applying a standard across different contexts will be challenging. For example, if a standard = average across multiple groups, that might create problems with issues related to subgroups' diversity. Perhaps applying different timelines or windows of time/measurement may be ways to differentiate measurement between different healthcare contexts. Regardless, you should include patients in this process, and we would be happy to be considered a partner to help convene patients to weigh in on this project."
>
> – Patient organization



Key Stakeholder Differences

Key differences emerged across stakeholder groups in three areas: measurement priority, scope of inclusion, and implementation focus. Research and clinical stakeholders emphasized standardized, validated measurement tools, while patient advocacy representatives favored flexible, patient-centered assessments. The scope of relevant criteria varied from direct health outcomes to broader social and economic factors. Clinical stakeholders concentrated on practical measurement considerations, while policy representatives prioritized systematic application across health care contexts. All stakeholders acknowledged that quantitative patient preferences could balance the demands for standardized approaches with accommodation of domains beyond traditional biometric measures.



Financial Considerations and Economic Impact Not Included

Analysis of stakeholder interviews revealed nuanced perspectives on incorporating financial impacts into the definition of patient benefit, without reaching clear consensus. While stakeholders broadly recognized that patient financial factors, including financial stress, significantly influence treatment adherence and outcomes, they advocated for separating financial considerations from the core definition of patient benefit. Health economists subsequently suggested that financial considerations should be analyzed separately from the core benefits assessment. Their recommendation positioned financial aspects as part of traditional cost analyses, incorporating patient and family financial burdens alongside health care system and societal costs, rather than integrating them into the fundamental definition of patient benefit.

Challenges and Required Practice Changes

Many stakeholders expressed concerns with how patient benefit information might be used. Clinical stakeholders, fearing they might be held responsible for metrics over which they had no, or little, control, emphasized practical measurement and decision-making changes, proposing a dual-track approach where providers and patients select key measures while adhering to evidence-based core outcomes. Research stakeholders focused on methodological adaptations, noting how standardization could enhance cross-disease comparative analysis.

> "If patients are going to go to the effort of contributing to a process designed to assess patient clinical benefit, it better be used."
> – Patient advocate

Core Considerations

System adaptation emerged as a primary concern, emphasizing modified measurement systems, updated decision processes, and enhanced stakeholder engagement. Process changes received significant attention, focusing on workflow procedures, documentation requirements, and decision protocols. Success would require attention to both technical and cultural organizational changes.

Key Areas for Practice Change

For successful integration, three fundamental areas require systematic change. Measurement system adaptation requires developing dual-track systems capturing both provider-selected and patient-selected metrics while maintaining validity. Decision-making reform necessitates restructured clinical processes that integrate standardized assessments while preserving flexibility. Stakeholder engagement requires new organizational structures facilitating meaningful input while maintaining operational efficiency.

Implementation Framework

> "There is a great fear of "what are you going to do with the information?" Points of happiness/dollar as a threshold makes people nervous. You are going to get a lot of pushback from clinicians because it will always come down to money. You need to start with the: "Why are we doing this? What is it going to be used for? What is it going to change?" Need a clear set of expectations of what we can expect coming from this approach."
>
> – Hospital executive/clinician

Successful implementation requires development of comprehensive measurement frameworks accommodating both standardized and customized metrics, creation of flexible decision-making protocols preserving clinical autonomy, and establishment of robust stakeholder engagement mechanisms.

Stakeholders should have agency in every phase of testing and adoption. Model development must prioritize patient engagement on the patient groups terms. Solicitation of patient feedback must not be overly demanding, intimidating, or burdensome and researchers should implement a number of feedback mechanisms to meet patients where they are. Interviews, surveys, virtual and in-person meetings are all options for stakeholder engagement.

Furthermore, to ensure that patient benefit can be adapted across policy settings, an incremental approach to model development and testing will be required. Separate workstreams should evaluate the validity of the patient benefit process definition within specific disease states, demonstrate the questions that will need to be addressed in different policy environments, identify different stakeholder needs and inputs, and identify new research questions.

DEFINING PATIENT BEENFIT

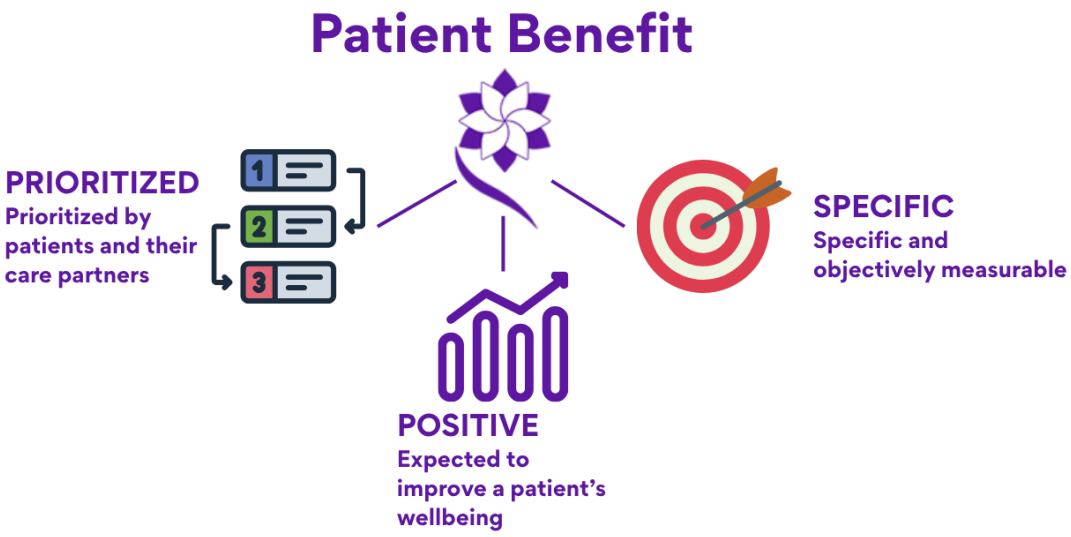
Based on the research conducted for this project, it is clear that "patient benefit" cannot be a standard definition applicable to all patients and disease states. Rather, we must endeavor to define a standard against which to measure the *process* of evaluating patient benefit. This standard can then be included in different environments like clinical research, physician payment incentives, coverage decisions, and even price negotiations. What ultimately becomes the measure of benefit for each patient population within each of these contexts will vary based on the perspectives of the population it impacts (and, as the process is refined, each subpopulation).

At the end of the process, the patient community will determine:

"Patient Benefit" is improvement in health-related outcomes that are:

1. Prioritized by patients and their care partners.
2. Specific and objectively measurable.
3. Expected to improve a patient's wellbeing and/or ability to engage with their communities (*e.g.*, home, work, neighborhood, society).

This improvement encompasses positive impact on outcomes like quality of life, functional ability for patients to engage with their community, and well-being in ways that matter to patients. These outcomes include all relevant outcomes, including those measured through traditional biometrics (typically "clinical outcomes") and patient-reported outcomes.

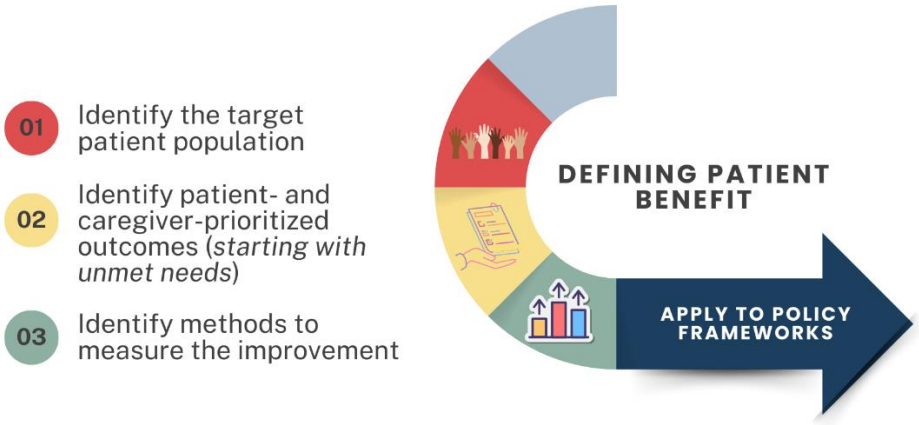


Process for Defining Patient Benefit

To reflect the patient communities' evolving goals and needs, defining patient benefit needs to be an iterative process that refreshes on a regular basis to ensure it accounts for immediate and long-term impacts on patients' lives while demonstrating responsiveness to evolving patient goals and needs. The process would include:

1. Identifying the target patient population for the item, therapy or service to be evaluated for use in the health care setting.
2. Identifying patient and care giver prioritized outcomes:
    a. Through engaging and collaborating with patients and their communities identified in step 1, identify all the health-related outcomes that matter to them and their care partners, starting with unmet needs.
    b. Using scientifically validated approaches, assess the relative priorities and weights of each outcome through quantitative patient preference methods.
    c. Through engaging and collaboration with patients and their communities, establish a focused set of health-related outcomes that can be measured.
3. Identifying methods to measure the improvement in the prioritized outcomes.

Out of scope of this process and definition includes financial metrics impacts, including costs to the health care system or the individual patients and their care partners. While these factors can be considerable factors in the outcome of a potential treatment or service, they can more adequately be quantified through health economics methods.



Challenges in Creating a Standardized Definition

There are many challenges in implementing this process for developing, quantifying and measuring patient benefit. While it would be easier to come up with one definition of patient benefit, all stakeholders acknowledged in our research the importance and challenges related to heterogeneity of patient populations and the related need for equity and representation in efforts to standardize a process for determining patient benefit. Concerns will persist about this approach, including:

- Methodological Challenges: Technical challenges in creating standardized measurements and metrics that could be consistently applied while maintaining validity across different contexts.
- Implementation Barriers: Systemic barriers related to existing health care structures and processes.
- Equity Considerations: Challenges related to ensuring fairness and representation of diversity of people and their perspectives, particularly as it relates to disadvantaged populations.

> A better, more standardized approach would help inform healthcare decisions. Without it, we are using more subjective measures that are subjected to political influence or arguments not based in evidence. A standardized approach makes the decisions more legitimate and comparable."
>
> – Health economics researcher

RESEARCH NEEDS AND FUTURE DIRECTIONS

The analysis revealed several critical areas requiring further research attention. Methodology development emerged as a primary need, particularly regarding validated measurement tools that can effectively combine objective and subjective measures while maintaining scientific validity. Implementation research received significant attention, with emphasis on investigating best practices for measurement programs and analyzing effective evaluation methods. Evidence standards development emerged as a critical research priority, particularly regarding frameworks for evaluating non-traditional evidence sources and methods for combining different types of preference data.

CONCLUSIONS AND RECOMMENDATIONS

The comprehensive analysis reveals that while developing and implementing a standardized definition of patient benefit presents significant challenges, substantial agreement exists on core principles and approaches. Success requires attention to both technical and human factors, particularly emphasizing multiple perspective integration, balance between standardization and flexibility across disease states, attention to equity and access, and commitment to continuous improvement in implementation.

Applications for Use: Near and Long Term

A standard and consistent definition of patient benefit has multiple potential applications across health care systems. In regulatory and payment contexts, applications include CMS guidance for drug price negotiations, value assessment models incorporating patient preferences, and risk adjustment in payment models. For medical product development, the definition could drive evidence development on patient-centered outcomes, standardize clinical trial outcome measures, and reduce market inefficiencies due to development risks. This definition can also be used to better demonstrate the benefit of expanded access to covered interventions in various patient populations.

In clinical settings, applications extend to comparing outcomes across institutions with different patient populations and enhancing bundled payment models to understand intervention value across settings. Within specific practice areas, the definition could transform primary care by shifting focus from standardized metrics to personalized care planning, while in cancer care, it could better address evolving patient goals throughout treatment progression.

The following patient stories illustrate how current healthcare policies, focused on narrow clinical metrics, often fail to capture the full scope of patient experiences and needs. Each case demonstrates how traditional measures of medical success can overlook crucial quality-of-life impacts, caregiver burden, access barriers, and other real-world challenges that profoundly affect patients and their families. These examples highlight the critical importance of expanding our understanding of patient benefit beyond conventional clinical outcomes.

- A construction professional with COPD faces severe quality-of-life limitations in basic daily activities despite medication successfully reducing their hospital visits, highlighting how clinical success metrics fail to capture the erosion of independence and dignity
- A caregiver to a child with cystic fibrosis sacrifices their career and personal wellbeing to manage complex daily treatments, demonstrating how therapeutic success measurements overlook the substantial burden on family care providers
- A patient with a rare genetic disorder experiences devastating but intermittent neurological symptoms that disrupt their professional life, yet these symptoms are classified as "non-consequential variations" because they don't fit standard clinical assessment frameworks
- A cancer survivor achieves clinical remission but faces devastating cognitive impacts from treatment that end their engineering career, revealing how traditional recovery metrics fail to account for long-term professional and quality-of-life outcomes
- A public health professional encounters systematic barriers to accessing HIV prevention medication despite clear risk factors, illustrating how clinical authorization criteria can fail to recognize individual patient circumstances and community vulnerability
- A rural patient faces multiple non-clinical barriers to receiving breast cancer screening, including transportation challenges and cultural factors, demonstrating how traditional healthcare metrics fail to capture access limitations
- A young patient with a rare neurological condition is denied access to a promising international treatment because marginal improvements in clinical trials don't meet standard statistical thresholds, despite the treatment's potential to preserve critical quality-of-life functions

CASE STUDY: POTENTIAL USE OF PATIENT BENEFIT IN IRA DRUG PRICE NEGOTIATIONS

Medicare Part D, the Medicare prescription drug benefit, has existed since the passage of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. However, it wasn't until passage of Inflation Reduction Act of 2022[13] (IRA) that the Medicare program had the ability to create a process to engage with manufacturers directly regarding the Medicare price for prescription drugs. Unlike private health plans that employ various tools and third parties to leverage their purchasing power to lower costs, CMS had no authority to engage with drug companies in a negotiation process. When the IRA was passed, CMS had to articulate how it would implement its new powers.

In a series of guidances published in the months following passage, CMS outlined its priorities and procedures for the complicated negotiations. One such guidance document conveyed CMS' intention to consider clinical benefit as a part of the process:

> To evaluate the clinical benefit conferred by the selected drug compared to its therapeutic alternative(s), as applicable, CMS will broadly evaluate the body of clinical evidence, including data received from the public and manufacturers as described in section 50.2 of this revised guidance, and data identified through a CMS-led literature review. CMS may also analyze Medicare claims or other datasets for utilization patterns of the selected drug versus its therapeutic alternative(s), clinical data, or other information relevant to the selected drug and its therapeutic alternative(s) and may consult with clinicians, patients or patient organizations, academic experts, and/or the FDA. As described in section 60.4 of this revised guidance, CMS will provide additional engagement opportunities for interested parties—specifically, meetings with manufacturers and patient-focused listening sessions—after the October 2, 2023, deadline for submission of section 1194(e)(2) data (further described in section 60.4 of this revised guidance).
>
> This approach provides a pathway for CMS to consider the multitude of information expected from public input, including but not limited to peer-reviewed research, expert reports or whitepapers, clinician expertise, real-world evidence, and patient experience. This approach also provides flexibility for CMS to consider multiple perspectives on the clinical benefit (emphasis added) of the selected drug and its therapeutic alternative(s), including potential risks, harms, or side effects, and any unique scenarios or considerations related to clinical benefit, safety, and patient experience[14].

The CMS approach was notable in that regulators identified the value of clinical benefit and wanted to capture that information in the drug price negotiations. Equally notable, however, was CMS' inability to identify how exactly clinical benefit would be determined or expressed, and how it would impact the negotiation process.

But these are just a few of the flaws in how CMS failed to adequately define and incorporate clinical benefit into its IRA implementation. Despite the positive intentions of the patient listening sessions identified in the June 2023 guidance, CMS failed to properly capture patient and caregiver feedback. Even with resources like recommendations from The Partnership to Improve Patient Care (PIPC) for a process centered on patients and people with disabilities[15], CMS preceded with a series of patient listening sessions that received considerable criticism for their lack of opportunities for patient and caregiver feedback, and poor execution[16]. Ostensibly responding to criticisms, CMS shifted its approach to holding only one public listening session and a series closed-door meetings with patient stakeholders. This change only adds to existing concerns about the lack of transparency in the price "negotiation" process. Despite being implemented in good faith, the IRA patient listening sessions and closed-door meetings were ineffective and potentially burdensome to the patients they hoped to reach.

Using the proposed process for determining patient benefit (instead of clinical benefit) for CMS evaluation of drugs in the IRA price negotiation process, CMS and stakeholders could have collaborated with relevant patient organizations, drug manufacturers and other key stakeholders to:

1. Identified the target patient population(s) for each drug and its therapeutic alternative (arguably already determined based on the FDA label, but consideration should be made for off-label uses as well as updates to clinical practice guidelines and real-world evidence). CMS could consider setting diversity and inclusion goals for this process, not unlike FDA's approach in clinical trial recruitment efforts.[17]

2. Identify patient and care giver prioritized outcomes by:
    a. Working in partnership with patient advocacy organizations, engage and collaborate with patients and their communities (identified in step 1) to identify all of the health-related outcomes and unmet needs that matter to them and their care partners. This could be done by:
        i. Leveraging existing, published information (if available) on outcomes related to the disease/condition and their therapeutic alternatives, particularly the therapeutic alternative to which CMS will be comparing the chosen drug
        ii. Holding patient advisory board sessions and conducting surveys with patient communities
        iii. Collecting qualitative and quantitative research already conducted with patients and their care partners related to the condition identified in step 1

    b. Using scientifically validated approaches, assess the relative priorities and weights of each outcome through quantitative patient preference methods. If not already available, this could be done by conducting an online survey of patients and their communities using a best-worst scaling method,[18,19] to assess the patient community's priorities and relative weights of each outcome, broken down by subpopulations to determine if priorities differ between patient populations.

c. Through engaging and collaboration with patients and their communities, CMS and stakeholders could review the results of the surveys and agree to an established set of health-related outcomes that can be measured.

3. Identify methods to measure the improvement in the prioritized outcomes.
    a. CMS or other stakeholders could identify the metrics that could be used to evaluate a drug's performance in addressing each of the health-related outcomes identified in step 2.
    b. Ideally at the stage of price negotiations under the IRA, techniques or methods to evaluate a drug based on the health-related priority outcomes identified in step 2 would already exist. However, should metrics not be available, CMS and stakeholders could work with sponsors to identify ways to identify or develop such measures and evaluate the drug's performance on those measures.

CASE STUDY: CALCULATING PATIENT BENEFIT AND PHYSICIAN PAYMENT

Under fee-for-service payment systems like Medicare, health care providers are paid a set rate for a specific service and therefore have an incentive to provide more care, if not necessarily better or more efficient care. Value-based payment (VBP) is intended to change that incentive structure with the goal of giving patients access to the right care at the right time, every time. Based on a simple formula: value equals measured health care quality divided by accrued cost, VBP is also intended to help "bend the cost curve," slowing the exponential rate of growth in health care spending year-over-year. Unfortunately, to date, the VPB experiment has not played out as well as policymakers had hoped.

$$\text{VALUE} = \frac{\text{QUALITY}}{\text{COST}}$$

The VBP system needs to improve how it measures quality across health care settings, medical specialties, or different patient needs. This has resulted in lack of uniformity in quality measurement and inconstant participation in quality assessment models. Instead of utilizing the best of this health care quality science, CMS has tried to retrofit robust quality measurement into previously conceived notions of payment and incentives. VBP systems also assume that providers can control all factors that might increase care costs, even when they have no insight into the actual cost of the care they provide. Instead, VBP programs tend to assume that quality care is always less expensive and therefore do not adequately accommodate treatment plans that demand more expense. They rarely account for the up-front costs of innovation and/or the opportunity for cost savings from reduction in hospitalizations or additional interventions, and establish a disincentive for providers to adopt more innovative and potentially more effective (and potentially less costly) treatment options.

Under these conditions, providers are left with very few options to achieve positive value scores—scores that are directly linked to their level of reimbursement. As such, providers who have no meaningful way to influence a stagnating quality numerator have to find a way to cut costs in order to get paid. Faced with exponentially increasing costs that are outside their control, they must either take pay cuts and accept Medicare penalties or to ration necessary care, refuse to see Medicare patients, or avoid complex/high risk/outlier patients.

Current VBP policy not only needs to make progress in its execution, but it must also improve conceptually. VBP assumes that all patients experience quality care in the same way. The needs of patients and caregivers change over time, and it makes sense that two individuals might experience the same events in entirely different ways, yet policy consistently dictates that patient feedback is static and standardized.

Because of these issues, we can expect policy makers to take another look at Medicare physician payment reform in the next few years. During this debate, there is opportunity to lean on this critical patient benefit research and help Medicare physician payment to ask the questions: "Value to whom?" and "Why?" Rather than making tweaks to resolve the litany of VBP implementation obstacles, we have

to look at the entire value-based ecosystem; we must change the inputs and relative weights of the variables in the value equation to prioritize *patient benefit*.

One approach is to redefine the Q(uality) in the Q/C(ost) equation to PB(patient benefit)/C(ost). By giving weight to the care and outcomes that patients and caregivers care about the most, we can use the payment system to incentivize the right care at the right time, every time. This model will require a more hands-on approach to care planning, emphasizing the importance of frequent, candid conversations about patient experiences and expectations. However, by reweighting the inputs in the value equation, we obviate the need to retrofit incentives to prop up the beleaguered primary care providers at the expense of proceduralists. Only then will we be able to test the hypothesis that a Medicare program that pays for appropriate and desired care can result in a system that incentivizes the provision of the best, most efficient, and cost-effective care.

CASE STUDY: COVERAGE WITH EVIDENCE DEVELOPMENT FOR MEDICAL DEVICES

The Centers for Medicare & Medicaid Services (CMS) is tasked with making coverage decisions for new medical technologies based on whether they are "reasonable and necessary" for Medicare beneficiaries. While CMS's mandate is distinct from that of the Food and Drug Administration (FDA), there is ongoing debate about how CMS should approach coverage for FDA-approved technologies, particularly in cases where evidence may be limited or inconclusive for the Medicare population. CMS's current approach to evaluating new technologies primarily focuses on clinical outcomes and may not fully capture the holistic patient experience. Values such as incremental functional improvements, or delays in disease progression, or even the benefit that hope for just a little more time are often not explicitly factored into coverage decisions. This gap in assessment may lead to coverage determinations that do not align with patient priorities and expectations.

Coverage with Evidence Development (CED):
In cases where evidence is insufficient to meet the "reasonable and necessary" standard, CMS may implement Coverage with Evidence Development (CED) policies. Under CED, coverage is provided with specific constraints while additional evidence is collected. This approach has been used to allow Medicare beneficiaries to access new treatment options while gathering of real-world data to inform future decision-making. In 2012, CMS coined a phrase that helps to define the circumstances under which CED might be employed, saying that frequently CMS is challenged to cover “items and services when the expectations of interested parties are not adequately supported by the existing evidence base.”

Patient Benefit can be used to address the limitations of the current system, by incorporating patient experience factors into CMS coverage decisions, complementing traditional clinical outcome measures. By incorporating patient benefit into coverage decisions, CMS could:

- Make more nuanced and patient-centered coverage determinations.
- Align coverage policies more closely with patient priorities and values.
- Provide a clearer framework for evaluating technologies where traditional clinical endpoints may be limited or not fully representative of patient benefit.
- Encourage the development of technologies that prioritize patient experience alongside clinical efficacy.

Patient benefit represents a significant opportunity to enhance the agency's ability to make truly patient-centered determinations. By explicitly valuing and measuring aspects of patient experience beyond traditional clinical outcomes, CMS can ensure that its coverage policies more accurately reflect the priorities of the beneficiaries it serves. This approach could lead to more comprehensive, nuanced, and ultimately more beneficial coverage decisions for Medicare patients.

APPENDIX A: INTERVIEW GUIDE: DEFINING PATIENT BENEFIT

Introduction:

Thank you for participating in this interview. We're conducting research to develop a clear, consistent, patient-based definition of “clinical benefit,” which we're terming “patient benefit.” This definition aims to measure success throughout all stages of health care delivery, including innovations considered for price negotiation under the Inflation Reduction Act.

Core Questions on Patient Benefit

- How would you define "patient benefit" in your own words?
- What key elements or criteria do you believe should be included in a comprehensive definition of patient benefit?
- How do you think patient preferences and experiences should be factored into this definition?
- How can we balance clinical outcomes with patient-reported outcomes when defining clinical benefit?
- What challenges do you foresee in creating a standardized definition of patient benefit that can be applied across different health care contexts?
- How do you think the financial impact of positive patient experiences should be considered in the definition of patient benefit?
- Can you share any examples from your experience where a clear definition of patient benefit would have been particularly useful?
- How do you think the definition of patient benefit might vary across different patient populations or disease states?
- How does your organization currently measure or evaluate clinical benefit?
- What changes would you need to make in your practices if a standardized definition of patient benefit were implemented?
- How do you think a clear definition of patient benefit could impact health care decision-making?

Wrap-up

- Are there any specific studies, reports, or data sources you would recommend we review to inform our understanding of patient benefit?
- Can you suggest any other experts or stakeholders we should consider interviewing on this topic?
- Is there anything else you'd like to add about patient benefit that we haven't covered?

APPENDIX B: DEFINING PATIENT CLINICAL BENEFIT: A STAKEHOLDER ANALYSIS

Executive Summary

This analysis synthesizes stakeholder perspectives on defining, measuring, and evaluating patient clinical benefit across health care contexts. Through systematic examination of more than 20 hours of interview responses from key clinical/academic, patient/advocacy organization, and research/policy stakeholders, we present a draft integrated framework for understanding and implementing patient clinical benefit assessment. The analysis reveals both the complexity of developing standardized definitions and the critical importance of incorporating diverse stakeholder perspectives, while highlighting opportunities for meaningful progress through structured implementation approaches.

Introduction

The phrase "clinical benefit" appears in a number of health care contexts and is frequently used to focus on a specific set of benefits that can only be determined through scientific/medical assessment. But the phrase is used in several policy settings in which a broader, more "patient-centric" definition could dramatically improve the health care system by improving coordination of care, focusing disparate stakeholders on a common objective and purpose.

The examination of patient clinical benefit represents a critical area of health care policy development, with implications for improvements in care delivery, outcome measurement, and value assessment. This analysis draws from stakeholder interviews addressing three core areas: defining clinical benefit, current measurement practices, and the integration of patient preferences and experiences.

> *"For too long, we've compartmentalized healthcare into silos – clinical outcomes here, patient-reported outcomes there. This fragmentation is not just inefficient; it's detrimental to patient care. We need a new definition of clinical benefit that encompasses both the measurable clinical impacts and the profound effects on a patient's quality of life." – Patient advocate*

Method

This qualitative analysis synthesized stakeholder perspectives on patient clinical benefit definitions and implementation approaches across health care contexts. More than 20 hours of semi-structured interviews were conducted from July through September 2024 with 14 stakeholders representing three primary groups: clinical/academic experts, patient/advocacy organizations, and research/policy specialists. Interview protocols addressed core domains including benefit definition, measurement approaches, implementation considerations, and cross-population variation. Response coverage varied across questions, with stronger representation from clinical/academic and patient/advocacy perspectives and more limited input from research/policy stakeholders. Insights were cross-referenced

between questions to identify recurring themes and relationships. A formal analytical framework was applied to examine consensus areas, differences, research gaps, and implementation implications. Limitations include variable response coverage across stakeholder groups and questions, potentially affecting the comprehensiveness of certain analytical domains. The synthesis focused on informing the development and implementation of standardized definitions while maintaining equal consideration of all stakeholder perspectives represented in the source material.

"Improvement in health-related outcomes that are:
1) Prioritized by patients and caregivers
2) Specific and objectively measurable
3) Expected to improve a patient's wellbeing and/or ability to engage with their communities (home work, neighborhood, society) "

Defining Patient Clinical Benefit

Through synthesis of stakeholder perspectives, a proposed definition of "Patient Clinical Benefit" can be:

This definition encompasses positive impact on:

- quality of life
- functional ability to engage with their community
- and well-being

in ways that matter to patients, supported and validated through quantitative patient preference metrics that incorporate perspectives of all outcomes, including those measured through traditional biometrics (typically "clinical outcomes") and patient-reported outcomes. It accounts for immediate and long-term impacts on patients' lives while demonstrating responsiveness to evolving patient goals and needs.

> *"Patient clinical benefit should be defined as outcomes that allow the patient and caregiver to function and interact with their community (home, work, neighborhood, society), as defined by the patient/caregiver. Clinical (biometrics) and functional (e.g., walking) endpoints are means to the end. We are too often using proxies for what people really want and need." – Patient advocate*

What follows is a more detailed analysis of the input from key stakeholders in developing this definition.

Core Thematic Elements

Several fundamental themes emerged across all interview responses. The most persistent theme was the need to integrate objective clinical measures with subjective patient experiences. This appeared prominently in definitions, measurement approaches, and implementation considerations. Stakeholders consistently emphasized that these elements should not be viewed as competing factors but as complementary components of a comprehensive assessment system.

> *"A better, more standardized approach would help inform healthcare decisions. Without it, we are using more subjective measures that are subjected to political influence or arguments not based in evidence. A standardized approach makes the decisions more legitimate and comparable." – Health economics researcher*

On the other hand, a recurring tension emerged between the need for standardized definitions and the need for flexibility across different fields. This theme manifested in discussions of population variations, implementation challenges, measurement approaches, and practice changes.

Finally, considerations of equity and access emerged across multiple questions, particularly in financial impact considerations, population variations, implementation challenges, and additional insights.

Challenges in Creating a Standardized Definition

Patient advocacy stakeholders emphasized challenges related to equity and representation in standardization efforts. Some interviewees were concerned that a standardized definition of clinical benefit across populations—and the potential for baking that into policy—has the potential for negative implications. Therefore, from a patient perspective, it is absolutely critical there be a process for defining clinical benefit that is adaptable to different conditions and patient populations before considering its use in policy. Their responses also highlighted concerns about developing a definition that adequately addresses disparities in how diseases impact different demographic groups while remaining practical for implementation. These stakeholders particularly emphasized the risk of creating definitions that might inadvertently disadvantage certain patient populations or fail to account for important cultural and socioeconomic factors.

Clinical stakeholders focused on measurement and implementation challenges, emphasizing concerns about how standardized definitions might affect payment systems and public reporting. They highlighted potential resistance from clinicians and patients when standardized measures don't fit specific situations. These stakeholders also expressed concern about the risk of focusing too narrowly on measured outcomes at the expense of other important factors.

Research and policy stakeholders emphasized the technical and methodological challenges of standardization. They highlighted the difficulty of creating measures that work across different populations and disease states while maintaining scientific validity. These stakeholders particularly noted the challenge of balancing the need for standardization with the reality of diverse health care contexts.

Analysis of the responses revealed three key challenges:

1. Methodological Challenges: The vast majority of stakeholders identified significant technical challenges in creating standardized measurements. Most emphasized the difficulty of developing metrics that could be consistently applied while maintaining validity across different contexts.
2. Implementation Barriers: All stakeholders recognized substantial practical challenges in implementing standardized definitions. Most identified systemic barriers related to existing health care structures and processes.
3. Equity Considerations: Most stakeholders emphasized challenges related to ensuring fairness and representation in standardized definitions. Some particularly highlighted concerns about disadvantaged populations.

Key Elements and Criteria for Patient Clinical Benefit

The vast majority of stakeholders agreed that any comprehensive definition must include both objective clinical measures and patient-reported outcomes. Clinical outcomes emerged as a fundamental component, encompassing traditional medical metrics, disease-specific indicators, quality measurement instruments, and standardized assessment tools. Patient-reported outcomes were equally emphasized, including symptom improvement, functional ability changes, quality of life impacts, and treatment satisfaction.

Broader impact measures received significant attention, particularly from patient/advocacy organization stakeholders, who emphasized the importance of considering impacts on daily activities, work and productivity effects, family and caregiver considerations, and social participation levels.

Significant differences emerged in several areas:

1. Measurement Priority: Research/clinical stakeholders tended to prioritize standardized, validated measurement tools, while patient advocacy representatives emphasized the need for more flexible, patient-centered assessment approaches.
2. Scope of Inclusion: Variations existed in how broadly stakeholders defined relevant criteria. Some focused primarily on direct health outcomes, while others advocated for including broader social and economic factors.
3. Implementation Focus: Clinical stakeholders emphasized practical measurement considerations, while policy representatives focused more on systematic application across health care contexts.

All stakeholders acknowledged that quantitative patient preferences may provide a balance between the demands of clinicians and researchers for standardized approaches to prioritizing outcomes and the desire amongst patient organizations and policy experts to accommodate domains beyond traditional biometric measures.

Based on the stakeholder responses, a comprehensive set of criteria for defining patient clinical benefit should include:

1. Core Measurement Components Selected and Prioritized Through Scientifically Rigorous Methods to quantify Patient Perspectives:
    a. Validated clinical outcome measures
    b. Standardized patient-reported outcomes
    c. Functional assessment tools
    d. Quality of life indicators
2. Adaptable Elements:
    a. Heterogeneity of disease manifestation-specific metrics
    b. Population-specific considerations
    c. Setting-specific adaptations
    d. Temporal measurement frameworks
3. Implementation Considerations:
    a. Practical measurement capabilities
    b. Resource requirement assessments
    c. System integration requirements
    d. Stakeholder engagement processes
4. Broader Impact Assessment:
    a. Social function indicators
    b. Economic impact measures
    c. Family/caregiver effects
    d. Long-term outcome tracking

Financial Considerations and Economic Impact Not Included

The role of financial impacts in defining clinical benefit emerged in the interviews as a complex and nuanced consideration, without any clear consensus. The feedback included almost all stakeholders indicating that both direct and indirect patient financial factors—including financial stress—can have profound impacts on treatment adherence and outcomes. But all expressed concerns that financial impacts on patients should be considered separately from the core definition of clinical benefit.

After subsequent follow-up with health economists, it was suggested that financial considerations should not be “co-mingled” in to the “numerator” of the value equation (net benefits/costs). Instead, traditional cost analyses should include methods to consider the financial burdens on patients and their families in addition to health care system and/or societal costs.

Variation Across Patient Populations and Disease States

The analysis revealed significant complexity in addressing variations across different patient populations and disease states. Patient/advocacy organization stakeholders emphasized the need for flexibility while maintaining core principles across populations. They highlighted how diseases can disproportionately affect different demographic groups and noted the importance of considering disparities in disease impact across gender, racial, and ethnic lines.

> *"Applying a standard across different contexts will be challenging. For example, if a standard = average across multiple groups, that might create problems with issues related to subgroups' diversity. Perhaps applying different timelines or windows of time/measurement may be ways to differentiate measurement between different healthcare contexts. Regardless, you should include patients in this process, and we would be happy to be considered a partner to help convene patients to weigh in on this project." – Patient organization*

Clinical stakeholders focused on the technical aspects of variation, emphasizing how underlying patient baselines and specific disease characteristics influence outcome measurement. They noted the need to consider differences between acute and chronic conditions, and how comorbidities and socioeconomic factors affect outcomes.

Research and policy stakeholders advocated for broad, flexible definitions that could work across conditions while maintaining scientific validity. They emphasized the importance of focusing on eligible patient populations rather than just clinical trial populations, and suggested including language about "eligible population per FDA label or accompanying documents."

Framework flexibility emerged as a critical consideration, with all stakeholders recognizing the need for adaptable frameworks that maintain core principles while allowing for condition-specific variation. Population considerations received significant attention, with most stakeholders highlighting the importance of accounting for demographic and socioeconomic factors.

Key Stakeholder Differences

Cross-sectional analysis of interview responses revealed several consistent patterns in differing stakeholder perspectives:

1. Measurement Emphasis
    a. Clinical stakeholders consistently emphasized objective measures.
    b. Patient advocates emphasized experiential factors.
    c. Research stakeholders focused on methodological rigor.
    d. Organization representatives emphasized practical implementation.

2. Implementation Approaches
    a. Clinical stakeholders focused on workflow integration.
    b. Patient advocates emphasized accessibility.
    c. Research stakeholders emphasized validity.
    d. Organization representatives focused on systemic adoption.
3. Outcome Priorities
    a. Clinical stakeholders emphasized measurable outcomes.
    b. Patient advocates emphasized meaningful life impacts.
    c. Research stakeholders emphasized comparative validity.
    d. Organization representatives emphasized practical utility.

Implementation Challenges and Required Practice Changes

Implementation challenges emerged as a significant concern across all stakeholder groups. Response coverage for this section was primarily from clinical/academic stakeholders and research organizations, with more limited input from patient/advocacy organizations.

> *"If patients are going to go to the effort of contributing to a process designed to assess patient clinical benefit, it better be used." – Patient advocate*

Clinical stakeholders emphasized practical changes needed in measurement and decision-making processes, suggesting a dual-track approach where providers and patients each choose key measures to track while working within evidence-based core outcomes measures for specific conditions. They particularly emphasized the need to ensure measures are meaningful for both providers and patients while avoiding metrics that could be easily manipulated for payment or reporting purposes.

> *"There is a great fear of "what are you going to do with the information?" Points of happiness/dollar as a threshold makes people nervous. You are going to get a lot of pushback from clinicians because it will always come down to money. You need to start with the: "Why are we doing this? What is it going to be used for? What is it going to change?" Need a clear set of expectations of what we can expect coming from this approach." – Hospital executive/clinician*

Research stakeholders focused on methodological adaptations needed to implement standardized definitions. Their responses emphasized how standardization would benefit research by enabling better comparative analysis across diseases and conditions. The analysis revealed several key implementation requirements:

System adaptation emerged as a primary concern, with stakeholders emphasizing the need for modified measurement systems, updated decision processes, and enhanced stakeholder engagement. Implementation support was consistently highlighted, particularly the development of training programs, creation of implementation tools, and establishment of support systems.

Process changes received significant attention, with stakeholders emphasizing the need for updated workflow procedures, modified documentation requirements, and revised decision protocols. Success would require careful attention to both technical and cultural changes within health care organizations.

Critical Implementation Requirements

The analysis reveals three fundamental areas requiring systematic practice changes for successful implementation:

Measurement System Adaptation

Stakeholders consistently emphasized the need for substantial modifications to existing measurement approaches. Clinical stakeholders particularly highlighted the importance of developing dual-track measurement systems that can simultaneously capture provider-selected and patient-selected metrics while maintaining scientific validity. This suggests the need for significant infrastructure development to support more comprehensive data collection and analysis capabilities.

Decision-Making Process Reform

The findings indicate a clear requirement for restructured clinical decision-making processes that can effectively integrate standardized benefit assessments while preserving necessary flexibility. Clinical stakeholders emphasized the importance of avoiding overly rigid frameworks that might compromise individualized care decisions, while research stakeholders stressed the need for sufficient standardization to enable meaningful cross-context comparisons.

Stakeholder Engagement Enhancement

A consistent theme emerged regarding the need for more robust stakeholder engagement mechanisms, particularly in measure selection and implementation. The analysis suggests that successful implementation will require new organizational structures and processes to facilitate meaningful input from all relevant stakeholders while maintaining operational efficiency.

Recommendations for Practice Change Implementation

Based on the synthesized stakeholder perspectives, successful implementation will require:

1. Developing comprehensive measurement frameworks that can accommodate both standardized and customized metrics while maintaining validity and reliability.
2. Creating flexible decision-making protocols that preserve clinical autonomy while ensuring consistent application of standardized benefit assessments.
3. Establishing robust stakeholder engagement mechanisms that enable meaningful input while maintaining operational efficiency.

Research Gaps and Future Directions

The analysis revealed several critical areas requiring further research attention:
Methodology development emerged as a primary need, particularly regarding validated measurement tools that can effectively combine objective and subjective measures while maintaining scientific validity. Implementation research received significant attention, with stakeholders emphasizing the need for investigation of best practices for measurement programs and analysis of effective evaluation methods.

Evidence standards development emerged as a critical research priority, particularly regarding frameworks for evaluating non-traditional evidence sources and methods for combining different types of preference data.

Conclusions and Recommendations

The comprehensive analysis reveals that, while developing and implementing a standardized definition of patient clinical benefit presents significant challenges, there is substantial agreement on core principles and approaches. Success in implementation would require careful attention to both technical and human factors, with particular emphasis on:

1. The integration of multiple perspectives in the development of a standard definition.
2. A balance of standardization across disease states and flexibility within each disease state and population.
3. Equity and access.
4. Support for practical implementation and commitment to continuous improvement.

Several overarching recommendations emerged from the analysis:

1. A tiered definition structure should be developed, including:
    a. Core universal elements
    b. Condition-specific modules
    c. Population-specific considerations
    d. Implementation flexibility
2. A phased implementation strategy is recommended, beginning with core elements and adding complexity gradually while enabling local adaptation and maintaining measurement integrity.
3. Establishing a comprehensive measurement approach that integrates multiple data types, enables stakeholder input, supports continuous improvement, and maintains scientific validity

Support systems development received significant emphasis, particularly regarding implementation guidance, knowledge sharing, and stakeholder engagement.

The analysis suggests that, while challenges exist, careful attention to stakeholder needs and systematic implementation approaches can enable meaningful progress in standardizing patient clinical benefit assessment while maintaining necessary flexibility and responsiveness to diverse health care contexts.

Applications for Use: Near and Long Term

A standard and consistent definition of Patient Clinical Benefit could be applied in a number of use cases:

- In developing CMS guidance related drug price negotiations.
- In creating value assessment models that incorporate patient preferences.
- To drive evidence development on outcomes that matter to patients.
- To help standardize outcome measures across clinical trials.
- To reduce medical product development risks and uncertainties that lead to market inefficiencies.
- In bundled payment models, to understand the value of interventions across different settings.
- For risk adjustment in payment models.
- In comparing outcomes across institutions with different patient populations.
- In primary care, to shift focus from checkbox medicine to personalized care planning.
- In cancer care, to better address patients' changing goals throughout treatment

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